UNIVERISTY OF MILANO-BICOCCA

Department of Psychology

DOCTORAL PROGRAM IN EXPERIMENTAL PSYCHOLOGY,
LINGUISTICS, AND COGNITIVE NEUROSCIENCE
XXVII CYCLE

Exploring bodily representations: spatial maps around, in, and on the body

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Academic Year: 2014-2015

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RIASSUNTO

Questa tesi di dottorato ha come oggetto le rappresentazioni del corpo e dello spazio, come sono modulate e modificate da stimolazioni multisensoriali, e alcuni correlati fisiologici di tali modificazioni.

Nel capitolo #1, “Lo spazio attorno al corpo”, sono illustrati tre studi di adattamento prismatico, una tecnica che sfrutta la plasticità cerebrale nella formazione e rimappaggio di rappresentazioni spaziali sensorimotorie. Lo Studio #1 ha indagato il contributo della visione dell’arto nella formazione degli effetti postumi, in due differenti versioni dell’adattamento prismatico: l’effetto postumo determinato da adattamento tramite l’esecuzione di attività “ecologiche” è massimizzato da una completa visione dell’arto durante i compiti; al contrario, dopo adattamento ottenuto tramite puntamenti ripetuti, si ottengono effetti maggiori quando la visione dell’arto è preclusa per la maggior parte del movimento. Lo Studio #2 ha esaminato l’effetto di una stimolazione multisensoriale visuo-acustica durante adattamento, dimostrando che la riduzione dell’errore di puntamento avviene più rapidamente quando lo stimolo-bersaglio è multisensoriale, piuttosto che unisensoriale visivo o acustico. Lo Studio #3, condotto su un paziente cerebroleso, ha dimostrato come l’integrità del circuito parieto-cerebellare dell’emisfero sinistro sia necessaria per un corretto processo di rimappaggio spaziale propriocettivo, e come la neuromodulazione di tali aree durante la fase di esposizione possa normalizzare temporaneamente l’effetto postumo.

Nel capitolo #2, “Lo spazio nel corpo”, si esamina la relazione tra rappresentazioni spaziali e corporee e regolazione omeostatica. Il parametro fisiologico della temperatura cutanea, considerato indice di integrità del senso di appartenenza corporea, si modifica in seguito a manipolazioni delle rappresentazioni corporee. Le rappresentazioni spaziali e corporee di partecipanti sani sono state manipolate tramite tre differenti tecniche in grado di indurre effetti spaziali e attentivi direzione-specifici, misurando il loro effetto sulla regolazione termica. Lo Studio #4 ha dimostrato una diminuzione della temperatura delle mani dopo adattamento prismatico con una deviazione del campo visivo verso destra e effetti postumi verso sinistra, ma non durante adattamento verso sinistra. Lo Studio #5 ha dimostrato una modulazione della temperatura delle mani durante stimolazione ottico-cinetica verso sinistra, ma non verso destra. I dati preliminari dello Studio #6 suggeriscono che il solo orientamento dell'attenzione visiva non è sufficiente a indurre una specifica modulazione della temperatura.

Il capitolo #3, "Lo spazio sul corpo", riporta i risultati dello Studio #7, che ha investigato la percezione di distanze tattili, ovvero come e a che livello delle mappe somatosensoriali il cervello elabori la relazione spaziale tra oggetti che toccano la cute. Con un paradigma di adattamento sensoriale è stato indotto un effetto postumo di distanze tattili, che ha caratteristiche simili a quelle dei classici effetti postumi visivi di basso livello (specificità di orientamento e di localizzazione somatica). Questo suggerisce che l'elaborazione di distanze tattili avviene a un livello precoce di elaborazione somatosensoriale.

In conclusione, i risultati di questa tesi suggeriscono che: 1) alcune rappresentazioni del corpo e dello spazio sono modulabili da stimolazioni multisensoriali, specialmente quelle implicate nel senso di localizzazione del corpo nello spazio, e sostenute dall'attività della corteccia parietale posteriore; 2) la temperatura cutanea è un indice fisiologico delle modificazioni a carico di tali rappresentazioni multisensoriali; 3) le mappe corporee che contengono informazioni riguardanti la metrica del corpo, utilizzate nell'elaborazione delle relazioni spaziali tattili, originano presumibilmente a livelli precoci di elaborazione somatosensoriale.

Parole chiave: rappresentazioni corporee-spaziali, adattamento prismatico, temperatura

ABSTRACT

My Doctoral Thesis investigated different aspects of bodily and spatial representations, how they are modulated by multisensory stimulation, and some physiological correlates of their manipulation.

Chapter #1, “The space around the body”, reports three studies on prism adaptation, a technique that takes advantage of brain plasticity in the generation and modification of spatial bodily maps. Specifically, Study #1 investigates how the vision of the limb during two different versions of prism adaptation modulates their aftereffects: larger aftereffects take place with a concurrent vision of the limb after prism adaptation achieved through “ecological” visuo-motor activities; conversely, the vision of the very last part of the movement brings about larger aftereffects after the repeated pointing task. Study #2 examines the effect of a multisensory stimulation during prism adaptation, showing that the pointing error reduction is obtained with fewer pointing movements when the target is a visual-acoustic (multisensory), rather than unisensory stimulus. Finally, Study #3, which was performed in a brain-damaged patient, showed that the integrity of the left parieto-cerebellar circuit is required for an appropriate spatial remapping of proprioceptive maps to occur, and that the modulation through transcranial Direct Current Stimulation of these cortical areas temporarily restores the aftereffects.

Chapter #2, “The space in the body”, reports studies on the link between bodily spatial representations and homeostatic regulation. Skin temperature has been recently considered as a physiological parameter of disembodiment, and can be modulated by the manipulation of bodily representations. Three experiments in which spatial bodily maps were manipulated by means of different techniques, inducing direction-specific and lateralized effects, are presented. Specifically, Study #4 showed a reduction of hands’ skin temperature after adaptation to right shifting, but not to left shifting, optical prisms.

In Study #5, a modulation of temperature during leftward, but not rightward, optokinetic stimulation was found. Preliminary results from Study #6 show that the sole lateral shift of visual attention is not sufficient to induce a specific skin temperature modulation.

Chapter #3, “The space on the body”, concerns the perception of tactile distances, namely, the spatial relationships between single objects that simultaneously touch the skin. In Study #7 a sensory adaptation-aftereffects paradigm was used to show that a tactile distance aftereffect can be induced; this tactile aftereffect shares many lower-level characteristics of classic visual aftereffects, such as orientation and location specificity. These findings suggest that the processing of spatial relationships among tactile events takes place at an early stage of somatosensation.

Overall these results suggest the following: firstly, some bodily and spatial representations are susceptible to multisensory stimulations, especially those underpinning the sense of location of the body, sustained by the high-order posterior parietal cortex; secondly, modulation of skin temperature may be considered as an index of modifications of the multisensory representation of the body; thirdly, other bodily maps, such as those providing information about its metric, used in order to process tactile spatial relationships, are lower-level, likely arising at early stages of somatosensory processing.

Keywords: bodily-spatial representations, prism adaptation, temperature

INTRODUCTION

Even though our body is a unique object in the world, the way in which the body is represented in the brain is not. We can perceive and experience our body in many different ways, and this is reflected by the variety of mental bodily representation. For instance, we can feel the body from the inside, as a spatial entity for the direct perception of sensory events. We can also experience our body as a physical and biological object immerged in the external space.

This Thesis aimed to explore some of these mental representations of the body.

If we want to grasp an object in front of us, we need to represent the spatial coordinates about the location of the object with respect to our body. Information from several sensory modalities can signal this location in the external space (such as vision, proprioception, etc.), and need to be integrated in a common frame of reference. In Chapter #1 I explored this kind of mental bodily spatial representations; in particular I investigated their plasticity in response to the introduction of discordant or converging sensory inputs, and the consequences of a unilateral brain lesion in their remapping.

Changes in the perception and self-consciousness about our body can result in changes and modifications of physiological parameters; Chapter #2 investigated the effect of bodily and spatial remapping on one of those parameters, the skin temperature.

Finally, when an object touches our body, we can perceive its shape and size, its metric properties. When visual information is not available, in order to estimate the metric properties of an object, we need to use our body as a ruler, and use information about the size of the body part being touched as the frame of reference. Chapter #3 investigates this kind of mental body representations, where the metric properties of the body, such as body part size, are mapped.

CHAPTER 1

The space around the body:
Prism adaptation and its aftereffects

This Chapter examines some aspects of prism adaptation, a technique that takes advantage of brain plasticity in order to study how the spatial bodily maps are modified by visuo-motor adaptation to a multisensory conflict, between discordant visual and proprioceptive information about the location of the body in the external space. Which factors influence and modulate visuo-motor adaptation to visual displacing prisms, enhancing its aftereffects? Which brain areas are involved in the realignment of the bodily spatial maps during prism adaptation?

1.1. Introduction

Visuo-motor adaptation to wedge prism inducing a lateral displacement of the visual field is a well-known technique for investigating short-term sensorimotor neuroplasticity in healthy participants (Redding, Rossetti, & Wallace, 2005). While looking through prismatic goggles (figure 1), the participants' first attempts to point to a visual target deviate toward the direction of the prism-induced visual field displacement (the so-called "direct effect"). This sensorimotor discrepancy between the planned and the actual movement toward the target enhances a correction in subsequent movements. In fact, after repeated manual pointings, the error progressively decreases, until the visual target is correctly reached, and the sensorimotor discrepancy reduced, completing the prism adaptation (PA, adaptation as reduction of the pointing error). Following prisms' removal, participants still make a pointing error, but now in a direction opposite to that of the displacement induced by the prisms, the so-called aftereffects (AEs), which are considered the main index that PA has taken place (Redding et al., 2005).

Figure 1. Goggles fitted with base-left prismatic lenses, inducing a rightward shift of the visual field.

Two main processes occur during PA. First, the recalibration process, the mainly "strategic" (voluntary) component of PA, which leads to an early correction of the pointing error, supported by the posterior parietal cortex (PPC). The second and more "automatic" process of PA, the spatial visuo-motor realignment, contributes to both the error reduction during the repeated pointing movements and the AEs, namely the "true adaptation", and is supported by the cerebellum (Pisella, Rode, Farnè, Tilikete, & Rossetti, 2006; Weiner, Hallett, & Funkenstein, 1983). The resolution of the sensorimotor discordance between visual and proprioceptive information induced by optical prisms displacing the visual scene, occurs during the realignment process, and requires a remapping of bodily and space coordinates into a new egocentric spatial frame of reference. The occurrence of sensorimotor AEs, that index successful adaptation, is assessed by measuring the egocentric straight ahead, both before (pre-), and after (post-) prismatic exposure. Usually, straight ahead measures are obtained for the visual, the proprioceptive, and the visual-proprioceptive sensorimotor systems. Proprioceptive and visual-proprioceptive AEs are shifted in the opposite direction with respect to the displacement of the visual scene induced by exposure to optical prisms, while visual AEs are shifted in the same direction of it (Redding et al., 2005). PA also has been successfully used for improving temporarily (in the time range of hours) a number of clinical manifestations of the syndrome of left unilateral spatial neglect (Angeli, Benassi, & Làdavas, 2004; Rode, Rossetti, & Boisson, 2001; Rossetti et al., 1998; Vallar, Zilli, Gandola, & Bottini, 2006), and for the rehabilitation of this disorder, with long lasting effects, in the time range of months (Fortis et al., 2010; Frassinetti, Angeli, Meneghello, Avanzi, & Làdavas, 2002; Serino, Bonifazi, Pierfederici, & Làdavas, 2007). This now large literature has been recently reviewed (Barrett, Goedert, & Basso, 2012; Jacquin-Courtois et al., 2013; Newport & Schenk, 2012). Given the clinical and rehabilitative impact of PA, it has been pointed out the need of a systematic investigation of the technique, in order to determine the optimal parameters of its application.

One debated factor influencing PA, is the amount of visual feedback provided during the exposure phase (Freedman, 1968; Gaveau, Prablanc, Laurent, Rossetti, & Priot, 2014; Làdavas, Bonifazi, Catena, & Serino, 2011; Michel, Pisella, Prablanc, Rode, & Rossetti, 2007; Redding & Wallace, 1988). In the so-called “terminal exposure” condition, the finger or hand can only be seen at the very end of the pointing. This is usually achieved by placing a screen across the workspace, so that the arm is hidden for the majority of the movement, only being visible when it reaches the target plane (figure 2, left).

Figure 2. Apparatus for the repeated pointings (left) and the ecological (right) prism adaptation procedures.

Instead, "concurrent exposure" refers to the condition in which the arm can be seen for some, or all, of the reaching movement, so that vision and proprioception are available concurrently. In terminal exposure condition, the spatial discrepancy between the planned and the actual movement, and the feedback about the initial pointing error are maximised, whereas the online visual correction of the movement during the pointing is minimal. Conversely, in the concurrent exposure condition, as the vision of the limb is available for the entire pointing, participants can correct online the trajectory of the movement, minimizing the spatial discrepancy between planned and actual movement, and thus the initial pointing error is diminished.

One recent study (Làdavas et al., 2011) crucially compared the effects of two PA treatments for neglect patients, one based on a terminal and the other on a concurrent exposure condition, of the classic repeated pointing procedure. During the terminal feedback exposure patients could only see their hand during the final part of their pointing movements. This was contrasted with a condition where patients observed their hand during the second half of their movement (continuous feedback procedure). The terminal-feedback exposure produced a significantly greater reduction of neglect symptoms than the continuous-feedback one. The results suggest a better neglect improvement for patients treated with terminal exposure, correlated to a stronger error reduction effect (Làdavas et al., 2011). According to Ladavas et al.'s earlier findings, evidence from a recent study by Herlihey and colleagues on healthy participants (Herlihey, Black, & Ferber, 2012), showed that terminal, but not concurrent exposure, produces perceptual AEs, as assessed by the shifts in manual and perceptual bisection tasks. Moreover, evidence from a recent study by Gaveau and colleagues (Gaveau et al., 2014), suggested a critical role of hand-to-target feedback error signals in visuomotor adaptation in order to elicit sensorimotor AEs.

However, Michel and colleagues (Michel et al., 2007), manipulated participants awareness of the optical deviation induced by the prisms; interestingly, they found that the condition in which participants were unaware of the optical deviation, because of its progressive stepwise increase, was associated with larger AEs, transfer to the non-exposed hand for the visual and auditory pointing tasks, and greater robustness, compared to the condition in which they were aware of the visual shift. This evidence suggest that it does not appear to be necessary for PA and the induction of AEs that participants are aware of pointing errors. Moreover, it has been also shown that PA therapeutic effect can be achieved using ecological visuomotor activities, instead of laboratory pointing tasks (Fortis et al., 2010; Shiraishi, Yamakawa, Itou, Muraki, & Asada, 2008). Particularly, in the study of Fortis and colleagues (Fortis et al., 2010), the classical terminal-feedback pointing PA procedure was compared with a more ecologically relevant version, where patients manipulated common objects, such as coins, jars, jigsaw puzzles (figure 2, right). Interestingly, in the ecological version patients were given continuous feedback and the vision of the limb was available during the entire movement throughout the session (concurrent exposure). Given Ladavas et al.'s earlier findings, demonstrating the superiority of terminal feedback, one might expect that the classical procedure is superior to the ecological version. However, the two procedures (classical and ecological) turned out to be equally effective in ameliorating neglect symptoms. Moreover, a following study by Fortis and colleagues (Fortis, Ronchi, Calzolari, Gallucci, & Vallar, 2013) compared the effects of ecological PA (concurrent exposure) to those of the classic repeated pointing procedure (terminal exposure) in two groups of healthy participants (young and elders), showing that the ecological procedure induced greater proprioceptive (for both the young and the elders) and visual-proprioceptive AEs (for young group), than the repeated pointing PA (Fortis et al., 2013). This evidence suggest that different factors could modulate the building up of the AEs during the repeated pointing and the ecological PA procedures. For instance, the authors suggest that the more varied patterns of movements during the manipulation of several everyday objects of the ecological task may have required the allocation of more attentional resources than the repetitive pointing task, resulting in enhanced AEs. Additionally, participants may have been more engaged and motivated during the ecological than during the pointing procedure, as assessed by the questionnaire.

To this end, in Study #1, we further investigated the effects of the vision of the limb during both the ecological (Experiment #1) and the repeated pointing PA (Experiment #2), in healthy participants, comparing, in each experiment, a terminal exposure with a concurrent exposure version of the PA procedure. If the critical factor in order to obtain larger AEs is a stronger error reduction (as it occurs during terminal exposure, when the vision of the limb is reduced), one might predict that the execution of the ecological task in a terminal exposure condition could bring about greater AEs, compared with the ecological PA executed in the concurrent exposure condition. On the other hand, as argued by Fortis et al. (2013), if different factors could modulate the building up of the

AEs during the repeated pointing and the ecological PA procedures, one might expect that the concurrent and terminal exposure conditions could affect differently the two PA procedures.

In healthy participants, several parameters can modulate adaptation, such as movement speed (Kitazawa, Kimura, & Uka, 1997), presence or absence of visual feedback (Freedman, 1968), realistic characteristic of the conflict (Norris, Greger, Martin, & Thach, 2001), simultaneity between movement execution and visual reafference (Hay & Goldsmith, 1973; Kitazawa, Kohno, & Uka, 1995) (see Redding et al., 2005 for a review). However, so far, the effect of the sensory modality of the target stimulus has never been assessed. Bornschlegl and colleagues (Bornschlegl, Fahle, & Redding, 2012) suggested that pacing the pointing movements during PA toward a visual target with a rhythmic auditory signal, which is usually employed to control movement speed, could have enhanced overall activation of the PA neural network, and might have enable multisensory integration, including auditory spatial information that selects the more reliable proprioceptive signal for movement control. However, in this study, the stimulus itself was purely visual. Multisensory integration is a powerful mechanism for maximizing sensitivity to sensory events; cross-modal spatial integration between auditory and visual stimuli is a common phenomenon in space perception, and the principles underlying such integration (such as the so-called *spatial*, *temporal*, and *inverse effectiveness* rules) have firstly been outlined by neurophysiological and behavioral studies in animals (Stein & Meredith, 1993). Subsequent studies, provided evidence that similar principles occur also in humans, improving visual detection (Bolognini, Frassinetti, Serino, & Làdavas, 2005; Frassinetti, Bolognini, & Làdavas, 2002), visual localization (Hairston, Laurienti, Mishra, Burdette, & Wallace, 2003), auditory localization (Bolognini, Leo, Passamonti, Stein, & Làdavas, 2007), and reducing saccadic reaction times (Arndt & Colonius, 2003; Colonius & Arndt, 2001; Corneil, Van Wanrooij, Munoz, & Van Opstal, 2002; Harrington & Peck, 1998; Hughes, Nelson, & Aronchick, 1998). Moreover, it has been found that a sound, spatially and temporally coincident to a visual stimulus, can improve visual perception both in neglect patients (Frassinetti, Pavani, & Làdavas, 2002), and in the blind hemifield of hemianopic patients (Bolognini, Rasi, Coccia, & Làdavas, 2005; Frassinetti, Bolognini, Bottari, Bonora, & Làdavas, 2005), can temporarily ameliorate visuospatial attention deficits in patients with neglect (Van Vleet & Robertson, 2006), and can improve the ability to localize a sounds in a patient with severe auditory localization defect (Bolognini, Rasi, & Làdavas, 2005). In Study #2, we investigated the effect of the nature of the target (unimodal visual, acoustic or bimodal), both on the AEs magnitude and the pointing error reduction, during the classical repeated pointing PA procedure.

As far as the neural basis of PA is concerned, it has been suggested that a bilateral network is involved in PA, which includes two key cortical areas: the PPC, and the cerebellum, which mainly support, respectively, the recalibration process, and the spatial visual-proprioceptive realignment (Chapman et al., 2010; Clower et al., 1996; Danckert, Ferber, & Goodale, 2008; Luauté et al., 2006; Saj, Cojan, Vocat, Luauté, & Vuilleumier, 2013; Sekiyama, Miyauchi, Imaruoka, Egusa, & Tashiro, 2000). Several studies, both in the animal (Baizer, Kralj-Hans, & Glickstein, 1999), and in humans (Block & Bastian, 2012; Martin, Keating, Goodkin, Bastian, & Thach, 1996a; Pisella et al., 2005), show that cerebellar lesions disrupt both the PA and the AEs components. Conversely, the integrity of the PPC does not appear necessary for the occurrence of PA and the subsequent AEs. Indeed, patients with left unilateral spatial neglect, which is frequently, though not exclusively, caused by right hemispheric lesions involving the inferior PPC, the temporo-parietal junction, and their connections (Vallar & Bolognini, 2014; Vuilleumier, 2013), exhibit both PA and AEs phenomena, with the latter being, if anything, even larger than those occurring in healthy participants (Farnè, Rossetti, Toniolo, & Làdavas, 2002; Pisella, Rode, Farnè, Boisson, & Rossetti, 2002; Rossetti et al., 1998). In line with these findings, the on-line guidance of action, such as in target-driven pointings, appears preserved in right-brain-damaged patients with left neglect (Harvey & Rossit, 2012). There is some evidence that right occipital damage reduces the extent of error correction in PA, and negatively affects neglect recovery; these negative correlations are specific for occipital damage (Serino, Angeli, Frassinetti, & Làdavas, 2006; Serino et al., 2007). However, other reports have shown that both unilateral occipital damage and hemianopia neither affect the PA process, nor the PA-induced recovery of left neglect (Frassinetti, Angeli, et al., 2002; see Jacquin-Courtois et al., 2013 for a review; Sarri, Kalra, Greenwood, & Driver, 2006). Finally, spared PA and AEs have been described in a patient with bilateral optic ataxia, due to bilateral damage to the PPC (Pisella et al., 2004). In Study #3, we investigated the neural basis of the cerebral network involved in PA and in the production of normal and atypical proprioceptive AEs, and how changes in the cortical excitability of a brain-damaged patient may affect abnormal AEs after PA.

1.2. Study #1: The vision of the limb in ecological and repeated pointing PA

1.2.1. Aim of the study

This study investigated the contribution of the vision of the limb in the generation of AEs, during ecological (Experiment #1), and repeated pointing (Experiment #2) PA. As previously reported, in terminal exposure condition the vision of the limb is restricted to very last part of the movement, so that both the spatial discrepancy between the planned and the actual movement, and the feedback about the initial pointing error are maximised, whereas the online visual correction of the movement during the pointing is minimal. In the concurrent exposure condition the opposite occurs: as the vision of the limb is available for the entire pointing, participants can correct online the trajectory of the movement, minimizing the spatial discrepancy between planned and actual movement, and thus the initial pointing error is diminished. Previous studies showed an advantage of the repeated pointing PA in terminal exposure condition both in the amelioration of neglect symptoms (Làdavas et al., 2011), and in the generation of perceptual AEs (Herlihey et al., 2012). However, it has been shown that awareness of pointing errors during repeated pointing PA is not necessary in order to complete the adaptation procedure and to induce AEs (Michel et al., 2007). Moreover, the ecological PA has been shown to be equally effective in the rehabilitation of neglect patients (Fortis et al., 2010), and to bring about greater AEs in healthy participants (Fortis et al., 2013).

In Experiment #1 we compared the amplitude of the AEs in the proprioceptive, visual and visual-proprioceptive straight-ahead tests after ecological PA in a concurrent and in a terminal exposure condition.

In Experiment #2 the same two condition were applied to the repeated pointing PA.

If the two PA procedures are sustained by the same mechanism, we should expect an advantage of the terminal exposure condition in both experiments; otherwise, if different factors could modulate the building up of the AEs during the repeated pointing and the ecological PA procedures, we might reasonably expect that the concurrent and terminal exposure conditions bring about a different amount of AEs according to the PA procedure used.

1.2.2. Materials and methods

Participants

Forty-eight healthy right-handed (Oldfield, 1971) adults took part in the experiment (24 for each experiment; Experiment #1: 12 females; mean±SD age: 64.88±6.66 years, range: 51-77; mean education : 14.04±4.04 years, range: 5-18; Experiment #2: 12 females; mean age: 67.50±5.00 years, range: 57-80; mean education: 13.63±3.75 years, range: 5-17). Participants were recruited from the inpatient population of the Neurorehabilitation Unit of the IRCCS Istituto Auxologico Italiano, Milan, Italy, had normal or corrected-to-normal vision and no history or evidence of neurological or psychiatric disorders. The study was approved by the local Ethical Committee and performed according to the ethical standards laid down in the 1991 Declaration of Helsinki. All participants gave informed consent, after a brief session that outlined the nature of the study.

Procedure

In both experiments, participants underwent two sessions, in two consecutive days. Each session lasted about one hour and included 1) a pre-exposure phase, 2) a prism adaptation exposure phase, 3) a post-exposure phase, identical to phase 1).

Pre- and post-exposure phases. In order to assess the presence and the magnitude of AEs, in each session participants performed the three typical tests to measure the perception of the straight-ahead position (sagittal to their body midline) in the proprioceptive, visual and visual-proprioceptive systems (Redding et al., 2005) (figure 3). Each participant performed the three tests in the same order, both in the pre- and in the post-exposure phases, in both sessions; the tests order was counterbalanced across participants. For each test 10 trials were given.

- *Proprioceptive test (P).* Each participant, seated in front of a table, with eyes closed, received instructions to point with the right index finger to a location on the table surface, perceived as the subjective straight-ahead. A graduated panel, aligned with the body-midline, allowed the recording (degrees of visual angle in 1° steps) of the participant’s deviation from the objective body-midline, with an accuracy of 0.5° (figure 3, first illustration).
- *Visual test (V).* In darkness, each participant received instructions to stop verbally a red light moving horizontally just above eye level, at a distance of 85cm from the participant’s mid-sagittal plane, when the light was perceived as straight-ahead. The 10 trials (5 with the light moving from the right to the left visual periphery, 5 from left to right) were given in a random fixed order. A ruler was fixed on the track edge facing the experimenter, to register the deviation of the visual judgment (cm, converted in degrees of visual angle) from the objective midline (figure 3, second illustration).
- *Visual-proprioceptive test (VP).* In darkness, each participant received instructions to fixate a red LED placed in the straight-ahead position, and to point with the right index finger to the location on the table surface subjectively perceived as the projection of the light on the table. No information was given about the actual LED location, and a wooden box precluded participants from viewing the pointing movement, which then took place without any visual feedback. A graduated panel,

aligned with the body-midline, allowed the recording (degrees of visual angle in 1° steps) of the participant’s deviation from the straight-ahead position of the LED, with an accuracy of 0.5° (figure 3, third illustration).

In every test, the difference between the post-exposure and pre-exposure deviations was taken as index of the AEs magnitude, as the shift from the perceived body midline: positive values indicated a rightward deviation from the perceived body midline, negative values a leftward deviation.

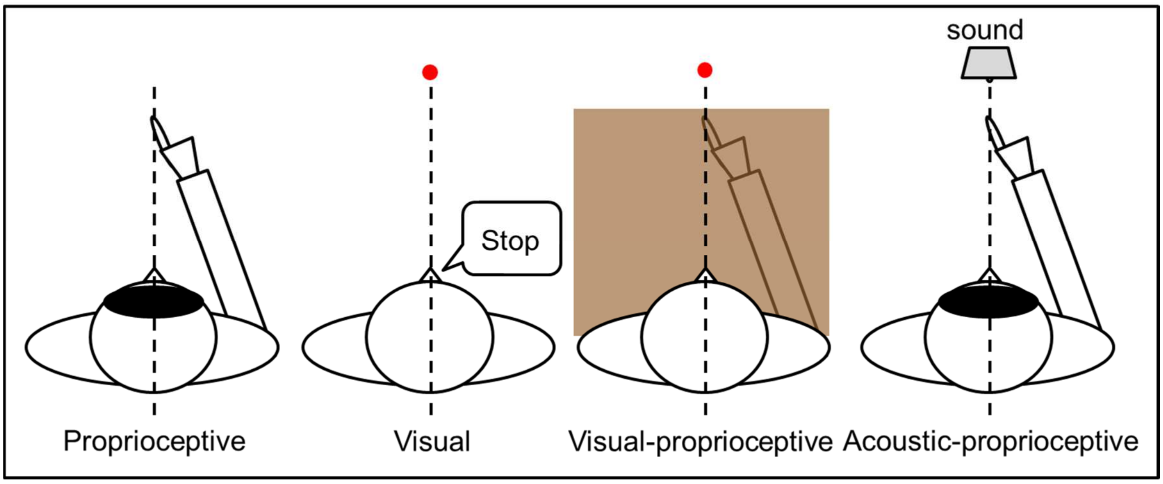


Figure 3. Schematic representation of the four straight-ahead tests used in the different studies. The dashed lines indicate the objective straight-ahead position. The red dot indicates the visual target (a red LED) in the Visual-proprioceptive and Visual tests. The black ovals indicate that participants were blindfolded during the tasks (Proprioceptive and Acoustic-Proprioceptive). The brown board in the Visual-proprioceptive task indicates that participants could not see the their arm during the pointing to the visual target.

Prism adaptation exposure phase Experiment #1: ecological tasks. During the prism adaptation exposure phase, participants were adapted to an 11.4° rightward visual shift induced by 20-diopter, base-left prism glasses (Optique Peter, Lyon, France), while performing the ecological tasks. The ecological tasks PA lasted about 15-20 mins. Participants performed the ecological tasks in two different conditions, concurrent and terminal, in two consecutive days. The order of the adaptation condition were counterbalanced across participants (half of the sample group performed the ecological tasks in the concurrent condition on day one, and in the terminal condition on day two; the other half did the opposite). In the concurrent condition, during the execution of the ecological tasks, the vision of the limb was available for the entire movement, during the whole adaptation session (Fortis et al., 2010, 2013). In the terminal condition, a covering apparatus was fixed on the table in front of participants, in order to prevent participants from seeing the initial arm position and the subsequent arm movement, until the last part of it, when the hand became visible on the table surface. The covering apparatus consisted of a horizontal beam (80cm long) fixed on the top of two adjustable in height vertical lateral beams placed on the table surface. A black cloak, fixed to the horizontal beam, was fasten to participants' neck, occluding the limb view. The elevation of the horizontal beam could be adjusted, depending on participant height. Moreover, before wearing the prismatic glasses, participants were asked to protrude the right hand on the table, underneath the covering apparatus, until they were able to see their hand from the fingertip of the middle finger to the wrist. This procedure was repeated for three positions (on the left, center and right with respect to the participant body midline), and these locations were marked with a piece of tape, in order to delimit the table surface within it was allowed to place the ecological tasks materials (so that, during the execution of the ecological tasks, participants were able to see just their right and the objects). The workspace delimitation was marked also in the concurrent condition, even though the covering apparatus was then removed. Just eight of the original twelve ecological tasks (Fortis et al., 2010, 2013) were included in the study, and performed by participants in this order for both conditions (figure 2, right): (1) collecting coins on the table and putting them in a money box, (2) selecting rings and bracelets from a box and wearing them on the left hand and fingers, (3) assembling jigsaw puzzles, (4) moving blocks from one compartment of a box to another compartment, (5) sorting cards, (6) threading a necklace with 12 spools and rope, (7) copying a chessboard pattern on an empty chessboard, (8) composing a dictated word using letters printed on a square. We decided to exclude two of the tasks (closing jars with the corresponding lid, and serving a cup of tea) because their execution (that implied also broad movements directed upward) was not suitable for the terminal condition, permitting the vision of a greater part of the movement even though the presence of the covering apparatus (figure 4, upper panels).

Prism adaptation exposure phase Experiment #2: repeated pointing task. Participants performed the repeated pointing task in two different conditions, concurrent and terminal, in two consecutive days. The order of the adaptation condition were counterbalanced across participants (half of the sample group performed the repeated pointing task in the concurrent condition on day one, and in the terminal condition on day two; the other half did the opposite). In the concurrent condition participants sat in front of the table and, while wearing wedge prisms, they perform the pointing tasks, with their right hand, with the vision of the arm available for the entire movement, during the whole adaptation session. In the terminal condition, the same covering apparatus of Experiment #1 was fixed on the table in front of participants, in order to prevent participants from seeing the initial arm position and the subsequent arm movement, until the last part of it, when just the hand became visible on the table surface. The repeated pointing task consisted in the execution of 92 pointing movements toward one of four visual targets. The targets were four colored stickers dots (1.6 cm diameter), stuck on the surface of a wooden board (80 x 40 x 1.4cm) that was placed in front of the participant. The dots were fixed on the distal edge of the board, with respect to the participant location, at 10° and 20° to the right and to the left of the participant body midline, within reaching distance (about 40cm distance from the starting hand position). On each trial, participants were asked to point toward the visual target named by the experimenter, with their right index finger, with a ballistic movement, at a fast but comfortable speed, and then return to the starting position (a point on the board, close and aligned to participant body midline). The board side facing the experimenter was graduated in cm, in order to register the deviation of the index finger from the target. Each measure was then converted in degrees of visual angle, with positive values corresponding to rightward deviation from the target, negative values to leftward deviations. Participants performed 23 pointing movements to each target, in a pseudorandom fixed order, with a brief break after the first 46 pointing movements (figure 4, lower panels).

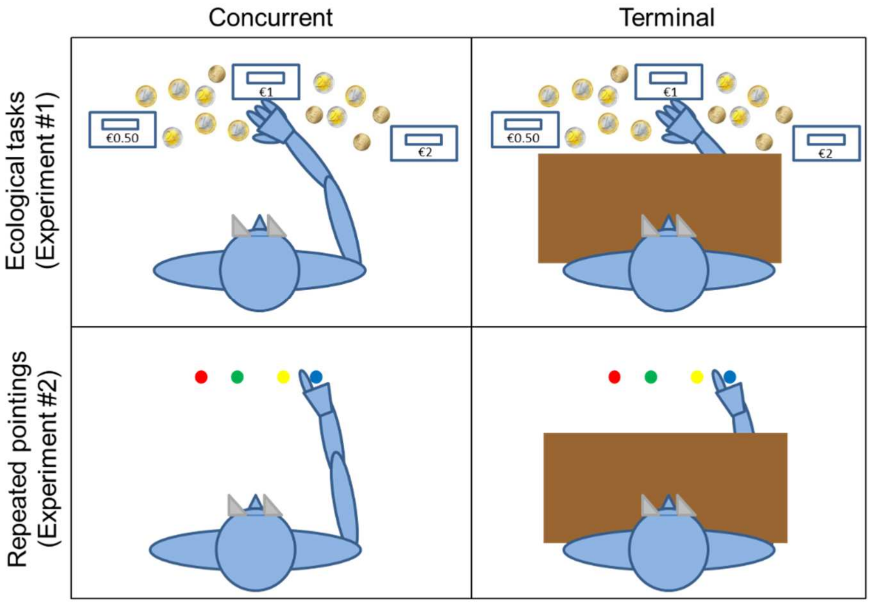


Figure 4. Schematic representation of the prism adaptation conditions in the two experiments. The upper panels depict the first task (collecting coins) of the ecological PA (Experiment #1), respectively in the concurrent (left) and terminal (right) exposure conditions. The lower panels depict the same conditions during the repeated pointings PA (Experiment #2).

1.2.3. Statistical analysis

The statistical analyses were carried out with the software Statistica (StatSoft, Tulsa, OK, USA, version 7.0). In all ANOVAs, significant effects and interactions were investigated with Duncan *post hoc* multiple test comparisons. Significance was set at $\alpha = 0.05$. Partial eta squared (η_p^2) of significant effects were also computed in order to determine the effect sizes (Cohen, 1988).

For each experiment, possible differences in the AEs brought about by the different exposure conditions were assessed by running three repeated-measures ANOVAs, one for each test, performed on the participants' straight-ahead mean shifts, with the within-subjects factor of "Condition" (terminal/concurrent) and the between-subjects factor of "Order of Condition" (terminal-concurrent/concurrent-terminal).

Moreover, just in Experiment #2, in order to assess the presence of adaptation, as the reduction of the initial pointing error, a repeated-measure ANOVA was performed, on the mean deviation from the target of the first and last four pointing movements, with the within-subjects factors of "Condition" (terminal/concurrent) and of "Pointing" (first four/last four), and the between-subjects factor of "Order of Condition" (terminal-concurrent/concurrent-terminal).

1.2.4. Results

Experiment #1: ecological PA

Sensorimotor AEs.

The repeated-measures ANOVA ran on the proprioceptive straight-ahead shifts showed that, in both conditions, the shift after prism exposure was significant, as revealed by the intercept of the ANOVA, that compares the mean shift against zero [$F_{(1,22)} = 51.52$, $p < 0.001$, $\eta_p^2 = 0.70$], thus demonstrating the presence of a proprioceptive AE in the expected leftward direction. The ANOVA failed in showing any other significant effect or interaction [Condition $F_{(1,22)} = 1.41$, $p = 0.25$; Order of Condition $F_{(1,22)} = 1.65$, $p = 0.21$; Condition by Order of Condition $F_{(1,22)} = 0.17$, $p = 0.69$], demonstrating that the magnitude of the proprioceptive shift was equivalent after both conditions in all participants (terminal M±SD° -2.37±2.18°, concurrent -3.25±3.03°; figure 5, lower bars).

The repeated-measures ANOVA ran on the visual straight-ahead shifts showed that, in both conditions, the visual shift after prism exposure was significantly shifted in the expected rightward direction, as revealed by the intercept [$F_{(1,22)} = 6.90$, $p < 0.05$, $\eta_p^2 = 0.24$]. The ANOVA failed in showing any other significant effect or interaction [Condition: $F_{(1,22)} = 0.05$, $p = 0.83$; Order of Condition: $F_{(1,22)} = 0.32$, $p = 0.58$; Condition by Order of Condition: $F_{(1,22)} = 0.41$, $p = 0.53$], demonstrating that the magnitude of the visual shift was equivalent after both conditions in all participants (terminal 0.73±1.88°, concurrent 0.85±2.08°; figure 5, middle bars).

The repeated-measures ANOVA ran on the visual-proprioceptive straight-ahead shifts showed that, in both conditions, the visual-proprioceptive shift after prism exposure was significantly shifted in the expected leftward direction, as revealed by the intercept [$F_{(1,22)} = 45.62$, $p < 0.001$, $\eta_p^2 = 0.67$]. The ANOVA showed a significant effect of Condition [$F_{(1,22)} = 4.93$, $p < 0.05$, $\eta_p^2 = 0.18$], demonstrating that the magnitude of the visual-proprioceptive shift after the ecological concurrent condition was bigger than after the ecological terminal condition (terminal: -2.54±2.74°, concurrent: -4.34±3.49°; figure 5, top bars). The effect of Order of Condition [$F_{(1,22)} = 0.32$, $p = 0.58$] and the Condition by Order of Condition interaction [$F_{(1,22)} = 0.11$, $p = 0.75$] were not significant.

Experiment #2: repeated pointing PA

Sensorimotor AEs.

The repeated-measures ANOVA ran on the proprioceptive straight-ahead shifts showed that, in both conditions, the proprioceptive shift after prism exposure was significantly shifted in the expected leftward direction, as revealed by the intercept [$F_{(1,22)} = 89.78$, $p <$

0.001, $\eta_p^2 = 0.80$]. The ANOVA showed a significant effect of Order of Condition [$F_{(1,22)} = 4.70$, $p < 0.05$, $\eta_p^2 = 0.18$], revealing a greater proprioceptive AE in the group of participants which did the repeated pointing PA in the terminal condition on the first day and the concurrent condition on the second day (-3.78±1.59°), compared to the group that did the opposite order (-2.38±1.59°, figure 6, lower bars). The effect of Condition [$F_{(1,22)} = 0.37$, $p = 0.55$], and the Condition by Order of Condition interaction [$F_{(1,22)} = 2.88$, $p = 0.10$] were not significant.

The repeated-measures ANOVA ran on the visual straight-ahead failed in revealing any significant effects or interactions [Intercept: $F_{(1,22)} = 1.22$, $p = 0.28$; Order of Condition: $F_{(1,22)} = 2.63$, $p = 0.12$; Condition: $F_{(1,22)} = 1.47$, $p = 0.24$; Condition by Order of Condition: $F_{(1,22)} = 2.04$, $p = 0.17$, figure 6, middle bars].

The repeated-measures ANOVA ran on the visual-proprioceptive straight-ahead shifts showed that, in both conditions, the visual-proprioceptive shift after prism exposure was significantly shifted in the expected leftward direction, as revealed by the intercept [$F_{(1,22)} = 55.45$, $p < 0.001$, $\eta_p^2 = 0.72$]. The ANOVA showed a significant interaction of Condition by Order of Condition [$F_{(1,22)} = 6.28$, $p < 0.05$, $\eta_p^2 = 0.22$]. The Duncan post hoc multiple comparisons test showed a greater visual-proprioceptive AE after the repeated pointing exposure in the terminal condition (-5.20±3.07°) compared to the concurrent condition (-2.09±3.28°), but just in the group which did the terminal condition the first day and the concurrent condition the second day (figure 6, top bars), thus demonstrating that a greater visual-proprioceptive shift can be obtained through repeated pointing in the terminal condition rather than in the concurrent condition, when the terminal condition was executed the first day. The effects of Order of Condition [$F_{(1,22)} = 0.73$, $p = 0.40$] and of Condition [$F_{(1,22)} = 0.83$, $p = 0.37$] were not significant.

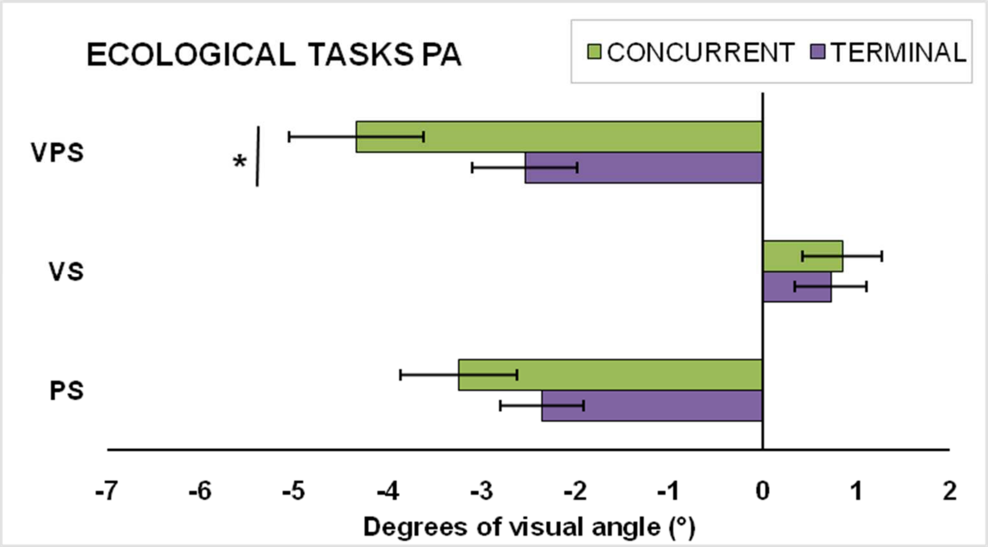


*Figure 5. Mean (Standard Error, SE) deviation from body midline in the proprioceptive (PS), visual (VS), and visual-proprioceptive (VPS) straight-ahead tests, expressed as a shift (post- minus pre- exposure performance), after the terminal (violet) and concurrent (green) conditions of ecological adaptation, in degrees of visual angle (°); positive values correspond to rightward deviation from the perceived body midline, negative values to leftward deviations. p < 0.001***, < 0.01**, < 0.05*.*

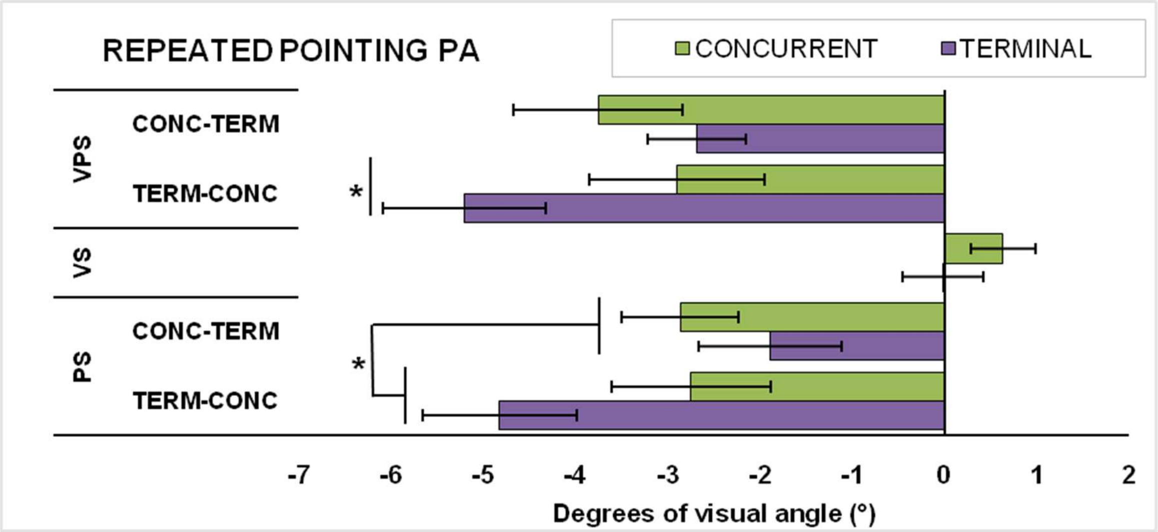


*Figure 6. Mean (SE) deviation from body midline in the proprioceptive (PS), visual (VS), and visual-proprioceptive (VPS) straight-ahead tests, expressed as a shift (post- minus pre- exposure performance), after the terminal (violet) and concurrent (green) conditions of repeated pointing PA, in degrees of visual angle (°); for PS and VPS tests, results for the two sub-groups (terminal-concurrent, n=12 and concurrent-terminal, n=12) are reported separately. Positive values correspond to rightward deviation from the perceived body midline, negative values to leftward deviations. p < 0.001***, < 0.01**, < 0.05*.*

Error reduction.

The repeated-measures ANOVA ran on the mean deviation of the first and last four pointing movements during the adaptation exposure showed that all the effects and interactions were significant: Order of Condition [$F_{(1,22)} = 4.65$, $p < 0.05$, $\eta_p^2 = 0.17$], Condition [$F_{(1,22)} = 12.29$, $p < 0.01$, $\eta_p^2 = 0.36$], Pointing [$F_{(1,22)} = 59.33$, $p < 0.001$, $\eta_p^2 = 0.73$], Condition by Order of Condition [$F_{(1,22)} = 5.59$, $p < 0.05$, $\eta_p^2 = 0.20$], Pointing by Order of Condition [$F_{(1,22)} = 7.48$, $p < 0.05$, $\eta_p^2 = 0.25$], Condition by Pointing [$F_{(1,22)} = 8.22$, $p < 0.01$, $\eta_p^2 = 0.27$], and Condition by Pointing by Order of Condition [$F_{(1,22)} = 10.44$, $p < 0.01$, $\eta_p^2 = 0.32$].

The triple interaction Condition by Pointing by Order of Condition was further investigated by means of two repeated-measures ANOVAs, one for each group of participants, Order of Condition terminal-concurrent (N=12), and concurrent-terminal (N=12) (figure 7). The ANOVA conducted on the group terminal-concurrent showed significant effects of Condition [$F_{(1,11)} = 10.63$, $p < 0.01$, $\eta_p^2 = 0.49$], Pointing [$F_{(1,11)} = 38.71$, $p < 0.001$, $\eta_p^2 = 0.78$], and of Condition by Pointing interaction [$F_{(1,11)} = 11.10$, $p < 0.01$, $\eta_p^2 = 0.50$]. Post hoc comparisons showed that the first pointing movements were more rightward deviated than the last pointing movements, which were directed correctly to the target, in both conditions (terminal first 2.34±1.65°, terminal last -0.09±0.26°, $p < 0.001$; concurrent first 0.94±0.69°, concurrent last -0.06±0.27°, $p < 0.01$). Moreover, while the last pointing movements were equally directed to the target between condition ($p = 0.94$), the first pointing movements were more rightward deviated in the terminal than in the concurrent condition, thus confirming previous evidence (Làdavas et al., 2011) that seeing just the last part of the movement (terminal condition) led to a greater initial pointing error compared to the condition (concurrent) where participants could see the entire movement ($p < 0.001$). The ANOVA conducted on the group concurrent-terminal showed a significant effects of Pointing [$F_{(1,11)} = 20.81$, $p < 0.001$, $\eta_p^2 = 0.65$], demonstrating that overall, in both conditions, the first pointing movements were more rightward deviated than the last pointing movements (concurrent first 0.74±0.75°, concurrent last -0.11±0.23°, terminal first 0.83±0.51°, terminal last 0.06±0.22°). The main effect of Condition [$F_{(1,11)} = 1.72$, $p = 0.22$], and the Condition by Pointing interaction [$F_{(1,11)} = 0.20$, $p = 0.66$] were not significant.

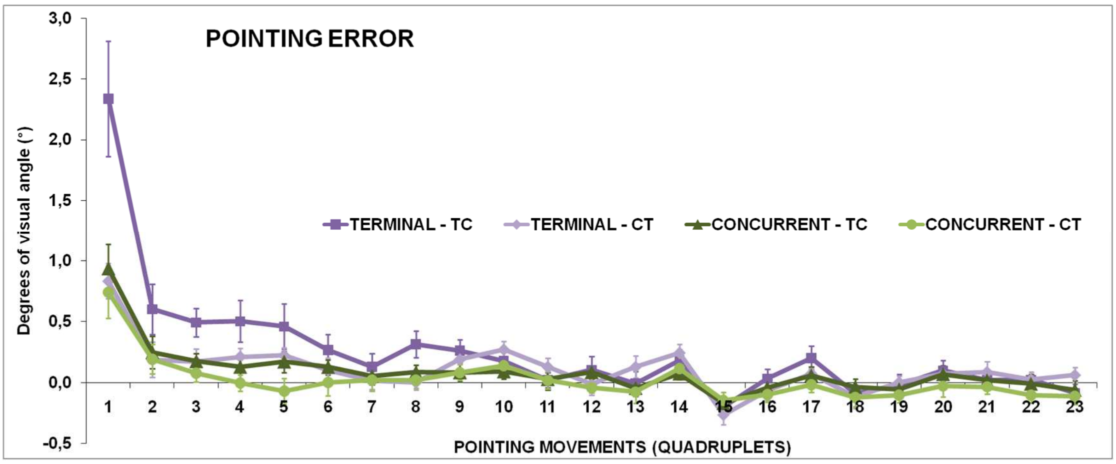


Figure 7. Mean (SE) deviation of the pointing movements (average of four pointings, resulting in 23 quadruplets) of the right index finger from the visual target in the pointing adaptation task, in degrees of visual angle (°); positive values correspond to rightward deviations from the visual target, negative values to leftward deviations. Violet: terminal condition for the terminal-concurrent (TC, n=12, dark violet) and the concurrent-terminal (CT, n=12, light violet) sub-groups. Green: concurrent condition for the terminal-concurrent (TC, n=12, dark green) and the concurrent-terminal (CT, n=12, light green) sub-groups. The ANOVA reported in the text, was conducted on the quadruplet #1 (first four pointing) and #23 (last four pointings).

1.2.5. Conclusion

In Experiment #1, participants underwent two sessions of ecological PA, in two different exposure condition, varying the vision on the limb during the execution of the tasks: terminal, and concurrent. In Experiment #2, the same two exposure conditions were applied to the repeated pointing PA. In both experiments, before and after the exposure phase, participants executed three tests assessing the perception of the straight-ahead position in the proprioceptive, visual, and visual-proprioceptive domains. Experiment #1 showed that a greater visual-proprioceptive AE was induced through ecological PA in the concurrent exposure condition, compared to the terminal one. No differences were found in the amount of visual and proprioceptive AEs, between the two exposure conditions. Thus, the ecological PA procedure benefits the most from an exposure condition where visual and proprioceptive information are available together, bringing about greater AEs in the visual-proprioceptive system.

Conversely, the results of Experiment #2 indicated that a greater proprioceptive AE was induced through repeated pointing PA in the sub-group which did the terminal exposure condition in the first session and the concurrent exposure condition in the second day, compared to the other sub-group, which did the two sessions in the opposite order, irrespective of the specific exposure condition. Moreover, a greater visual-proprioceptive AE was induced through repeated pointings in the terminal exposure condition, but only in the sub-group where the terminal condition was executed in the first session. Finally, the greatest initial pointing error was found in terminal exposure condition, but only in the sub-group which did the terminal exposure condition in the first day. Thus, confirming previous evidences (Làdavas et al., 2011), the repeated pointing PA procedure benefits the most from an exposure condition that maximize the visual and proprioceptive discrepancy and the terminal pointing error, increasing the AEs in visual-proprioceptive system.

Taken together these results suggest that the amount of visual feedback during visuo-motor adaptation to displacing prisms, affects in an opposite direction the ecological and repeated pointing PA procedure. Thus, even though the two procedures might share the same main PA processes, one might argue that different factors could affect distinctively the two procedures.

1.3. Study #2: Multisensory integration in PA

1.3.1. Aim of the study

In the present study we tested the hypothesis that the sensory nature of the target could be one factor affecting PA. And specifically, that multisensory integration (i.e., cross-modal spatial integration between auditory and visual stimuli) could enhance the PA components. Participants underwent three sessions of repeated pointing PA, with the target presented in three different modality, one per session: unimodal visual, unimodal acoustic, and bimodal. Firstly, we compared the magnitude of the AEs after the three different PA conditions. Secondly, we tested the possible advantage to point to a multisensory target in the correction of the pointing error. Lastly, we tested for the first time the possibility to adapt through repeated pointing movement toward an acoustic target (unimodal acoustic condition of PA), in the absence of a visual target.

1.3.2. Materials and methods

Participants

Twenty-four healthy right-handed (Oldfield, 1971) students recruited in the Department of Psychology of the University of Milano-Bicocca took part in the experiment (12 females; mean age: 23.25±1.42 years, range: 21-28; mean education: 15.25±1.33 years, range: 13-16). Participants had normal or corrected-to-normal vision and no history or evidence of neurological or psychiatric disorders. The study was approved by the local Ethical Committee and performed according to the ethical standards laid down in the 1991 Declaration of Helsinki. All participants gave informed consent, after a brief session that outlined the nature of the study.

Procedure

Participants underwent three sessions, in three different days (the intersessions interval was at least 24 hours). Each session lasted about one hour and included 1) a pre-exposure phase, 2) a prism adaptation exposure phase, 3) a post-exposure phase, identical to phase 1).

Pre- and post-exposure phases. In order to assess the presence and the magnitude of AEs, in each session participants performed four tests to measure the perception of the straight-ahead position (sagittal to their body midline): in addition to the three classic proprioceptive (P), visual (V) and visual-proprioceptive (VP) straight-ahead tests, a fourth acoustic-proprioceptive (ACP) straight-ahead test was included (adapted from Michel, Pisella, Prablanc, Rode, & Rossetti, 2007, and Pavani, Farnè, & Làdavas, 2003). Each participant performed the four tests in the same order, both in the pre- and in the post-exposure phases, in both sessions; the tests order was counterbalanced across participants. For each test 10 trials were given. The procedure for the proprioceptive, visual and visual-proprioceptive straight-ahead tests is the same used in Study #1 (see p. 18), with the only exception of the distance from the LED in the visual and visual-proprioceptive straight-ahead tests, which in this study was 65cm, instead of 85cm. Thus, only the procedure for the acoustic-proprioceptive straight-ahead test is reported:

- *Acoustic-proprioceptive test (ACP).* In darkness, each participant received instructions to point with the right index finger to the location on the table surface subjectively perceived as the projection of a sound source. The sound presented was a 1200Hz tone, lasting 250ms, emitted by a speaker placed 65cm distant, aligned with participant' body-midline. No information was given about the actual LED location. A graduated panel, aligned with the body-midline, allowed the recording (degrees of visual angle in 1° steps) of the participant's deviation from the straight-ahead position of the speaker, with an accuracy of 0.5° (figure 3, fourth illustration).

In every test, the difference between the post-exposure and pre-exposure deviations was taken as index of the AEs magnitude, as the shift from the perceived body midline: positive values indicated a rightward deviation from the perceived body midline, negative values a leftward deviation.

Prism adaptation exposure phase. In each session, participants adapted to an 11.4° rightward visual shift, induced by 20-dioptre, base-left prism glasses (BLP; Optique Peter, Lyon, France). Visuo-motor adaptation was achieved by the execution of 92 manual pointing movements towards a target presented at 4 different positions (+10°, +20° rightwards, and -10° and -20° leftwards, with respect to the participant's body midline), in a pseudorandom fixed order. The target stimulus varied according to the adaptation condition:

- unimodal visual (red led);
- unimodal acoustic (white noise burst);
- bimodal (simultaneous presentation of the light and the white noise burst).

The order of the three adaptation conditions was counterbalanced across participants. In each session of adaptation, just one type of target stimulus was presented. In order to induce a multisensory integration in the bimodal condition, the stimuli in all the sessions lasted 150ms. The apparatus for the target stimuli was adapted from the one by Frassinetti and colleagues (Frassinetti, Bolognini, et al., 2002). Four LEDs and four piezoelectric loudspeakers were mounted in couple, on a semicircular black board, arranged horizontally at the participant's ear level and located at an eccentricity of 10° and 20° to the left and right of the centre of the apparatus, which was aligned with participant's body midline. Participants were unable to see the loudspeakers, which were mounted behind the board. Participants received instructions to point with their right fingertip to the target stimulus, with a fast and accurate movement, and then to return to the initial position (right finger on the sternum). The view of the pointing movement was occluded by means of a wooden box and a cape that covered the participant's arms, with the finger becoming visible at the very last part of the movement. The external side of the wooden box, the one facing the experimenter, was graduated in degrees of visual angle, so that the experimenter measured the deviation of each pointing from the target with an accuracy of 1°; rightward deviations from the target were scored with positive values, leftward with negative values. The pointing adaptation procedure lasted about 20 min.

1.3.3. Statistical analysis

The statistical analyses were carried out with the software Statistica (StatSoft, Tulsa, OK, USA, version 7.0). In all ANOVAs, significant effects and interactions were investigated with Newman-Keuls test post hoc for multiple comparisons. Partial eta squared ($\eta_p{}^2$) of significant effects were also computed, in order to determine the effect sizes (Cohen, 1988). Significance was set at $\alpha = 0.05$.

Possible differences in the AEs brought about by the different exposure conditions were assessed by running four repeated-measures ANOVAs, one for each test (P, ACP, VP, V), performed on the participants' straight-ahead mean shifts (post- *minus* pre- exposure phase performance), with the within-subjects factor of "Adaptation condition" (Visual, Acoustic, Bimodal).

In order to assess the presence of adaptation, as the reduction of the initial pointing error, a repeated-measure ANOVA was performed, on the mean deviation from the target of the first and last four pointing movements, with the within-subjects factors of "Adaptation condition" (Visual, Acoustic, Bimodal) and of "Pointing" (first four/last four).

Moreover, we were interested in assessing the minimum number of pointing movements necessary in order to point correctly to the target, in the different adaptation conditions. To this end, a series of 92 t-test for dependent samples were performed between each pointing deviation against zero, for each condition of adaptation, where zero corresponded to the absence of pointing error.

1.3.4. Results

Sensorimotor AEs.

The four repeated-measures ANOVAs ran on the straight-ahead shifts failed in revealing any significant effects of Adaptation condition [P: $F_{(2,46)} = 2.27$, $p = 0.11$; ACP: $F_{(2,46)} = 0.62$, $p = 0.54$; VP: $F_{(2,46)} = 0.36$, $p = 0.70$; V: $F_{(2,46)} = 0.80$, $p = 0.45$], thus demonstrating that the three adaptation conditions brought about the same amount of AEs in the four straight-ahead tests, in the expected direction (figure 8). Specifically, after the exposure phase, participants perceived the straight-ahead position deviated toward the left in the proprioceptive (PS: visual = M±SD°, -3.12±2.17°; acoustic = -1.78±2.70°; bimodal = -2.00±2.37°), acoustic-proprioceptive (ACPS: visual = M±SD°, -1.94±2.94°; acoustic = -2.33±3.37°; bimodal = -1.49±4.06°), and visual-proprioceptive tests (VPS: visual = M±SD°, -2.65±2.18°; acoustic = -2.38±2.80°; bimodal = -2.95±2.23°), and toward the right in the visual test (VS: visual = M±SD°, 0.11±1.62°; acoustic = -0.06±1.02°; bimodal = 0.45±1.81°).

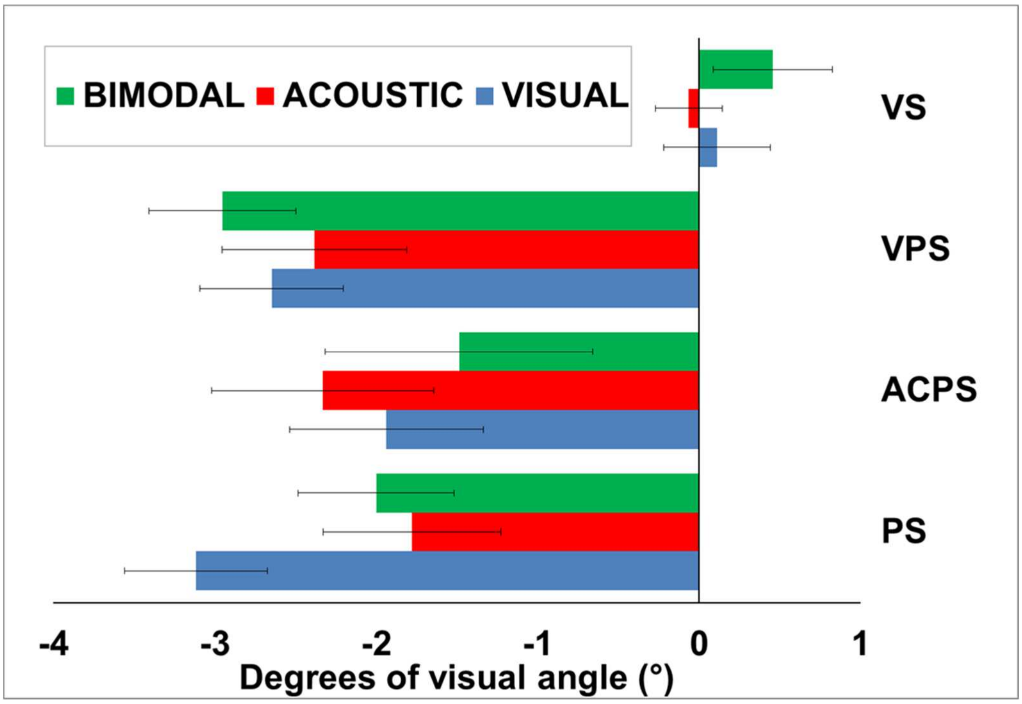


Figure 8. Mean (SE) deviation from body midline in the proprioceptive (PS), acoustic-proprioceptive (ACPS), visual-proprioceptive (VPS), and visual (VS) straight-ahead tests, expressed as a shift (post- minus pre- exposure performance), after the bimodal (green), acoustic (red), and visual (blue) conditions of PA, in degrees of visual angle (°); positive values correspond to rightward deviation from the perceived body midline, negative values to leftward deviations.

Error reduction.

The repeated-measures ANOVA ran on the mean deviation of the first and last four pointing movements during the adaptation exposure showed a main effect of Adaptation condition [$F_{(2,46)} = 7.22$, $p < 0.01$, $\eta_p^2 = 0.24$], of Pointing [$F_{(1,23)} = 205.68$, $p < 0.001$, $\eta_p^2 = 0.90$], and of the interaction Adaptation condition by Pointing [$F_{(2,46)} = 3.29$, $p < 0.05$, $\eta_p^2 = 0.12$]. Post hoc comparisons showed that, in the visual and bimodal conditions, the first pointing movements were more rightward deviated than the last pointing movements, which were directed correctly to the target (visual first M±SD° 4.20±1.44°, visual last 0.18±0.39°, $p < 0.001$; bimodal first 3.74±1.85°, bimodal last 0.15±0.28°, $p < 0.001$; figure 9). Moreover, both the first and the last pointing movements did not differ between the two conditions (both *p-values* > 0.13). In the acoustic condition the first pointing movements were more rightward deviated than the last pointing movements, which were more leftward deviated (acoustic first 3.21±1.94°, acoustic last -1.46±2.39°, $p < 0.001$), and which differed from the last pointings in the other two conditions (both *p-values* < 0.001). Moreover, the first pointings in the acoustic condition differed from the first pointings of the visual condition ($p < 0.01$), but not from those of the bimodal condition ($p = 0.09$).

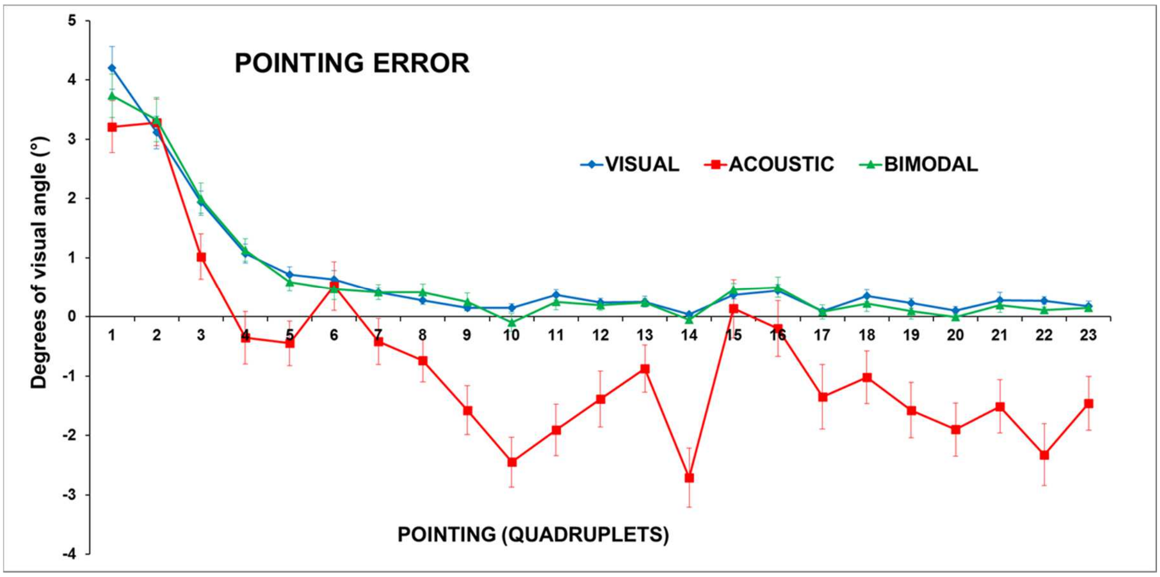


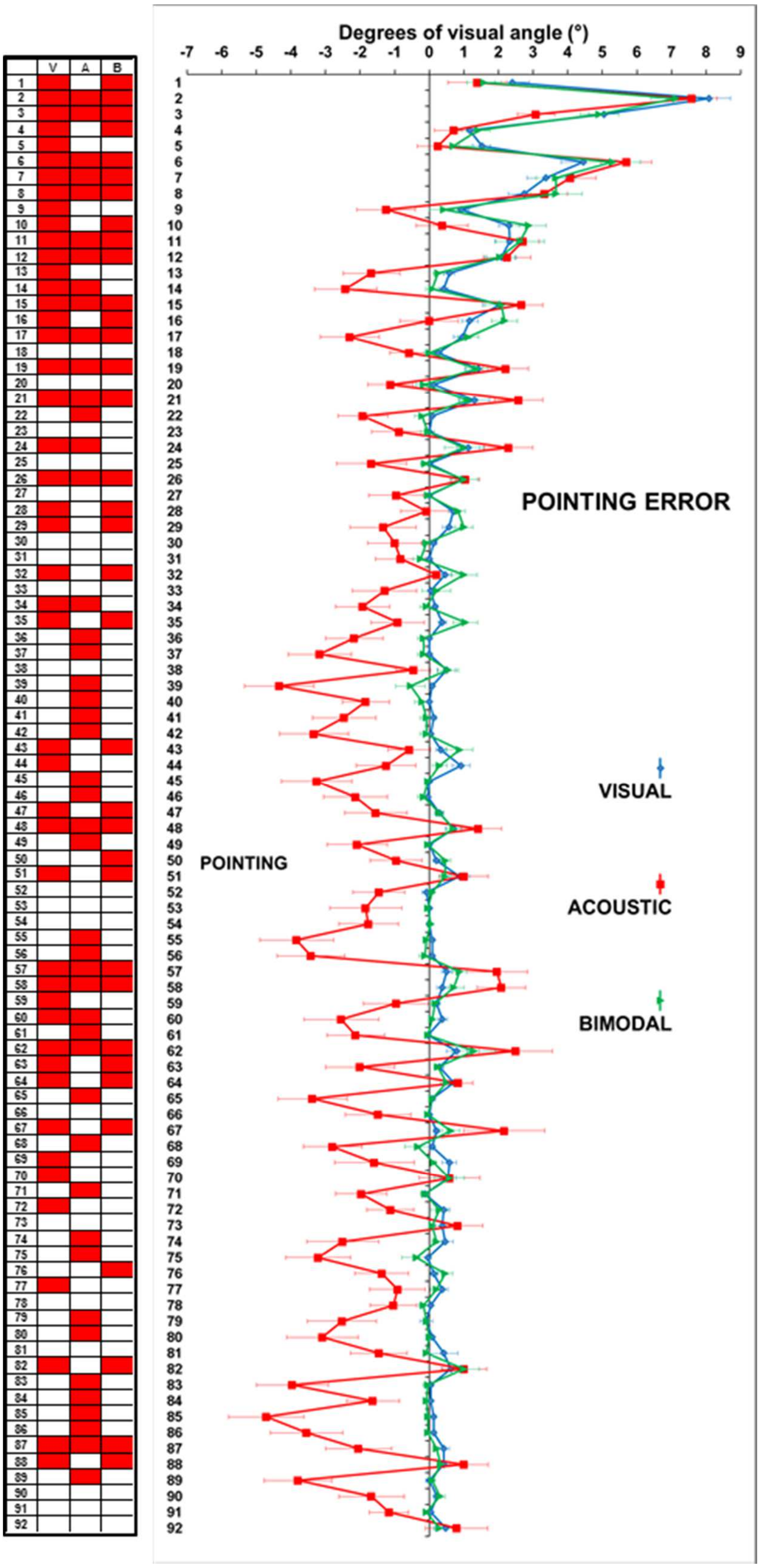
Figure 9. Mean (SE) deviation of the pointing movements (average of four pointings, resulting in 23 quadruplets) of the right index finger from the visual target in the pointing adaptation task, in the visual (blue), acoustic (red), and bimodal (green) conditions, in degrees of visual angle (°); positive values correspond to rightward deviations from the visual target, negative values to leftward deviations. The ANOVA reported in the text, was conducted on the quadruplet #1 (first four pointing) and #23 (last four pointings).

Evolution of the error reduction.

As shown in figure 10 (left panel), which depicts the *p-values* of the t-test comparisons between each pointing movement against zero, for each condition of adaptation, participants firstly pointed correctly to the target at pointing #18 in the visual (pointing #18 vs. 0, $p = 0.08$), #1 in the acoustic (pointing #1 vs. 0, $p = 0.12$), and #5 in the bimodal pointing #5 vs. 0, $p = 0.22$) condition. Beside the quantitative description of the results, several qualitative observations can be made. The visual and bimodal adaptation conditions, show the classic evolution of the error reduction of the repeated pointing PA (Bornschlegl et al., 2012; Redding & Wallace, 2011): that is, initially, pointing errors are made in the direction of the visual displacement. Such errors diminish over repeated trials with visual feedback, and disappear in as few as 15 trials; thus the person has "adapted" to the prismatic displacement (Redding & Wallace, 2011). Conversely, the evolution of the pointing correction in the acoustic condition (red lines in figures 9 and 10) does not show this initial bias, being the first pointing already correctly directed to the target (pointing #1 vs. 0, p = 0.12). Moreover, the following pointings are not consistently directed toward the target, as one might expect if participants adapted to the prismatic displacement; instead, they oscillate between those pointings correctly directed to the target (50%), those rightward deviated (17%), and those leftward biased (*overcompensation*, 33%) (Table 1). During both visual and bimodal adaptations participant did not overcompensate (0% in both conditions); moreover during bimodal adaptation, on average, participants pointed the 62% of the time correctly to the target, compared to the visual condition, where the unbiased pointings are equal to 50%.

Table 1. Number (proportion) of unbiased, rightward and leftward biased pointing, in the three exposure phase conditions.

	Pointing		
Type of adaptation	Unbiased	Rightward biased	Leftward biased (*overcompensation*)
VISUAL	46 (50%)	46 (50%)	0 (0%)
ACOUSTIC	46 (50%)	16 (17%)	30 (33%)
BIMODAL	57 (62%)	35 (38%)	0 (0%)



	V	A	B
1	🟥		🟥
2	🟥	🟥	🟥
3	🟥	🟥	🟥
4	🟥		🟥
5	🟥		
6	🟥	🟥	🟥
7	🟥	🟥	🟥
8	🟥	🟥	🟥
9	🟥		
10	🟥		🟥
11	🟥	🟥	🟥
12	🟥	🟥	🟥
13	🟥		
14	🟥	🟥	
15	🟥	🟥	🟥
16	🟥		🟥
17	🟥	🟥	🟥
18			
19	🟥	🟥	🟥
20			
21	🟥	🟥	🟥
22		🟥	
23			
24	🟥	🟥	
25			
26	🟥	🟥	🟥
27			
28	🟥		🟥
29	🟥		🟥
30			
31			
32	🟥		🟥
33			
34	🟥	🟥	
35	🟥		🟥
36		🟥	
37		🟥	
38			
39		🟥	
40		🟥	
41		🟥	
42		🟥	
43	🟥		🟥
44	🟥		
45		🟥	
46		🟥	
47	🟥		🟥
48	🟥	🟥	🟥
49		🟥	
50			🟥
51	🟥		🟥
52			
53			
54			
55		🟥	
56		🟥	
57	🟥	🟥	🟥
58	🟥	🟥	🟥
59	🟥		
60	🟥	🟥	
61		🟥	
62	🟥	🟥	🟥
63	🟥		🟥
64	🟥		🟥
65		🟥	
66			
67	🟥		🟥
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79		🟥	
80		🟥	
81			
82	🟥		🟥
83		🟥	
84		🟥	
85		🟥	
86		🟥	
87	🟥	🟥	🟥
88	🟥		🟥
89		🟥	
90			
91			
92			

Figure 10. Left panel: significant (red) and not significant (white) p-values of the t-test comparisons between each pointing movement (form 1 to 92) against zero, for each condition of adaptation (V: visual, A: acoustic, B: bimodal). Right panel: mean (SE) deviation of the pointing movements of the right index finger from the visual target in the pointing adaptation task, in the visual (blue), acoustic (red), and bimodal (green) conditions, in degrees of visual angle (°); positive values correspond to rightward deviations from the visual target (0°), negative values to leftward deviations. The ANOVA reported in the text, was conducted on the mean of the first and last four pointings.

1.3.5. Conclusion

Participants underwent three repeated pointing PA session, with the target presented in three different modality: unimodal visual, unimodal acoustic, and bimodal. Before and after the exposure phase, they performed four tests to measure the perception of the straight-ahead position, in the proprioceptive, visual, visual-proprioceptive, and acoustic-proprioceptive domains. The results showed that the three adaptation conditions brought about AEs of the same magnitude, in each straight-ahead test (proprioceptive, visual, visual-proprioceptive and acoustic-proprioceptive straight-ahead). This suggest that the sensory nature of the target does not affect the process underlying the induction of the AEs, namely the spatial realignment.

As far as the pointing error reduction during the exposure phase is concerned, results showed that participants adapt to all the three stimulation conditions, as, overall, the first pointings were significantly rightward biased, compared to the last pointings, which were directed toward the target in the visual and bimodal conditions, and biased toward the left in the acoustic PA. More interestingly, results showed that, with bimodal stimulation, participants needed fewer trials to point correct to the target, compared to the visual one. Moreover, with visuo-acoustic targets, participants made a greater number of unbiased pointings, with respect to the visual condition. This last evidence suggests a possible effect of the sensory nature of the target on the process underlying the error reduction during PA, namely the recalibration process.

Finally, even if the evolution of the adaptation did not show the same curve of the classic error reduction, participants were able to adapt to the visual displacement also when asked to point to an acoustic stimulus, in the absence of visual information about the target location.

1.4. Study #3: Abnormal proprioceptive AEs restored by neuromodulation: a single case study

[Calzolari, E., Bolognini, N., Casati, C., Marzoli, S. B., & Vallar, G. (2015). Restoring abnormal aftereffects of prismatic adaptation through neuromodulation. *Neuropsychologia, 74,* 162–9]

1.4.1. Aim of the study

So far, no evidence is available as to how changes in the cortical excitability of brain-damaged patients may affect abnormal AEs after PA. The present single-case study addresses this issue in a patient with a stroke lesion involving the left cerebellum, and the occipital cortex bilaterally. Based on the evidence described in the introduction, we explored firstly whether and how such a lesion may alter PA itself, and its AEs in the proprioceptive, visual, and visual-proprioceptive domains. Secondly, by means of transcranial Direct Current Stimulation (tDCS) delivered during the PA procedure, we investigated whether the neuromodulation (Vallar & Bolognini, 2011) of the activity of the PPC and the cerebellum, could restore in this patient the defective AEs, and the efficacy of PA. To this aim, the anodal stimulation was used in order to up-regulate the activity of the parieto-cerebellar network recruited by PA.

1.4.2. Materials and methods

Participants

Participants were recruited from the inpatient population of the IRCCS Istituto Auxologico Italiano, Milan, Italy. The study was approved by the local Ethical Committee, and performed according to the ethical standards of the Declaration of

Helsinki laid down in 1991. Participants gave their informed consent to participate in the study.

Case report. Patient MM

Patient MM was a right-handed (Oldfield, 1971), 56 year-old male with 13 years of education. On February 2014, the patient had been referred to the Neuropsychological Laboratory of the Istituto Auxologico Italiano by the Neurophthalmology outpatient ward, for a general neuropsychological evaluation. Six months before (September 2013), MM had been admitted to another hospital, due to the sudden onset of dizziness, vertigo, unsteadiness, dysarthria, and burning and prickling sensation in the left side of the face; the patient also reported photophobia. At a neurological exam the patient was alert, cooperative, and oriented in time and space; a confrontation test revealed a bilateral visual deficit in the lower quadrants; a right-beating horizontal and rotatory nystagmus was noted; speech was slurred; gait was wide-based and irregular, with a positive Romberg sign with eyes open; dysmetria and adiadochokinesia in the left upper limb were present; no motor and somatosensory deficits were found. A MRI scan (September 2013) showed left cerebellar and bilateral occipital ischaemic lesions. A successive MRI scan, performed at the time of the neuropsychological assessment (on February 2014), confirmed the presence of lesions involving the occipital cortex bilaterally, and the left lateral cerebellum (figure 11). A neurological control exam at the time of the study showed left facial weakness, mild dysarthria, dysmetria, and dysdiadochokinesia in the left upper limb, and gait ataxia. Humphrey visual field perimetry showed a bilateral deficit in the lower quadrants (figure 12).

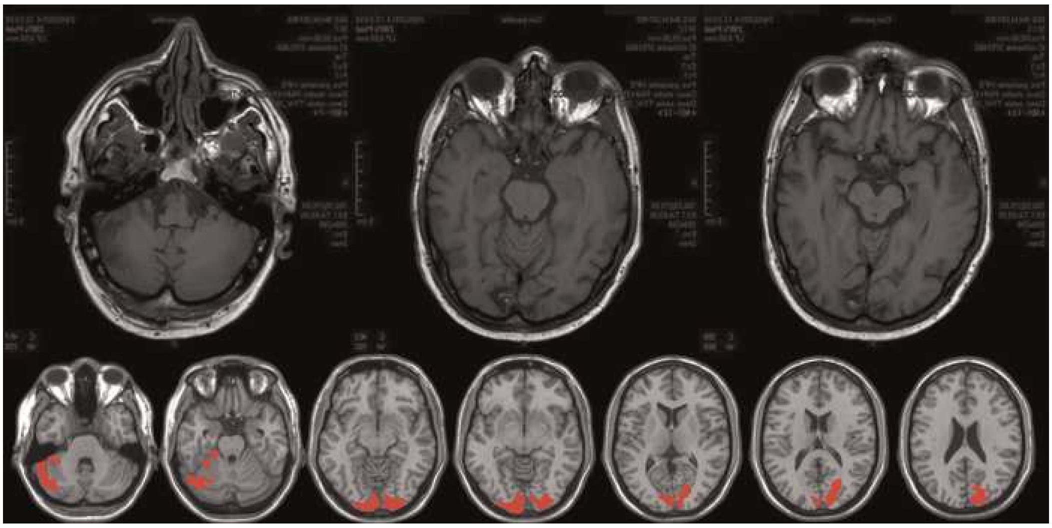

Figure 11. Patient MM. Occipital bilateral and left cerebellar lesion.

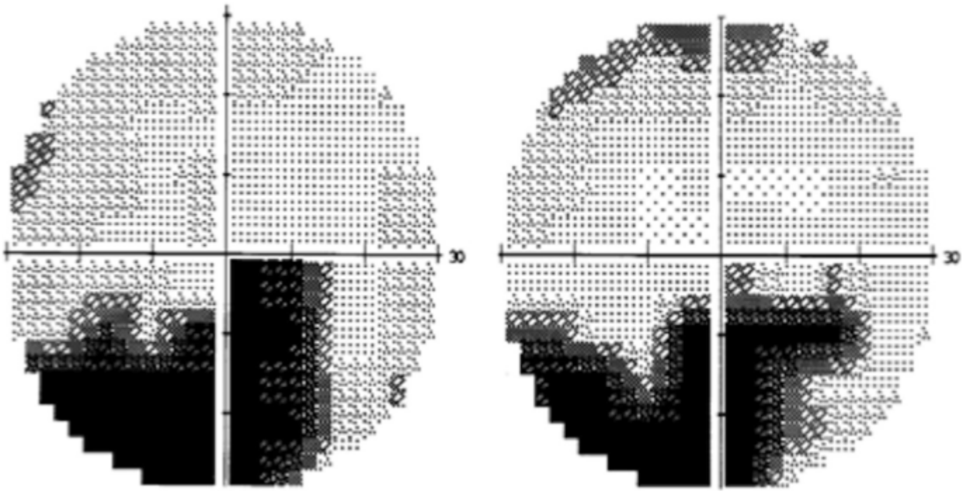

Figure 12. Patient MM. Bilateral deficit in the lower quadrants.

The neuropsychological evaluation is summarised in Table 2. The patient was not aphasic, while showing some reading difficulties, related to the bilateral visual field defect. The defective performance in visual exploration at the Test of Attentional Performance (TAP), and in the number barrage test, did not show any lateralized pattern. No evidence of reasoning deficits was found. As for visual perception, defective scores in the Position discrimination subtest of the Visual Object and Space Perception Battery (VOSP), and in the Poppelreuter-Ghent Test were found. At the initial evaluation, a mild left spatial neglect was found at the Letter and Bell cancellation tasks, and at Line Bisection (Table 2).

Table 2. Patient MM. Baseline neuropsychological assessment.

MMSE[a]	30/30
LANGUAGE	
Token Test[b]	35.25/36
ENPA[c] reading	
Words	6.3/10*
Non-words	3/5*
Phrases	0.9/5*
Boston Naming Test[d]	56/60
MEMORY	
Digit Span[e]	5.75
Corsi's visuo-spatial span[e]	4.75
Short Story[f]	10.5/28
VISUO-SPATIAL COGNITION	
Target cancellation[g]	
Letter	55/104*
	(L = 26, R = 23, D = 3)♠
Bell	26/35*
	(L = 6, R = 3, D = 3)♠
Star	55/56
Line Bisection[h]	+7.6%*
Number Barrage[i]	29/60*
Alertness[j]	
with cues	397 ms (100%)
without cues	403 ms (100%)
Visual exploration[j]	
target	4616 ms (69%)
no target	8657 ms (100%)
REASONING	
Raven CPM[k]	34.5/36
Verbal Reasoning[l]	41.25/60
Cognitive Estimates[l]	12/42
VOSP[m]	
Shape detection screening test	20/20
Incomplete letters	17/20
Silhouettes	16/30
Object decision	16/20
Progressive silhouettes	11/20
Dot counting	9/10
Position discrimination	17/20*
Number location	8/10
Cube analysis	6/10
LINE ORIENTATION[n]	26/30
BORB[o]	
Copy	8/8
Memory copy	5/6
Object decision task	
A	28/32
B	30/32
Associative matching task	30/30
Naming	15/15
POPPELREUTER-GHENT TEST[p]	29/71*

* Defective performance according to available norms.

♠ Missed targets L/R: left/right; D: L–R difference.

[a] Grigoletto et al. (1999)
[b] De Renzi & Faglioni (1978)
[c] Capasso & Miceli (2001)
[d] Kaplan et al. (1983)
[e] Orsini et al. (1987)
[f] Novelli et al. (1986)
[g] Vallar et al. (1994)
[h] Fortis et al. (2010)
[i] Spinnler & Tognoni (1987)
[j] Zimmermann & Fimm (2014)
[k] Basso et al. (1987)
[l] Della Sala et al. (2003)
[m] Warrington & James (1991)
[n] Benton et al. (1983)
[o] Riddoch & Humphreys (1993)
[p] Della Sala et al. (1995)

This mild deficit may be traced back to the left cerebellar lesion, on the basis of reports of spatial neglect ipsilateral to a cerebellar damage (Silveri, Misciagna, & Terrezza, 2001). Be as it may, at a later evaluation, before the experimental study, MM omitted 19 left-sided and 21 right-sided letter targets, and made no omissions in the Bell, and Star cancellation tasks; at Line Bisection the rightward deviation (+2.20%) was within the normal range (Fortis et al., 2010). MM had no contraindication to non-invasive brain stimulation, and the accepted recommendations for the safe use of tDCS were applied (Nitsche et al., 2003; Rossi, Hallett, Rossini, & Pascual-Leone, 2009).

Control participants.

Ten right-handed participants [5 males, mean age 67.80 years (Standard Deviation, SD 76.30, range 60–77), mean education 13.90 years (SD75.72, range 5–18)], with no history and evidence of neurological and psychiatric disorders, and normal or corrected-to-normal vision, served as controls.

Procedure

PA procedure.

A standard PA protocol of the laboratory was used (Fortis et al., 2013). Both patient MM and control participants adapted to an 11.4° rightward visual shift, induced by 20-dioptre, base-left prism glasses (BLP; Optique Peter, Lyon, France), using for pointing the right hand, in which the patient showed no dysmetria. Visuo-motor adaptation was achieved by the execution of 90 manual pointing movements towards a visual target (a red pen) presented at 2 different positions (+10° rightwards, and -10° leftwards, with respect to the participant's body midline), in a pseudorandom fixed order. Participants received instructions to point with their right fingertip to the pen, with a fast and accurate movement, and then to return to the initial position (right finger on the sternum). The view of the pointing movement was occluded by means of a wooden box and a cape that covered the participant’s arms, with the finger becoming visible at the very last part of the movement. The pointing adaptation procedure lasted about 15 min, with 3 min of rest after 30 pointing trials. The external side of the wooden box, the one facing the experimenter, was graduated in degrees of visual angle, so that the experimenter measured the deviation of each pointing from the target with an accuracy of 1°; rightward deviations from the pen were scored with positive values, leftward with negative values.

Assessment of AEs.

The pre- and post-exposure phases included the execution of the three tests (proprioceptive, visual and visual-proprioceptive straight-ahead tests) used to assess the presence of the PA-induced AEs (see Study #1 for further details, p. 18); for each test 10 trials were given. In every test, the difference between the post-exposure and pre-exposure deviations was taken as index of the AEs: positive values indicated a rightward deviation from the subjective straight-ahead, negative values a leftward deviation. Both MM and healthy control participants underwent the PA, and the pre- and post-exposure phases.

Transcranial direct current stimulation (tDCS).

Anodal tDCS was applied, using a battery-driven constant current stimulator (BrainStim, E.M.S. s.r.l., Bologna, Italy, http://brain stim.it), and a pair of surface saline-soaked sponge electrodes ($5x5cm^2$). Current intensity was of 1.5 mA (Fade-in/-out=8s), for a total duration of 15 min. The stimulation started and it was delivered 5 min before PA, and continued for 10 min, during PA. MM underwent 6 experimental sessions, 1 per day (mean intersessions interval = 91.2 h, range 24–144, SD±54.73), given in the following order:

1. Without tDCS (PA alone).

2. Right cerebellar (R-Cer) tDCS: the electrode was placed 2 cm below the inion, and 1 cm medially from the right mastoid process, while the reference electrode was placed over the ipsilateral right deltoid (Ferrucci et al., 2012).

3. Right parietal (R-PPC) tDCS: the electrode was placed over P4, while the reference electrode was placed over the contralateral supraorbital area (Bolognini, Fregni, Casati, Olgiati, & Vallar, 2010).

4. Sham tDCS: the same montage of the second session was used (R-Cer tDCS), but the stimulator was turned off after 30 s (Gandiga, Hummel, & Cohen, 2006).

5. Left cerebellar (L-Cer) tDCS: the electrode was placed 2 cm below the inion and 1 cm medially from the left mastoid process, while the reference electrode was placed over the ipsilateral left deltoid (Ferrucci et al., 2012).

6. Left PPC (L-PPC) tDCS: the electrode was placed over P3, while the reference electrode was placed over the contralateral supraorbital area (Bolognini et al., 2010).

Each session lasted about 1 h, and included: (1) a pre-exposure phase, immediately before wearing the prismatic goggles; (2) an exposure phase, namely PA, during which tDCS was delivered over one of the target areas; (3) a post-exposure phase, after goggles' removal. Since our aim was to use tDCS for improving MM's abnormal responses to PA, and given that the patient showed pathological AEs only in the proprioceptive test (see below), the effect of tDCS were assessed only with respect to this task.

1.4.3. Statistical analysis

Firstly, in the control group and in MM, we assessed the presence of PA in the PA alone session (without tDCS), as a reduction of the initial pointing errors during prism exposure; two independent sample t-tests on the deviation scores of the first 4 and the last

4 pointings of the exposure phase were performed. Secondly, t-tests for case-control comparisons were performed, to compare MM’s first 4 and last 4 pointing deviations in the PA alone condition with the average deviations of the 10 control participants (Crawford & Howell, 1998). Thirdly, a t-test for case-control comparisons was performed on the correction index of MM vs. the average score of the control group; the index was computed as the deviation in the last 4 pointings minus the deviation in the first 4 pointings, with a negative value indicating a leftward correction of the initial rightward deviation. Finally, t-tests for case-control comparisons were performed, in order to compare MM’s AEs scores in the V, P, and VP straight ahead tests, with those of healthy controls; AEs were the straight-ahead shifts (post-exposure *minus* pre-exposure deviations) in each test in the PA alone condition. For all t-tests, two-tailed *p-values* were used, with a level of significance set at $\alpha = 0.05$. The effects of tDCS were then assessed only with respect to the P straight-ahead task, in which MM showed abnormal AEs at baseline, as detected by the analysis described above. To this aim, a mixed ANOVA was performed on the patient’s P straight-ahead scores in the pre-exposure and post-exposure deviations, with the within-subjects factor Condition (2 levels: Pre-exposure, Post-exposure), and the between-subjects factor tDCS Session (6 levels: PA alone without tDCS, R-Cer tDCS, R-PPC tDCS, Sham tDCS, L-Cer tDCS, L-PPC tDCS). In all ANOVAs, significant main effects and interactions were analysed by multiple comparisons with the Bonferroni post hoc test, with the significance level being set at $\alpha =$ 05. Partial eta squared (η_p^2) of significant effects were also computed in order to determine effect sizes (Cohen, 1988). Analyses were carried out with the software Statistica (StatSoft, Tulsa, OK, USA, version 7.0).

1.4.4. Results

PA as pointing error reduction.

As shown in figure 13, both control participants and patient MM made an initial rightward pointing error during prism exposure, which decreased at the end of the exposure phase. In the controls' group and in MM's scores, t-test showed a significant difference between the first 4 and the last 4 trials (control group: $t_{(18)} = 5.51$, $p < 0.001$; MM: $t_{(6)} = 9.02$, $p < 0.001$), with the first 4 pointing trials (controls: 3.75±2.45°; MM: 8.75±1.50°) being more rightward deviated than the last 4 (controls: 0.45±0.71°; MM: 1.5±0.58°). These findings indicate that the prism-induced rightward pointing error decreased, in both controls and patient MM. Crawford-Howell's t-tests for case-control comparisons showed that the mean score of the control group did not differ from the patient's score in the PA alone session, indicating that MM's initial deviations ($t = 1.946$, $p = 0.084$), final deviations ($t = 1.410$, $p = 0.192$), and the reduction of the initial error ($t = -2.092$, $p = 0.066$) (control group -3.30±1.80°, MM -7.25°) were comparable to those of control participants.

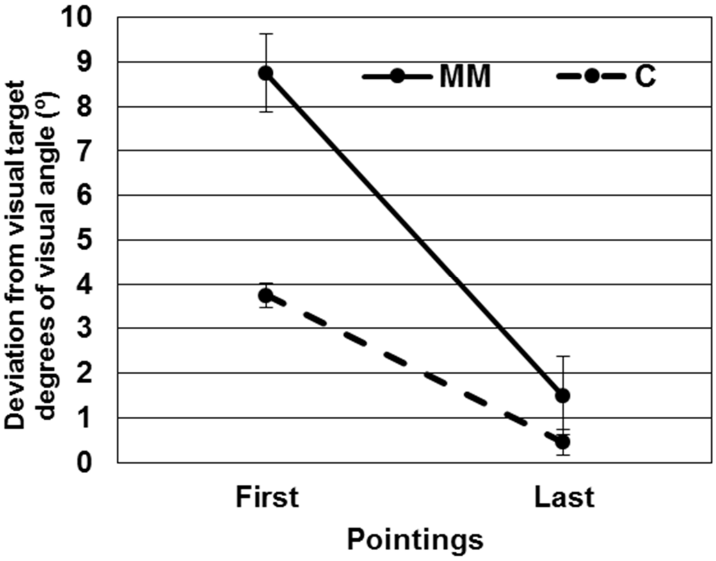

Figure 13. Adaptation as pointing error reduction. Mean (SE) deviations from the visual target of the first 4, and of the last 4 pointing movements of the right index finger in the pointing adaptation task, in degrees of visual angle (°). Positive values indicate rightward deviations from the visual target, negative values leftward deviations. Solid line: patient MM. Dashed line: control group (C).

Assessment of AEs.

As shown in figure 14, after the exposure to rightward deviating prisms, in the P test, control participants exhibited the expected leftward AEs. Conversely, MM, in the PA alone session, showed a rightward deviation, in the opposite direction. Crawford-Howell t-tests for case-control comparisons showed that the mean score of the control group (-1.37±1.60°) differed (t = 2.37, $p < 0.05$) from the patient's score in the PA alone session (2.60±1.60°). In the V (t = 0.42, $p = 0.68$), and in the VP (t = 0.74, $p = 0.48$) tests no differences were found between the scores of the control group (V test: 0.69±1.77°; VP test: -4.54±3.59°), and those of MM (V test: 1.47±2.52°; VP test: -1.75±2.11°).

tDCS effects on the abnormal proprioceptive AEs of MM.

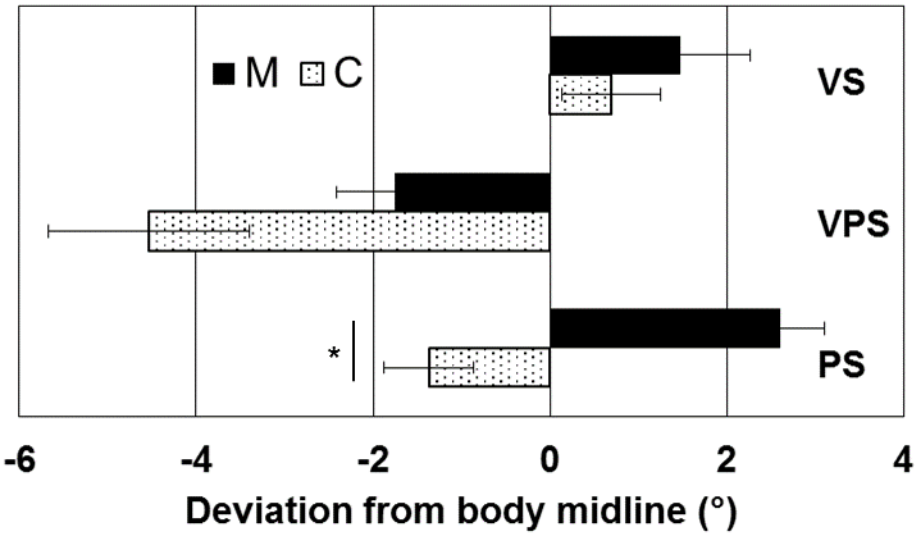

*Figure 14. AEs. Mean (SE) deviation from body midline in the proprioceptive (PS), Visual-proprioceptive (VPS) and Visual (VS) straight-ahead tasks, as difference between the Post- and the Pre- adaptation phase, in degrees of visual angle (°). Positive values: rightward deviation from the subjective body midline; negative values: leftward deviations. Black bars: patient MM's deviations. Dotted bars: control group (C). p < 0.001***, < 0.01**, < 0.05*.*

As shown in figure 15, in the pre-exposure phase of every session patient MM showed a rightward deviation, that became disproportionately larger in the post-exposure phase of the PA alone session, being reversed toward the left in the post-exposure phase of the L-PPC tDCS session only. In the L-Cer tDCS session the post-exposure deviation was close to zero. A repeated-measures ANOVA showed a significant main effect of Condition [$F_{(1,54)} = 26.40$, $p < 0.001$ $\eta_p^2 = 0.33$], while the main effect of Session was not significant [$F_{(5,54)} = 1.76$, $p = 0.14$]. The Condition by Session interaction was significant [$F_{(5,54)} = 20.48$, $p < 0.001$, $\eta_p^2 = 0.65$]. Multiple comparisons showed a significant difference between the pre-exposure and the post-exposure deviations in the PA alone session, in which the post-exposure deviation became more deviated rightward (pre-exposure = 1.05±1.17°, post-exposure = 3.65±0.91°, $p < 0.01$). The difference between the pre-exposure and post-exposure deviations was significant also in the L-Cer tDCS (pre = 3.50±1.22°, post = 0.00±1.03°, $p < 0.001$), in which the rightward deviation was reduced to zero, and in the L-PPC tDCS sessions (pre = 3.75±.01°, post = -1.20±2.51°, $p < 0.001$), in which the leftward AEs were restored. In the other sessions, the adjuvant use of tDCS during PA did not alter the straight-ahead deviations in the post-exposure assessments, as compared to the pre-exposure ones (R-Cer tDCS session: pre = 1.00±0.78°, post-exposure = 1.90±1.37°, $p = 1.00$; R-PPC tDCS session, pre = 3.25±1.40°, post = 1.30±1.32°, $p = 0.17$; Sham tDCS session, pre = 2.10±1.17°, post = 1.25±2.15°, $p = 1.00$). The leftward post-exposure deviation of the L-PPC tDCS session differed significantly from those of all of the other sessions (all *p-values* < 0.04), but the L-Cer tDCS ($p = 1$). Instead, the post-exposure deviation of the L-Cer tDCS session differed only from that of the PA alone session ($p < 0.01$). Importantly, pre-exposure deviations did not differ across the first 4 sessions (PA alone, R-Cer tDCS, R-PPC tDCS, Sham tDCS, all *p-values* > 0.08), while the rightward deviation was larger in the last two sessions (L-Cer PPC and L-

PPC tDCS), as compared with the first two ones (PA alone, R-Cer tDCS, *p-values* < 0.01). These results rule out a possible carry-over effect on AEs by multiple exposures to PA to rightward displacing prisms, which, if anything, would be expected to bring about a cumulative increase of leftward deviations in the proprioceptive straight ahead.

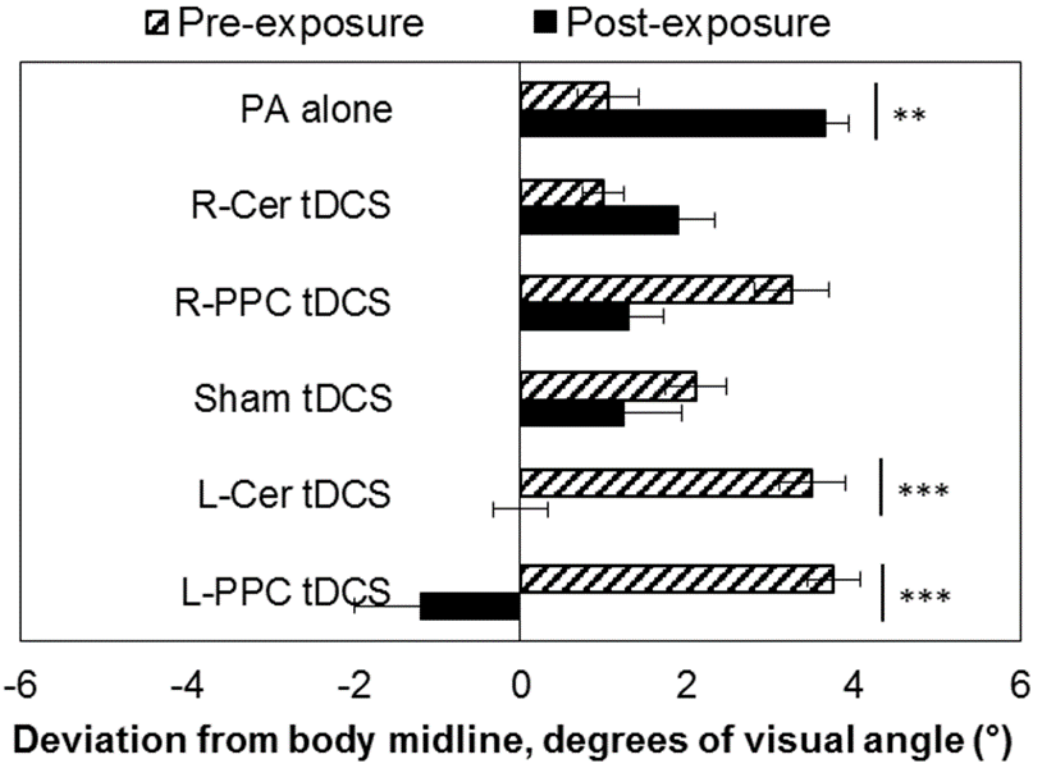

*Figure 15. Patient MM. tDCS modulation of proprioceptive AEs. Mean (SE) deviation, in degrees of visual angle, from the body midline in the P straight-ahead task, in the Pre-exposure and Post-exposure phases of each of the 6 experimental sessions. Pre- vs. Post-exposure differences, p < 0.001***, < 0.01**, < 0.05*.*

1.4.5. Conclusion

In this single case study, we investigated the effects of a left cerebellar and bilateral occipital lesion on the ability of patient MM to adapt to an optical prismatic displacement and to show AEs in the proprioceptive, visual, and visual-proprioceptive systems, as assessed by straight ahead tasks. Moreover, we investigated the effects of excitatory neuromodulation, by means of anodal tDCS, over the activity of the PPC and cerebellar cortices of either hemisphere on defective PA-induced proprioceptive AEs in MM. Firstly, we found that the bilateral occipital and left cerebellar lesion does not affect MM's ability to adapt to the optical displacement induced by the prisms. Indeed, patient MM shows an initial pointing error in the direction of the visual displacement (i.e., rightward), which diminishes progressively at the end of the exposure phase, as in the control group. Despite the presence of a lesion affecting the occipital cortex bilaterally, which determines a bilateral lower visual field defect, PA is not disrupted in MM, presumably because the patient still visually processes the error signal in the unimpaired upper quadrants. In line with these findings, there is evidence that both unilateral occipital damage and hemianopia do not affect the PA process, and the positive effects of prism exposure on recovery from left neglect (Frassinetti, Angeli, et al., 2002; Jacquin-Courtois et al., 2013; Sarri, Kalra, Greenwood, & Driver, 2006). The present findings are also in line with previous results from a single-case study, showing that a unilateral left cerebellar lesion does not impair the visuo-motor process of PA to a rightward visual field displacement, as indexed by a reduction of the pointing error (Pisella et al., 2005). On the other hand, in line with previous findings (Weiner et al., 1983), MM shows altered AEs (the 'true adaptation'), as compared to the control group. The directional alteration of the AEs is confined to the proprioceptive straight-ahead test. When vision is available to the patient (visual, and visual-proprioceptive straight- ahead), the AEs are preserved. This result is in line with findings suggesting a cerebellar involvement in active (rather than passive) proprioceptive tasks (Bhanpuri, Okamura, & Bastian, 2013), such as the present proprioceptive straight ahead, that involves an upper limb movement by the participant (Chokron, Colliot, Atzeni, Bartolomeo, & Ohlmann, 2004). In patient MM, the directionally altered proprioceptive AEs, after adaptation to rightward displacing prisms, are restored to their standard leftward direction, by up-regulating cortical excitability in the parieto-cerebellar network mediating the spatial realignment induced by PA (Prevosto, Graf, & Ugolini, 2010). In particular, MM’s altered proprioceptive AEs are reintegrated by the anodal (excitatory) tDCS over the spared left PPC. Rightward directionally altered proprioceptive AEs are also improved, namely reduced to zero, by the anodal stimulation over the left cerebellum.

1.5. Discussion

In this chapter, I tried to answer some questions about the processes underlying visuo-motor adaptation to visual displacing prisms and its neural correlates.

Study #1 demonstrated that ecological and repeated pointings PA procedures are differently affected by the vision of the limb during the prism exposure condition, as assessed by the amount of AEs in the visual-proprioceptive test, which was greater after concurrent exposure condition in ecological PA (Experiment #1), and after terminal exposure condition in repeated pointings PA (Experiment #2). Thus, even though the two procedures might share the same main PA processes, one might argue that different factors could affect distinctively the two procedures.

It has been proposed that the level of adaptation to displacing prisms, as assessed by the presence and magnitude of the AEs, may simply depend on the quantity of visual exposure and the feedback hand-to-target terminal error signals. In particular, it has been shown that those exposure conditions that maximize the error between final hand and target positions (i.e., direct effect) brought about greater sensorimotor AEs (Gaveau et al., 2014; Làdavas et al., 2011). However, evidence from both the present and previous studies, showed that AEs can be obtained (and in some cases even enhanced, as in Fortis et al., 2013) also when no direct effect of the prismatic displacement is observed, as occurs, for instance, when participants are not aware of the visual distortion (Dewar, 1971; Howard, Anstis, & Lucia, 1974; Jakobson & Goodale, 1989; Michel et al., 2007), and when performing ecological tasks in a natural environment, without any visual constraint of the hand, the manipulated objects, and the hand movements toward the objects (Fortis et al., 2010, 2013; Shiraishi et al., 2008). It is well established that both the ecological and repeated pointing procedures (as well as the terminal and concurrent exposure conditions) can give rise to adaptation and AEs, and results of Study #1 confirm this evidence, as assessed by the presence of sensorimotor AEs after both PA procedures. The evidence of the present study, showing that terminal and concurrent exposure conditions affect in an opposite manner the two PA procedures, corroborates the assumption that different factors could modulate the building up of the AEs during the repeated pointing and the ecological PA procedures, and that different mechanisms may affect distinctively the two procedures (Fortis et al., 2013). However, those mechanisms that brings about the differential pattern of results found in Experiment #1 and #2 remains unclear. Here, we can only make a few observations about the characteristics of the two procedures, and try to make some assumptions about the factors implied in the two PA procedures. One first hypothesis is that the two procedures may differ in the relative contribution of the two main PA components: namely, the strategic recalibration, which leads to an early correction of the pointing error, and the spatial realignment of sensorimotor reference frames, which contributes to both the error reduction during the repeated pointing movements and the AEs (Redding et al., 2005; Redding & Wallace, 2006). In the repeated pointing task, participants are asked to perform a series of fast and ballistic back-and-forth reaching movements toward a visual target. Classically, repeated pointing PA is performed in terminal exposure condition, in order to maximize the direct error, and both strategic recalibration and spatial realignment contribute to the error reduction (Michel et al., 2007). In the ecological PA, instead, participants are asked to complete several tasks comprising the manipulation of everyday objects (such as collecting coins, opening and closing jars, and assembling jigsaw puzzles), without any visual constraint of the limb or the movement. Thus, no evident direct pointing error is generated. Given the absence of the direct effect of pointing error in ecological PA, we might suggest that during this procedure the strategic component is limited, and that adaptation is be obtained mainly thorough the spatial realignment process (cf. Michel et al., 2007). However, this hypothesis does not account completely for the differences found in Study #1, otherwise we should have found a superiority of the same exposure condition in producing AEs, irregardless of the PA procedure used. Another possible explanation to our results can be found in the different nature and origin of the error signals involved in eliciting the adaptation, in the two PA procedures. Three main sources of error have been suggested to induce adaptation (Gaveau et al., 2014): 1) a discrepancy between vision and proprioception of the hand (Craske & Crawshaw, 1974; Redding & Wallace, 1992); 2) an inconsistency between predicted visual reafferences of the moving hand (derived from an efferent copy) and actual visual reafferences, as suggested by Held's efference–reafference theory (Held & Hein, 1958), or by more modern versions of this theory introducing internal models (Diedrichsen, Hashambhoy, Rane, & Shadmehr, 2005; Kawato, 1999; Shadmehr, Smith, & Krakauer, 2010; Wolpert & Miall, 1996); 3) a reaching feedback error, i.e., the simultaneous vision of the target and hand either during movement (Redding & Wallace, 1988), or at movement end (Harris, 1963; Kitazawa et al., 1995; Magescas & Prablanc, 2006; Martin, Keating, Goodkin, Bastian, & Thach, 1996b). Under most conditions, these sources of error are closely intertwined.

In order to clarify the relative contributions of reaching feedback errors (source of error #3), which correspond to visually perceived discrepancies between hand and target positions), and errors between predicted and actual visual reafferences of the moving hand (source of error #2), in the study by Gaveau and colleagues (Gaveau et al., 2014), participants underwent two different repeated pointing PA conditions: "terminal feedback error" condition, where the view of their hand was allowed only at the movement end, simultaneously with viewing of the target; and "movement prediction error" condition, where the view of the hand was limited to movement duration, in the absence of any visual target, and error signals arose solely from comparisons between predicted and actual reafferences of the hand. Adaptive AEs were observed in the “terminal feedback error” condition only, indicating that prediction error alone (source of error #2) was insufficient to induce adaptive AEs, and indicating a critical role of hand-to-target feedback error signals (source of error #3) in visuomotor adaptation. The Author concluded that a combination of feedback and prediction error signals is necessary for eliciting AEs during repeated pointing PA.

As far as the ecological PA procedure is concerned, it is worth noting that the source of the error inducing adaptive AEs is unlikely to be the reaching feedback error (source of error #3), as, during this procedure, the terminal error is minimal, if not absent. Instead, we suggest that the greatest source of error in this procedure could arise from the discrepancy between the predicted (efference copy) and the actual sensory reafferences of the moving hand during the action. The tasks of the ecological PA procedure involves the manipulation of different everyday objects, and a more varied and complex patterns of movements; during this procedure participants are asked to plan a series of subsequent actions and movements toward different objects, in order to complete them. One might suggest that the predictions of the motor output resulting from a motor command (i.e., efference copies) for the actions occurring during the manipulation of objects are more complex and varied, compare to those generated during repeated pointing PA. It has been suggested that visuomotor adaptation results from the progressive decrease of the conflict between the efference copy and visual reafferent signals (Held & Hein, 1958). During the typical exposure condition of ecological PA (i.e., concurrent) the visual reafferences resulting from the motor command (i.e., the vision of the actively moving hand) are available for a longer time, for the entire duration of the action, and from a greater part of the limb, as the vision of it is not occluded, as compared to the terminal exposure condition. Thus, during ecological PA in concurrent exposure condition the error signal between the internal model of the predicted action and the actual movement might be enhanced, and this, in turn, might bring about a stronger realignment, and subsequent greater AEs.

Study #2 explored the effect of the sensory nature of the target on the main process underlying the error reduction during PA, highlighting the multisensory characteristic of the strategic recalibration process of PA. The results provided evidence that participants were more accurate in pointing toward a multisensory (visuo-acoustic) stimulus, rather than toward unimodal ones. However, the nature of the target did not affect the generation of the sensorimotor AEs, which were induced with the same magnitude after the three PA sessions, suggesting that the sensory nature of the target does not affect the process underlying the induction of the AEs, namely the spatial realignment. Multisensory integration is a powerful mechanism for maximizing sensitivity to sensory events, and cross-modal spatial integration between auditory and visual stimuli is a common phenomenon in space perception, firstly outlined by neurophysiological and behavioral studies in animals (Stein & Meredith, 1993). Parietal cortex has long been known to be a site of sensorimotor integration (for a recent review, see Sereno & Huang, 2014). PPC is also involved in the spatial recalibration process and the error reduction phase of PA (Chapman et al., 2010; Clower et al., 1996; Danckert et al., 2008; Luauté et al., 2006; Pisella et al., 2006; Saj et al., 2013; Sekiyama et al., 2000; Weiner et al., 1983). On the basis of the results of Study #2, we might propose that the process of cross-modal integration occurring during visuomotor PA to a bimodal stimulus, supported by associative and multisensory areas in the PPC, could have enhanced the strategic recalibration component of PA, as assessed by the more accurate pointings and the faster reduction of the terminal pointing error. Even though the specific mechanisms underpinning this boosting effect remain unclear, however, one might speculate that multisensory stimulation might have contribute to the enhancement of the recalibration component at two different levels. Firstly, by the introduction of a third source of conflicting information about the location of the body relative to the target. One might suppose that, by augmenting the discrepancy between sensory inputs arising from different sensory modalities, could require a greater and more efficient contribution of the PA components implied in the resolution of the sensory conflict.

The sensorimotor maps involved in the spatial realignment and recalibration when pointing to a visual target are (Redding & Wallace, 2006):

- the visual–motor eye–head, signalling the position of the eyes with respect to the head, tested with the visual straight-ahead;
- the proprioceptive–motor hand–head system, signalling the position of the pointing limb with respect to the body midline, tested with the proprioceptive straight-ahead;
- the eye–hand sensorimotor coordination system, signalling the position of the pointing limb with respect to the position of the eyes, tested with the visuo-proprioceptive straight-ahead, and involving the coordination of the two above listed components.

During unimodal visual PA, the sensory discrepancy arises from contrasting visual and proprioceptive inputs about the spatial location of the different parts of the body with respect of the visually dislocated target. By contrast, during bimodal stimulation, in addition to vision and proprioception, a third sensory modality (i.e., audition) is signalling the position of the target. In fact, in the bimodal PA, the visuo-acoustic target is visually perceived displaced toward the direction of the visual displacement, but at the same time it might be heard in its actual location. This may in turn increase the potential number of systems involved (for instance, there might be one system signalling the position of the sound source with respect to the ear-head, and another one signalling the relative position between the heard sound and the limb, a coordination system similar to the visuo-proprioceptive one), and that have to be recalibrated and realigned into a new common egocentric reference frame. Thus, the augmented sensory discrepancy induced by a bimodal stimulus might need a greater allocation of strategic recalibration to be solved (Zwiers, Van Opstal, & Paige, 2003).

A second explanation might be that multisensory integration improves the target localization during PA. In their study, Bornschlegl and colleagues (Bornschlegl et al., 2012) suggested that pacing the pointing movements during PA toward a visual target with a rhythmic auditory signal, could have enhanced overall activation of the PA neural network, and might have enable multisensory integration, including auditory spatial information that selects the more reliable proprioceptive signal for movement control. In several studies, it has been shown that multisensory integration improves visual detection (Bolognini, Frassinetti, et al., 2005; Frassinetti, Bolognini, et al., 2002), visual localization (Hairston et al., 2003), auditory localization (Bolognini et al., 2007), and reduces saccadic reaction times (Arndt & Colonius, 2003; Colonius & Arndt, 2001; Corneil et al., 2002; Harrington & Peck, 1998; Hughes et al., 1998). The results found in Study #2 (that is, participants are more accurate in the pointing to bimodal targets, as assessed by a smaller pointing error, and are faster in the error correction, as assessed by the fewer trials needed in order to point correctly to the target), might reflect the effect of multisensory integration in improving the target detection.

Lastly, in Study #2, we demonstrated that participants were able to adapt to the prismatic displacement also when asked to point to an acoustic stimulus, as assessed by the presence of the AEs. However, the evolution of the adaptation did not show the same curve of the classic error reduction, as in the visual and bimodal conditions. It is worth noting that, during the acoustic PA, participants were not aware of the location of the loudspeakers. Thus, the source of pointing error in this condition might reflect a combination of three kind of errors: the visual bias induced by the prismatic displacement, producing a pointing error to the right of the target; the bias induced by the persistence of error-corrective strategies in the face of developing realignment, namely *overcompensation*, producing a pointing error to the left of the target (Redding & Wallace, 2011); the error in the localization of the sound source, which could be both to the left or to the right of the actual target.

Finally, in Study #3, we investigated the neural substrate of proprioceptive spatial realignment during PA. The brain lesion of patient MM involved the left cerebellum and the occipital cortices, bilaterally. After one session of visuomotor adaptation to rightward displacing prisms, MM did show an abnormal AEs in the proprioceptive straight-ahead task, compared to healthy controls (that is, after PA, controls showed a pointing bias toward the left, whereas MM's performance was biased toward the right of the perceived body midline). MM's altered proprioceptive AEs was reintegrated by the anodal tDCS over the spared left PPC. Rightward directionally altered proprioceptive AEs was also improved, namely reduced to zero, by the anodal stimulation over the left cerebellum.

Real-time proprioceptive control of active movement, which is involved in pointing and reaching tasks, requires predicting, monitoring, and updating representations or internal models of limb position, a function that is likely to be sustained by the cerebellum (Bhanpuri et al., 2013). Also, suggestions have been made that the cerebellum may participate in monitoring sensory information for spatial representation (Rondi-Reig, Paradis, Lefort, Babayan, & Tobin, 2014). In patient MM the unilateral cerebellar lesion may have brought about "a mismatch between the brain's modelled dynamics and the actual body dynamics, resulting in ataxia" (Bhanpuri, Okamura, & Bastian, 2014), thus interfering with the spatial realignment process during PA, and resulting in the altered proprioceptive straight-ahead AEs. The excitatory tDCS delivered over the left damaged cerebellar cortex, stimulating the spared neural cortical tissue, may have restored the cerebellar-based predictive and matching function about proprioception and limb position. In turn, this would reset the operation of the parieto-cerebellar network underlying the PA process of spatial realignment, also reducing the imbalance with the contralateral cerebellar hemisphere (Rossi & Rossini, 2004), and restoring the normal direction of the proprioceptive AEs. The PPC is a relevant target of output from the cerebellar motor (Clower, West, Lynch, & Strick, 2001), and non-motor (Bostan, Dum, & Strick, 2013) networks. In neurologically unimpaired participants, the left PPC is activated during movement updating and correction in reaching tasks executed with the right hand (Desmurget et al., 2001), and during PA achieved with that hand (Clower et al., 1996; Danckert et al., 2008). These pieces of evidence concur to suggest a role of the PPC in limb reaching tasks, and in PA, particularly of the left PPC with the right hand. In 7 right-brain-damaged patients with left neglect, after a PA treatment, fMRI showed a bilateral increase of activity in the fronto-parietal areas, including the PPC, associated with a reduction of the rightward bisection bias, and an improvement of visual search (Saj et al., 2013). In the present study excitatory tDCS over the left PPC, but not over the right PPC, brings about proprioceptive AEs more leftward than before the stimulation, a direction opposite to that of the prism-induced optical deviation. This hemispheric asymmetry of the effects of tDCS could be based on intra-hemispheric connections between the left PPC and the left damaged cerebellum, which would up-regulate the left PPC-cerebellar network. Furthermore, as noted above, the left PPC is particularly involved in reaching tasks and PA with the right hand (Clower et al., 1996; Danckert et al., 2008; Desmurget et al., 2001). Here, the restoration of AEs after PA performed using the right hand, brought about by the anodal tDCS over the left PPC, may be accounted for in terms of the more effective operation of the left hemispheric PPC-cerebellar network. Instead, the excitatory anodal tDCS over the contralateral right PPC may have proven to be not effective in this respect, compared to the left PPC tDCS, since the right-hemispheric PPC-cerebellar neural network is structurally undamaged, hence likely more functionally preserved, and therefore, less susceptible to the additional excitatory effects caused by anodal tDCS. Furthermore, the right-hemispheric PPC-cerebellar neural network, as noted above, is less involved in PA with the ipsilateral right hand.

CHAPTER 2

The space in the body:
Homeostatic regulation in humans

This Chapter investigates the relationship between bodily spatial representations and homeostatic regulation. Skin temperature has been recently considered as a physiological index of disembodiment, and it has been shown to be modulated by the manipulation of bodily representations. In three studies we examined if and how a change in bodily spatial maps affects skin temperature regulation in unimpaired participants, by means of different techniques that induce direction-specific and lateralized effects: prims adaptation, optokinetic stimulation and shift of visual attention.

2.1. Introduction: thermoregulation in human

The relationship between the sense of body ownership and the physiological regulation of bodily functions has recently drawn the attention of those researchers interested in understanding how the human brain develops, represents and maintains a bodily "self"

(Blanke, Slater, & Serino, 2015; Longo, Azañón, & Haggard, 2010; Moseley, Gallace, & Spence, 2012; Tsakiris, Hesse, Boy, Haggard, & Fink, 2007). In particular, the link between several physiological parameters (heartbeat, temperature regulation, skin conductance responses, pupil dilatation), different aspects of perception (tactile, thermal, proprioception, pain), and bodily consciousness has been investigated both in healthy participants, and in neurological patients showing autonomic dysfunctions or abnormalities in cortical representations of the body and the space around it (Barnsley et al., 2011; Blanke, 2012; Craig, 2002; Gentile, Guterstam, Brozzoli, & Ehrsson, 2013; Kammers, Rose, & Haggard, 2011; Moseley, Gallace, & Iannetti, 2012; Romano, Gandola, Bottini, & Maravita, 2014; Tsakiris, 2010).

One of the most recent approaches to study the relationship between brain mechanisms of bodily self-consciousness and the integrity of the body itself has made use of perceptual illusions in healthy participants and clinical populations. Within such paradigms, ambiguous and conflicting multisensory information about the location and the appearance of one’s own body is adopted with the purpose to alter the persons’ sense of body ownership, and the regulatory control of their physiological functions (Barnsley et al., 2011; Blanke, 2012; Lenggenhager, Tadi, Metzinger, & Blanke, 2007).

The Rubber Hand Illusion (RHI) has been used to test the hypothesis that hand skin temperature can be modulated by disrupting the sense of ownership over that limb. Specifically, when participants begin to perceive that an artificial limb is part of their own body, the temperature of their real hand (the one placed on the same side of the artificial limb) decreases (Hohwy & Paton, 2010; Moseley et al., 2008; Rohde, Wold, Karnath, & Ernst, 2013). Importantly, the temperature’s drop observed in the real ‘disowned’ hand is positively correlated with the vividness of the illusion (Moseley et al., 2008). In a complementary way, the strength of the Rubber Hand Illusion is more easily induced when a real hand is artificially cooled, while warming the hand decreases the strength of the illusion (Kammers et al., 2011). In other recent studies, the induction of a Full Body Illusion, obtained by immersing participants in a virtual reality environment, was found to be effective in modulating the exteroceptive sensitivity of the palm of the hand to thermal changes (Llobera, Sanchez-Vives, & Slater, 2013), and to cause a widespread drop of the participants’ skin temperature (Salomon, Lim, Pfeiffer, Gassert, & Blanke, 2013). Finally, a drop in temperature was found when conflicting visuo-vestibular bodily input was given to participants in a virtual reality environment (Macauda et al., 2015). Correspondingly, the sight of the reflection of the participant’s limb through a mirror, produced a limb-specific increase in skin temperature: this suggests that the vision of the body could result in an enhanced ownership over the seen limb, thus increasing temperature and homeostatic control, in a process opposite (and complementary) to that acting in the Rubber Hand Illusion (Sadibolova & Longo, 2014). Taken all together, this evidence suggest that, in healthy participants, the maintenance of the bodily self relies on the accurate integration of multisensory inputs, and that skin temperature is a plausible index of illusory body ownership. Specifically, a drop in temperature has been shown after different combinations of conflicting multisensory input about the appearance and location of one’s body, which might impact on body self-coherence: visuo-tactile (Hohwy & Paton, 2010; Moseley et al., 2008; Salomon et al., 2013), visuo-vestibular (Macauda et al., 2015), and visuo-kinesthetic (Llobera et al., 2013).

Disorders of bodily awareness and of thermal regulation have been found to be correlated in a number of different neurological and psychiatric conditions, such as schizophrenia (Bersani, Iannitelli, Pacitti, & Bersani, 2012; Boettger, Grossmann, & Bär, 2013; Chong & Castle, 2004; Thakkar, Nichols, McIntosh, & Park, 2011), autism (Kushki et al., 2013; Miyazaki et al., 2007), epilepsy (Boesebeck & Ebner, 2004; Holtkamp, Schmitt, Buchheim, & Meierkord, 2007), neuropathic pain (Moseley, 2008), anorexia nervosa, and bulimia (Papezová, Yamamotová, & Uher, 2005; Slade, 1985). The Complex Regional Pain Syndrome (CRPS) is another clinical condition, whose features include a disruption of thermoregulation (Moseley, Gallace, Di Pietro, Spence, & Iannetti, 2013; Moseley, Gallace, & Spence, 2009; Moseley, Gallace, & Iannetti, 2012), and an altered representation of the body in a number of patients (Bruehl et al., 1999; Bultitude & Rafal, 2010; Förderreuther, Sailer, & Straube, 2004; Lewis, Kersten, McCabe, McPherson, & Blake, 2007; Marinus et al., 2011; Moseley, 2005; Peltz, Seifert, Lanz, Müller, & Maihöfner, 2011; Reinersmann et al., 2010).

Interestingly, both patients affected by CRPS, and right-brain-damaged patients with left spatial neglect share a number of symptoms (Acerra, Souvlis, & Moseley, 2007; Frettlöh, Hüppe, & Maier, 2006; Galer, Butler, & Jensen, 1995; Galer & Jensen, 1999; Legrain, Bultitude, De Paepe, & Rossetti, 2012; Lewis et al., 2010, 2007; Moseley, 2004, 2005; Schwoebel, Friedman, Duda, & Coslett, 2001). In particular, CRPS patients exhibit a neglect-like, space-based tactile processing deficit (Moseley et al., 2009; for a study showing that also patients with chronic back pain may show spatial neglect-like symptoms under certain conditions of stimulus presentation, see Moseley, Gallagher, & Gallace, 2012). Specifically, in a temporal order judgment task, CRPS patients show a prioritization of vibrotactile stimuli presented on the unaffected hand, when arms are kept uncrossed, and a reversed prioritization when they are crossed over the body midline. These results suggest that the information processing deficits in CRPS patients may be related to body-centered (with reference to the patient's body midline) spatial, rather than to somatotopic (based on the somatosensory representation of the body in the primary somatosensory cortex, area SI) reference frames. CRPS patients show also a deficit in hand skin temperature regulation, with a cooling of the affected limb, related to the prioritization effect: the larger is the difference in temperature between the two hands, the earlier vibrotactile stimuli have to be delivered to the affected hand, in order to be perceived simultaneous to those delivered to the unaffected hand (Moseley et al., 2009). Interestingly, hand temperature of CRPS patients is modulated by manipulating the position of the hands in peri-personal space, namely: placing the unaffected hand in the "affected" side of space (the one where the affected hand is generally placed), in a position that crosses over the body midline, causes a decrement of hand temperature, suggesting a space-based (body-centered), rather than arm-based (somatotopic), modulation of skin temperature (Moseley, Gallace, & Iannetti, 2012). A further similarity between CRPS and neurological disorders of spatial cognition comes from a single case study. van Stralen and colleagues (van Stralen, van Zandvoort, Kappelle, & Dijkerman, 2013) induced the Rubber Hand Illusion (considered as an experimental measure of disownership of the real hand) on both hands of a right-brain-damaged patient suffering from left somatoparaphrenia, and recorded hand skin temperature before and after the induction of the illusion. A decrement in temperature after the induction of the illusion was found, but only in the left, disowned, hand. This result suggests that thermoregulatory control is related to the sense of body ownership, whose disruption may alter thermoregulation. Prism adaptation has been used to treat the symptoms of CRPS patients, achieving a substantial relief of pain, as well as the amelioration of other symptoms (Bultitude & Rafal, 2010; Sumitani et al., 2007). Moreover, prismatic lenses have been recently used in CRPS patients to test the hypothesis that its thermal manifestations depend on the perceived location of the hand relative to the body midline, rather than to its actual location. Prisms induced a deviation of the perceived position of the affected hand towards the affected (ipsilateral), or unaffected (contralateral), side of space, in the latter condition, illusorily crossing the body midline. The patients' pathological arm warmed up (with a reduction of the thermoregulatory dysfunction), when visually perceived in the unaffected, contralateral, side of space, and cooled down when perceived in the affected side, in both conditions regardless of its actual physical position (Moseley et al., 2013). Accordingly, those cortical mechanisms involved in processing the perceived position of the limbs in space, on the basis of visual and proprioceptive information, may also participate in modulating hand temperature.

As far as the neural basis of the higher-order modulations of thermoregulatory control is concerned, the temporary interference over the activity of the posterior parietal cortices (PPC) by means of rTMS, reduces hand temperature in healthy participants (Gallace, Soravia, Cattaneo, Moseley, & Vallar, 2014). The PPC, an area involved in the multisensory integration of stimuli in different sensory modalities (Caminiti, Innocenti, & Battaglia-Mayer, 2015; Sereno & Huang, 2014), the maintenance of spatial and body representations (Caminiti et al., 2015; Colby & Goldberg, 1999; Longo & Haggard, 2010), and the planning of goal-directed movements (Andersen, Andersen, Hwang, & Hauschild, 2014; Corbetta & Shulman, 2002; Vesia & Crawford, 2012), might be also part of a network that exerts a top-down modulation on physiological functions related to body ownership, such as thermoregulation. Finally, as already discussed in the first Chapter, the PPC is also involved in mediating PA processes and aftereffects (Calzolari, Bolognini, Casati, Marzoli, & Vallar, 2015; Chapman et al., 2010; Clower et al., 1996; Danckert et al., 2008; Luauté et al., 2006, 2009; Newport & Jackson, 2006; Saj et al., 2013; Sekiyama et al., 2000). Moreover, Macauda and colleagues (Macauda et al., 2015) suggested that visuo-vestibular modulation of the sense of self, possibly mediated by shared neural processes in the insula involved in vestibular and interoceptive signalling, thermoregulation and multisensory integration (Craig, 2002, 2009; Critchley, Wiens, Rotshtein, Ohman, & Dolan, 2004), might have cause the drop in hands' temperature found in their study. On the basis of these observations, we carried out three studies, in order to explore the link between bodily-spatial remapping and thermoregulatory control. In these studies, spatial bodily maps were manipulated by means of different techniques which are effective in inducing direction-specific and lateralized effects in healthy participants and in the temporary amelioration of several symptoms of right-brain-damaged patients with unilateral spatial neglect.

In particular, in Study #4, a PA procedure was used, in order to induce the typical sensorimotor remapping of bodily and spatial coordinates occurring to resolve the visual proprioceptive discrepancy induced by the prismatic displacement (cf. Chapter 1).

The technique employed in Study #5, is the optokinetic stimulation (OKS). Classically, OKS is obtained by means of a rotating striped drum, with black vertical bars superimposed to a white background. While fixating to the moving stripes, a horizontal optokinetic nystagmus is generated in response to the rotation movement, with a smooth pursuit movement in the same direction of the rotating stripes, and a quick saccade in the opposite direction (Howard, 1982). This stimulation has been efficaciously adopted in the rehabilitation of vestibular disorders (Pavlou, 2010) and of unilateral spatial neglect (Kerkhoff, Keller, Ritter, & Marquardt, 2006; Pizzamiglio et al., 2004). Studies on neglect patients demonstrated that OKS could modulate the subjective midpoint, as assessed by the displacement of line bisection in the direction of the movement during OKS (Pizzamiglio, Frasca, Guariglia, Incoccia, & Antonucci, 1990), and the position sense deficit, both vertical and horizontal (Vallar, Guariglia, Magnotti, & Pizzamiglio, 1995). Moreover, Vallar and colleagues, showed that an OKS stimulation with a leftward movement (contralateral to the side of the hemispheric lesion) improved the position sense deficit, while stimulation with a rightward (ipsilateral) movement produced a worsening of the performance level (Vallar, Antonucci, Guariglia, & Pizzamiglio, 1993).

In a study by Karnath (Karnath, 1996), the patients' horizontal displacement of the midsagittal plane (as assessed by a straight-ahead task), was reduced by OKS with a movement to the left and worsened by OKS with a movement to the right. These pieces of evidence suggest that in patients with neglect, the disorder of position sense is produced, at least in part, by an ipsilateral distortion of an egocentric coordinate system, which may be affected by direction-specific optokinetic stimuli (Vallar et al., 1995). Such direction-specific effects of OKS on spatial tasks, have been found also in healthy participants. In fact, it has been shown that haptic line bisection could be shifted in the direction of the OKS (Gallace, Auvray, & Spence, 2007). Moreover OKS could modulate postural control (Pavlou et al., 2011), and the position sense (Post & Lott, 1990; Revol et al., 2009) of healthy participants. A recent review about the vestibular and/or visual-proprioceptive stimulations that can transiently reduce left neglect signs, including left OKS, suggested the notion that the positive effects of these stimulation techniques may originate from a reorientation of attention towards the neglected side of space or from a recalibration of sensori-motor correlations, in the same fashion of PA (Chokron, Dupierrix, Tabert, & Bartolomeo, 2007). Thus, on the basis of both the results of Study #4, and the observations abovementioned about the direction-specific effects of OKS on neglect patients and healthy participants, we carried out the experiments comprised in Study #5, in order to investigate the effects of OKS on thermoregulatory control.

Lastly, on the basis of the results of both Study #4 and #5, we run two experiments, for which preliminary data are presented in Study #6, in order to assess the possible contribution of the sole visual spatial attention in temperature modulation (cf. Sadibolova & Longo, 2014). To this aim, we made use of an adapted version of the classical paradigm of visual attention orientation (Posner, 1980), in order to shift implicitly participants’ visual spatial attention toward the left (Experiment #1), and the right (Experiment #2) hemifield.

2.2. Study #4: Prism adaptation and thermoregulation

[Calzolari, E., Gallace, A., Moseley, L.G., & Vallar, G. (2016). Effect of prism adaptation on thermoregulatory control in humans. *Behavioural Brain Research*, *296*, 339-350.]

2.2.1. Aim of the study

In two experiments we test the hypothesis that the sensorimotor effects of PA, and its aftereffects on bodily spatial reference frames, can be effective in modulating thermoregulatory control in healthy participants. In particular, in Experiment #1, we tested the primary hypothesis that sensorimotor adaptation to right-displacing prisms, the ones that exert ameliorating effects on manifestations of left spatial neglect, affecting spatial representation and attention (Rossetti et al., 1998), could also affect body temperature regulation. Such a finding would suggest a relationship between spatial processing and basic physiologic parameters, such as body temperature. Specifically, we expected a different pattern of temperature change after sensorimotor adaptation to right displacing prisms with respect to the control condition (i.e., sensorimotor adaptation to neutral, not displacing lenses). In Experiment #2, we tested whether a change in body temperature is the result of an autonomic response to the visual-proprioceptive incongruence induced by the participants’ exposure to a lateral shift of the visual field, or if it reflects a more specific function sustained by cortical areas implied in spatial remapping during PA to rightward displacing prisms. Were the first hypothesis correct, we should expect a different hands’ skin temperature evolution following adaptation to left displacing prisms, compared to the control condition. Moreover, the temperature change should be in the same direction of that found using rightward displacing prism

(Experiment #1). Otherwise, no significant differences between the left displacing and the control conditions should be found.

2.2.2. Materials and methods

Participants

Forty-eight healthy right-handed (Oldfield, 1971) students, recruited in the Department of Psychology of the University of Milano-Bicocca, took part in the study (24 for each experiment; Experiment #1: 12 females, mean age: 26±3.54 years, range: 19-32; mean education: 16.54±1.67 years, range: 13-18; Experiment #2: 12 females, mean age: 25.08±3.12 years, range: 19-30; mean education: 16.21±2.17 years, range: 13-22). Participants had normal or corrected-to-normal vision, no history of diseases of the central or peripheral nervous system, epilepsy, migraine, ongoing flu, or other concurrent conditions that may alter body temperature (i.e., females were asked not to participate during the menstruation phase of their cycle).

The study was approved by the local Ethical Committee, and performed according to the ethical standards laid down in the 1991 Declaration of Helsinki. All participants gave informed consent, after a brief session that outlined the nature of the study. Students received credits for their participation.

Temperature measurement

Skin temperature was measured during the whole of the two sessions of each experiment by means of two wireless digital thermometers (Thermochron iButton® data loggers; model DS1922L, Maxim Integrated, San Jose, CA, USA) applied with two crossed strips of latex-free, hypoallergenic paper tape on the back of the participants' hands (3M™ Micropore™ Medical Tape). These thermometers are certified to measure human temperature with a resolution of 0.0625°C, from -10°C to +65°C (Smith, Crabtree, Bilzon, & Walsh, 2010; van Marken Lichtenbelt et al., 2006). The thermometers sampled at a rate of 0.2Hz (12 recordings per minute).

Prism adaptation task

In Experiment #1, in one session, participants were adapted to an 11.4° rightward visual shift induced by 20-diopter, base-left prism glasses (BLP; Optique Peter, Lyon, France). In the other session, they adapted to a normal vision condition using goggles with neutral lenses (NL; Optique Peter). In Experiment #2, in one session, participants were adapted to an 11.4° leftward visual displacement (20-diopter, base-right prism glasses, BRP; Bernell™ Deluxe Prism Training Glasses), and in the other session to the same neutral lenses used in Experiment #1. For both experiments, the order of sessions was counterbalanced between participants within the two experiments. The exposure visuo-motor adaptation task was the same used in Study #3 (cf. p. 44), with the same pseudorandom fixed order of trials presentation, maintained within the two conditions (prismatic and neutral lenses) for all participants, in both experiments. The deviation from the target of each pointing movement was measured with an accuracy of 1°, with rightward deviations from the pen being scored with positive values, leftward with negative values (see Fortis et al., 2013 for further details).

Proprioceptive straight-ahead test

The same task used in the previous studies was used (see Study #1, for further details, p. 18). Participants underwent the proprioceptive straight-ahead test before and after the adaptation session, and in the follow-up sessions of each experiment. For each of the 10 trials, the deviation of the finger position from the true body midline was measured in degrees of visual angle, with an accuracy of ±0.5°. Rightward deviations from the objective body midline were scored with positive values, leftward deviations with negative values.

Procedure

Each participant took part in two sessions, performed in two consecutive days; sessions were scheduled at the same time of the day for each participant, in order to prevent differences in body temperature due to the phase of the circadian rhythms (Aoki, Stephens, Saad, & Johnson, 2003; Hasselberg, McMahon, & Parker, 2013; Kräuchi & Wirz-Justice, 1994). During the whole session participants sat, in a comfortable position, with their arms leaning on a table, with the temperature of the room being recorded during each phase. Each block lasted about 90 minutes, and consisted of six sections: 1) thermometer stabilization and baseline, 2) pre-adaptation, 3) adaptation, 4) post-adaptation, 5) rest, and 6) follow-up (figure 16). In each of these phases, the experimenter recorded the initial and the final time of each activity, using the computer clock, which was synchronized with the thermometers.

1) *Stabilization phase*. The thermometers were activated and applied to the back of each participant's hands. Then the participant was asked to relax for a period of 20 minutes, in order for the thermometers to measure a stable baseline temperature of the hands. The mean of the samples recorded in the 5 minutes following this phase constituted the baseline temperature measure ($T_{baseline}$, see Gallace et al., 2014 for details).
2) *Pre-adaptation phase (and post-adaptation phase).* Each participant was firstly asked to perform the proprioceptive straight-ahead task, followed by 2 minutes of rest, and by 3 additional minutes of registration that constituted the pre-test measure (T_{pre}).
3) *Adaptation phase.* Each participant performed the pointing task. The order of the adaptation sessions was counterbalanced across participants: half of the participants were adapted to prism lenses in the first day and to neutral lenses in

the second day, the other half vice versa. In this phase, three temperature measures were computed, by averaging the temperature samples during the three adaptation blocks ($T_{AD1\text{-}30}$, $T_{AD31\text{-}60}$, $T_{AD61\text{-}90}$).

4) *Post-adaptation phase* (exactly the same as the pre-adaptation one). Temperature was measured for 3 minutes (T_{post}) and this was followed by the execution of the proprioceptive straight-ahead test to assess the aftereffects.
5) *Rest phase.* Each participant just sat at the table for 20 minutes, avoiding any arm movements, to prevent any direct loss of adaptation (Hatada, Miall, & Rossetti, 2006).
6) *Follow-up phase.* Participants performed the proprioceptive straight-ahead task again, to assess the possible persistence of the aftereffects, followed by other 3 minutes of temperature measurement ($T_{follow\text{-}up}$).

During the whole session the left hand was kept still, while the right hand executed the movements.

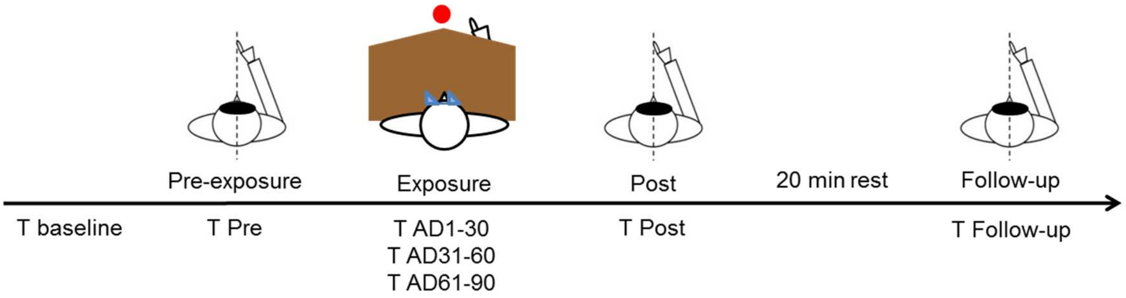

Figure 16. Schematic representation of Study #4 timeline. Hands skin temperature was recorded during the whole of the single session (12 recordings per minute).

2.2.3. Statistical analysis

Preliminary data processing

We excluded from all the analysis data from participants having > 50% of their temperature measurements (included $T_{baseline}$) more than 2SD lower than the mean of the entire group (Kammers et al., 2011).

Experiment #1

The statistical analyses were carried out with the software Statistica (StatSoft, Tulsa, OK, USA, version 6.0). The measures obtained by two participants were excluded from the analysis, according to our *a priori* policy. The analyses were thus carried on the remaining 22 participants.

Temperature

In order to assess the presence of temperature stability between the baseline and the pre adaptation phase, a repeated-measures analysis of variance (ANOVA) was performed on the average of the samplings collected during the 5-minute baseline period (mean of 60 registrations for each hand), and the pre-adaptation temperature 3-minute samplings (mean of 36 registrations for each hand). The ANOVA was performed with the within-subjects main factors of “Type of Lenses” used later during the adaptation phase (BLP/NL), and “Time” ($T_{baseline}$, T_{pre}). Afterward, in order to assess the presence of differences in hand skin temperature due to the adaptation to BLP or to NL, a repeated-measures ANOVA was performed on the six temperature samplings following the baseline: one before (T_{pre}), three during (T_{AD1-30}, $T_{AD31-60}$, $T_{AD61-90}$), and two after adaptation (T_{post}, $T_{follow-up}$). Each measure was the mean of the overall samples of that registration period. That is, each T_{pre}, T_{post}, and $T_{follow-up}$ value was the average of the 36 samplings, during the three minutes registration. Since the execution time of each of the three pointing blocks could slightly vary across participants (with a total pointing task lasting between 15 and 20 minutes, including some minutes of rest between blocks), the number of samplings of the three temperature measures during adaptation varied. The ANOVA was performed with the within-subjects factors of “Type of Lenses” used during adaptation (BLP/NL), “Hand” (left/right), and “Time” (T_{pre}, T_{AD1-30}, $T_{AD31-60}$, $T_{AD61-90}$, T_{post}, $T_{follow-up}$).

Behavioral measures: adaptation and aftereffects measures

In order to establish the occurrence of adaptation to prism exposure (in terms of reduction of the initial pointing error), a repeated-measures ANOVA was performed on the mean deviations from the position of the target (degrees of visual angle) of the first four and the last four pointing movements during the adaptation phase. In this analysis, the within-subjects factors were “Type of Lenses” (BLP/NL) and “Pointing” (first four/last four pointing trials).

In order to assess the presence and the magnitude of the aftereffects, caused by the adaptation to the lenses, on the proprioceptive straight-ahead task, a repeated-measures ANOVA, with the within-subjects factors of “Type of Lenses” (BLP/NL), and “Time” (Pre/Post/Follow-up), was performed on the pointing deviations from the true objective body midline.

In all ANOVAs, significant effects and interactions were investigated with Tukey's HSD (Honestly Significant Difference) test *post hoc* multiple comparisons. Partial eta squared (η_p^2) of significant effects were also computed, in order to determine the effect sizes (Cohen, 1988). Significance was set at $\alpha = 0.05$.

Experiment #2

The measures obtained by two participants were excluded from the analysis, according to our *a priori* policy. The analyses were thus carried on the remaining 22 participants. The same analyses adopted in Experiment #1 were performed on temperature and behavioral measures from Experiment #2; in this second experiment the two levels of the within-subjects factor of “Type of Lenses” used during adaptation were BRP and NL.

2.2.4. Results

Temperature

Experiment #1

The preliminary ANOVA assessing the temperature stability between $T_{baseline}$ and T_{pre} did not show any significant effect [Type of Lenses $F_{(1, 21)} = 0.02$, $p = 0.889$; Time $F_{(1, 21)} = 1.21$, $p = 0.284$] or interaction [Type of lenses by Time $F_{(1, 21)} = 0.03$, $p = 0.861$], thus demonstrating the stability between the baseline and the pre-adaptation temperature values.

Figure 17A (left panel) shows the hands skin temperature evolution during time, across the two sessions (values are summarized in Table 3). For NL, some increase of temperature was apparent in the final adaptation phase, while for BLP temperature decreased after adaptation. The ANOVA showed that the main effect of Time [$F_{(5, 105)} = 6.54$, $p < 0.001$, $\eta_p^2 = 0.24$] was significant, while those of Type of Lenses [$F_{(1, 21)} = 2.78$, $p = 0.11$], and Hand [$F_{(1,21)} = 2.31$, $p = 0.143$] did not attain the significance level. The Type of Lenses by Time interaction [$F_{(5,105)} = 2.34$, $p = 0.047$, $\eta_p^2 = 0.10$] was significant, while the Type of Lenses by Hand [$F_{(1, 21)} = 0.53$, $p = 0.475$], and Hand by Time [$F_{(5, 105)} = 0.42$, $p = 0.836$] interactions, as well as the Type of Lenses by Hand by Time [$F_{(5, 105)} = 0.52$, $p = 0.76$] interaction, were not significant. Multiple comparisons exploring the Type of Lenses by Time interaction showed that, when participants adapted to NL, the hand temperature in the last block of adaptation was significantly higher with respect to the pre-adaptation phase ($T_{AD61-90}$ *vs.* T_{pre} $p < 0.01$). During the follow-up (specifically after 15 minutes of rest), temperature was lower than it was during ($T_{follow-up}$ *vs.* T_{AD1-30} $p <$

0.05, *vs.* $T_{AD31\text{-}60}$ and $T_{AD61\text{-}90}$ *p-values* < 0.001) and after the adaptation phase ($T_{follow\text{-}up}$ *vs.* T_{post} $p < 0.001$), but it did not differ from the initial temperature during the pre-adaptation phase ($T_{follow\text{-}up}$ *vs.* T_{pre} $p = 0.58$). The increase in temperature found during the adaptation task, when participants wore neutral lenses, might be considered a consequence of the metabolic heat production during the prolonged motor effort, followed by a return to baseline thermal values once such motor activity ended (Bleichert, Behling, Scarperi, & Scarperi, 1973; Bonfiglioli et al., 2013; Schlader, Stannard, & Mündel, 2010). Interestingly, during the day in which participants adapted to BLP no such increase in temperature during the PA task occurred ($T_{AD1\text{-}30}$, $T_{AD31\text{-}60}$, $T_{AD61\text{-}90}$, T_{post} *vs.* T_{pre} all *p-values* > 0.993). Moreover, the hands temperature measured during the follow-up resulted to be significantly lower than the temperature measured in all the other phases of the experiment ($T_{follow\text{-}up}$ *vs.* T_{pre}, $T_{AD1\text{-}30}$, $T_{AD31\text{-}60}$, $T_{AD61\text{-}90}$, T_{post}, all *p-values* $<$ 0.001). The analysis also showed significant differences in temperature between the two types of lenses at the end of the adaptation phase ($T_{AD61\text{-}90}$ NL *vs.* $T_{AD61\text{-}90}$ BLP $p < 0.01$), after goggles removal (T_{post} NL *vs.* T_{post} BLP $p < 0.01$) and during the follow-up phase ($T_{follow\text{-}up}$ NL *vs.* $T_{follow\text{-}up}$ BLP $p < 0.01$). All of the comparisons showed a cooler temperature during and after the BLP adaptation, as compared to NL. No significant differences between right and left hand temperature were found. Notably, left hand temperature was affected as much as the right hand by the experimental manipulation even though the former remained still for the whole experimental session.

Experiment #2

The preliminary ANOVA assessing the temperature stability between $T_{baseline}$ and T_{pre} did not show any significant effect [Type of Lenses $F_{(1,\ 21)} = 0.09$, $p = 0.773$; Time $F_{(1,\ 21)} = 0.98$, $p = 0.333$] or interaction [Type of lenses by Time $F_{(1,\ 21)} = 1.37$, $p = 0.255$], thus demonstrating the stability between the baseline and the pre-adaptation temperature values.

Figure 17B (right panel) shows the hands skin temperature evolution during time, across the two sessions (values are summarized in Table 4). The main effect of Time [$F_{(5, 105)} = 5.13$, $p < 0.001$, $\eta_p^2 = 0.20$] was significant, while those of Type of Lenses [$F_{(1, 21)} = 0.02$, $p = 0.88$], and Hand [$F_{(1,21)} = 1.18$, $p = 0.29$] were not significant. The Hand by Time interaction [$F_{(5, 105)} = 3.89$, $p = 0.003$, $\eta_p^2 = 0.16$] was significant. The Type of Lenses by Hand [$F_{(1, 21)} = 0.05$, $p = 0.82$], Type of Lenses by Time [$F_{(5, 105)} = 0.45$, $p = 0.81$], and Type of Lenses by Hand by Time [$F_{(5, 105)} = 0.98$, $p = 0.43$] interactions were not significant. Multiple comparisons on the main effect of Time showed that hand temperature measured during the last block of adaptation significantly increased from that measured in the pre-adaptation phase ($T_{AD61\text{-}90}$ *vs.* T_{pre}, $p = 0.01$) and from that measured during the follow-up ($T_{AD61\text{-}90}$ *vs.*$T_{follow\text{-}up}$, $p < 0.001$). Moreover, during the follow-up, hands temperature did not differ from the initial temperature of the pre-adaptation phase ($T_{follow\text{-}up}$ *vs.* T_{pre}, $p = 0.90$). This was the same pattern of temperature changes found in Experiment #1 during adaptation to NL. Notably, in Experiment #2, no significant main effect of the factor Type of Lenses, or interactions involving it, were found, indicating that adaptation to BRP generated the same effect in hand temperature as the exposure to a non-deviating condition (i.e., adaptation to NL), as shown in figure 17B. As for the Time by Hand interaction, multiple comparisons showed a difference in temperature between hands during the adaptation task, where the right hand was cooler than the left hand, in the second and third adaptation blocks ($T_{AD31\text{-}60}$ left hand *vs.* $T_{AD31\text{-}60}$ right hand and $T_{AD61\text{-}90}$ left hand *vs.* $T_{AD61\text{-}90}$ right hand both *p-values* < 0.01).

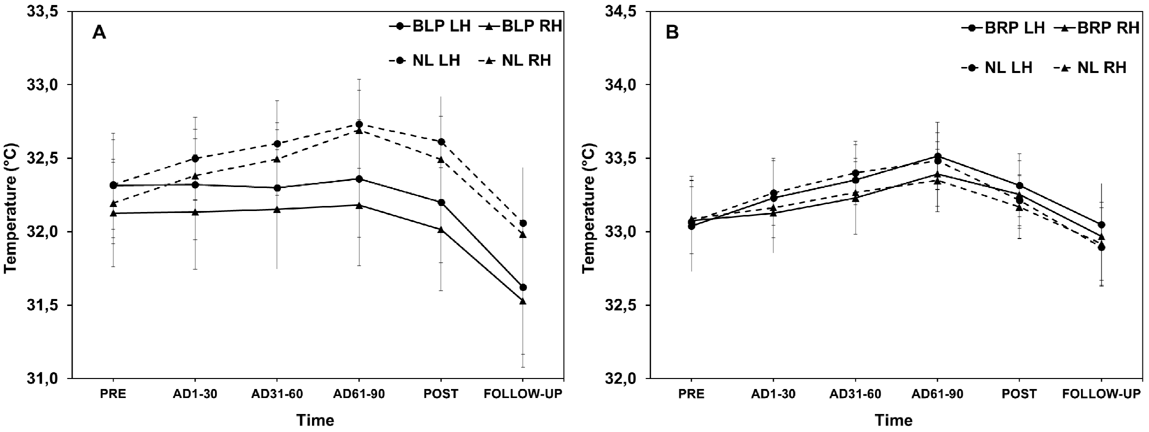

Figure 17. Mean (SE) skin temperature (°C) of the hands. Circles indicate temperature values for the left hand (LH), and triangles for the right hand (RH), before (pre), during (AD1-30, AD31-60, AD61-90), and after (post and follow-up) the pointing adaptation tasks. Experiment #1 A: adaptation to base-left prisms (BLP, solid line) and to neutral lenses (NL, dashed line). Experiment #2 B: adaptation to base-right prisms (BRP, solid line) and neutral lenses (NL, dashed line).

Table 3. Experiment #1. Mean (SE) skin temperature (°C) of the hands (average of left and right hand) before, during and after the prism adaptation tasks, by session (base-left prisms, neutral lenses).

Type of Lenses	T_{pre}	T_{AD1-30}	$T_{AD31-60}$	$T_{AD61-90}$	T_{post}	$T_{follow-up}$
BLP	32.22±0.36	32.23±0.38	32.23±0.40	32.27±0.40	32.11±0.41	31.58±0.45
NL	32.26±0.29	32.44±0.26	32.55±0.27	32.71±0.28	32.55±0.30	32.02±0.37

BLP Base Left Prisms, NL Neutral Lenses

Table 4. Experiment #2. Mean (SE) skin temperature (°C) of the hands before, during and after the pointing adaptation (average of values of the two prism adaptation sessions, base-right prisms and neutral lenses).

Hand	T_{pre}	T_{AD1-30}	$T_{AD31-60}$	$T_{AD61-90}$	T_{post}	$T_{follow-up}$
LEFT	33.05±0.25	33.25±0.23	33.38±0.21	33.50±0.19	33.26±0.18	32.97±0.25
RIGHT	33.08±0.26	33.15±0.24	33.25±0.23	33.37±0.20	33.21±0.21	32.94±0.28

Adaptation: pointing error reduction

Experiment #1

Figure 18A (left panel) shows the deviation of the first and last four pointing movements of the two adaptation phases, with the first pointing movements of adaptation to BLP being more deviated toward the right than the last pointing movements, that were more accurate; no such effects were found with NL. A repeated measures ANOVA showed that the main effects of Type of Lenses [$F_{(1, 21)} = 82.20$, $p < 0.001$, $\eta_p^2 = 0.80$], and Pointing [$F_{(1, 21)} = 85.33$, $p < 0.001$, $\eta_p^2 = 0.80$], as well as their interaction [$F_{(1, 21)} = 82$, $p < 0.001$, $\eta_p^2 = 0.80$] were significant. As shown by multiple comparisons, the first pointing movements of adaptation to BLP (6.01±2.91°) were more deviated toward the right ($p < 0.001$) than the last pointing movements, which, in turn, were more accurate (-0.28±0.59°). Adaptation to NL did not show such a significant difference ($p = 0.93$) between the first (-0.67±1.21°) and the last pointing movements (-0.36±0.43°). Moreover, the first pointing movements executed while wearing BLP were more shifted rightward than the first pointing movements while wearing NL (first pointing movements BLP 6.01±2.91° *vs.* first pointing movements NL -0.67±1.21°, $p < 0.001$). By contrast, the last pointing movements did not differ between the two conditions (last pointing movements BLP -0.28±0.59° *vs.* last NL -0.36±0.43°, $p = 0.999$). Accordingly, at the end of the pointing task, participants pointed correctly to the target, demonstrating the adaptation effect.

Experiment #2

Figure 18B (right panel) shows the deviation of the first four and the last four pointing movements of the two adaptation phases, with the first four pointing movements during the adaptation to BRP being more deviated toward the left than the last four pointing movements. The last four pointing movements were more accurate. No such effect was found with NL. A repeated measures ANOVA showed that the main effects of Type of Lenses [$F_{(1, 21)} = 103.45$, $p < 0.001$, $\eta_p^2 = 0.83$], Pointing [$F_{(1, 21)} = 54.08$, $p < 0.001$, $\eta_p^2 = 0.72$], as well as and the interaction between Type of Lenses and Pointing [$F_{(1, 21)} = 97.68$, $p < 0.001$, $\eta_p^2 = 0.82$] were significant. Multiple comparisons showed that the first four pointing movements during the adaptation to BRP (-6.34±2.59°) were significantly more deviated towards the left ($p < 0.001$), than the last four pointing movements (-0.47±0.42°). Adaptation to NL did not show such a difference ($p = 0.085$) between the first (1.20±1.87°) and the last pointing movements (0.09±0.48°). Moreover, the first pointing movements executed while wearing BRP were significantly shifted more leftward, as compared to those executed while wearing NL (BRP -6.34±2.59° *vs.* NL 1.20±1.87°, $p < 0.001$). By contrast, the last pointing movements did not differ between the two conditions (BRP -0.47±0.42° *vs.* NL -0.09±0.48°, $p = 0.88$). This finding indicates that, at the end of the pointing task, participants pointed correctly to the target, showing that the adaptation had been obtained.

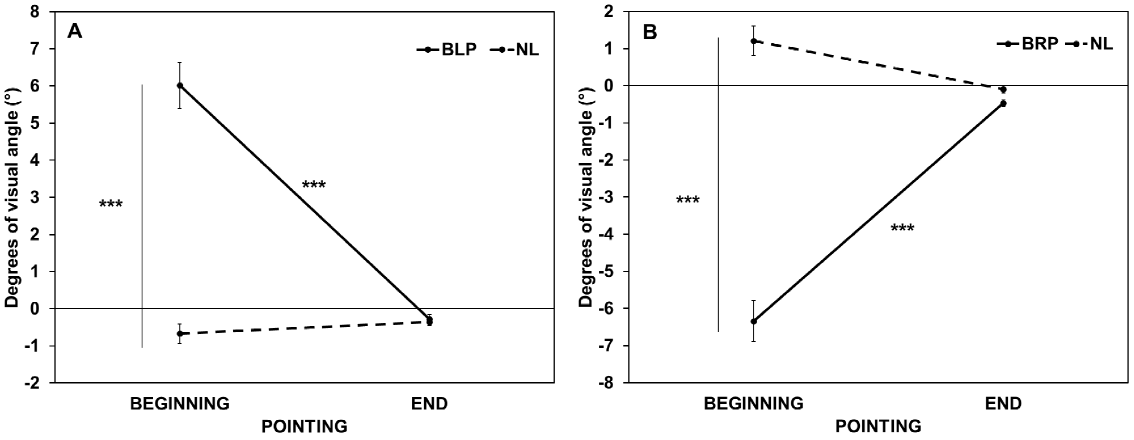

*Figure 18. Mean (SE) deviation of the first four pointing movements (beginning) and the last four pointing movements (end) of the right index finger from the visual target in the pointing adaptation task, in degrees of visual angle (◦); positive values correspond to rightward deviations from the visual target, negative values to leftward deviations. Experiment #1 A: prism adaptation to base-left prisms (BLP, solid line), and to neutral lenses (NL, dashed line); Experiment #2 B: prism adaptation to base-right prisms (BRP, solid line), and to neutral lenses (NL, dashed line). p < 0.001***, <0.01**, <0.05*.*

AEs: proprioceptive straight-ahead

Experiment #1

Figure 19A (left panel) shows the participants' performance in the proprioceptive straight-ahead task before (Pre), after (Post), and later after (Follow-up) the two adaptation sessions. Exposure to NL was ineffective, while that BLP brought about leftward aftereffects. The ANOVA showed that the main effects of Type of Lenses [$F_{(1,21)} = 1.21$, $p = 0.28$], and Time [$F_{(1,21)} = 2.26$, $p = 0.12$] were not significant. The Type of Lenses by Time interaction was significant [$F_{(2,42)} = 3.18$, $p = 0.05$, $\eta_p^2 = 0.13$]. Multiple comparisons showed that exposure to NL did not induce any shift of the subjective body midline, both immediately after exposure (M±SD° Pre -0.42±2.62° *vs.* Post -0.45±2.75°, $p = 0.999$), and in the follow-up (Pre *vs.* Follow-up -0.16±2.01°, $p = 0.991$, Post *vs.* Follow-up $p = 0.983$). Exposure to BLP induced an immediate leftward shift in the proprioceptive straight-ahead (Pre 0.01±2.16° *vs.* Post -1.57±3.12°, $p < 0.01$); during the Follow-up the shift was no longer present, and the participants' performance did not differ from the Pre and Post-adaptation phases (Pre *vs.* Follow-up -0.47±2.35°, $p = 0.873$, Post *vs.* Follow-up, $p = 0.137$).

Experiment #2

Figure 19B (right panel) shows the participants' performance in the proprioceptive straight-ahead task before (Pre), after (Post), and later after (Follow-up) the two adaptation sessions, with the first pointing movements of adaptation to BRP being more deviated toward the right than the last pointing movements, which were more accurate; no such effect was found with NL. The ANOVA showed that the main effect of Time [$F_{(2,42)} = 4.42$, $p < 0.02$, $\eta_p^2 = 0.17$] was significant, while that of Type of Lenses [$F_{(1,21)} = 3.02$, $p = 0.097$] did not attain the significance level. The Type of Lenses by Time interaction was significant [$F_{(2,42)} = 4.64$, $p = 0.015$, $\eta_p^2 = 0.18$]. Multiple comparisons showed that exposure to NL induced no shift of the subjective body midline, both immediately after exposure (M±SD° Pre -0.21±3.07° *vs.* Post 0.21±3.73°, $p = 0.92$), and in the follow-up (Pre *vs.* Follow-up 0.38±2.40°, $p = 0.73$, Post *vs.* Follow-up $p = 0.998$). Exposure to BRP induced a rightward shift in the proprioceptive straight-ahead (Pre -0.42±2.45° *vs.* Post 1.82±3.82°, $p < 0.001$; Pre *vs.* Follow-up 1.10±2.27°, $p = 0.01$). These findings are in line with previous evidence (Striemer & Danckert, 2010).

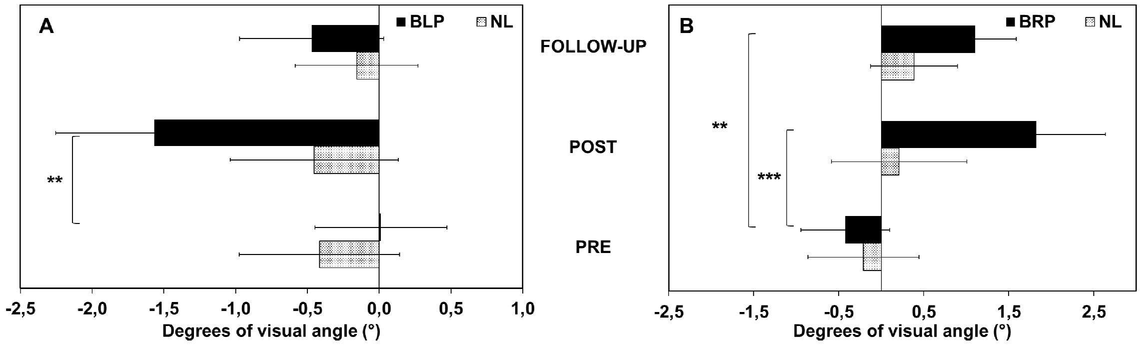

*Figure 19. Mean (SE) deviation from body midline in the proprioceptive straight-ahead pointing task before (pre), immediately after adaptation (post), and after the rest (follow- up), in degrees of visual angle (°); positive values correspond to rightward deviation from the objective body midline, negative values to leftward deviations. Experiment #1 A: prism adaptation to base-left prisms (BLP, solid black bars), and to neutral lenses (NL, dotted bars). Experiment #2 B: prism adaptation to base-right prisms (BRP, solid bars), and to neutral lenses (NL, dotted bars). p < 0.001***, <0.01**, <0.05*.*

2.2.5. Conclusion

This study assessed the hypothesis that the visuo-spatial manipulation occurring during PA, and its consequent aftereffects on body-spatial representations, can be effective in modulating thermoregulatory control in healthy participants. Hands' temperature was measured before, during, and after PA to lenses shifting the visual scene laterally (base-left prisms, shifting to the right, with leftward aftereffects; base-right prisms, shifting to the left, with rightward aftereffects), and to a control condition, where no displacement of the visual scene was induced (neutral lenses, without sensorimotor aftereffects). The two types of lenses worn by participants exert different effects on hands' temperature. Namely, adaptation to both leftward deviating prisms, and neutral glasses, result into an increase of hands' temperature, whereas adaptation to rightward deviating prisms does not. Particularly, the evolution of the hands' temperature during adaptation to neutral lenses (used as the control condition in both experiments), exhibits a gradual increase during the pointing motor task, and a subsequent coming back to baseline values 20 min after the end of it. This might reflect the natural increase in temperature caused by metabolic heat production during the prolonged motor effort done by participants (Bleichert et al., 1973; Bonfiglioli et al., 2013; Schlader et al., 2010). Notably, this evolution pattern was found in both experiments, and in different groups of participants. The main finding of this study is that the hands' temperature evolution during the adaptation to displacing prismatic lenses, as compared to that occurring during the control conditions (neutral lenses), shows a difference related to the lateral direction of the prism-induced displacement of the visual scene. When participants adapt to rightward displacing prisms (Experiment #1) no increase of temperature occurs during the adaptation motor task, at variance from the control condition. Moreover, 20 min after the end of the pointing motor task, a drop in temperature follows. By contrast, an increase in hands' temperature (just as in the control condition), and a subsequent return to baseline values, was found in the condition in which participants wore leftward displacing prisms (Experiment #2). Whereas, in spite of the different hands' temperature evolution exerted during the visuo-motor adaptation to right-displacing and left-displacing prisms, we found a similar and symmetric pattern of pointing error reduction and sensorimotor proprioceptive aftereffect. In fact, participants' pointing performance was initially biased toward the direction of the visual displacement, and gradually corrected toward the target at the end of the adaptation phase, and the proprioceptive straight-ahead aftereffect was biased in the opposite direction of the induced visual shift, namely: a leftward bias after rightward displacing prisms, and a rightward bias after leftward displacing prisms.

2.3. Study #5: Optokinetic stimulation and thermoregulation

2.3.1. Aim of the study

In two experiments we test the hypothesis that, given its directionally-specific effects on bodily spatial reference frames, both in neglect patients (Karnath, 1996; Kerkhoff et al., 2006; Pizzamiglio et al., 2004, 1990; Vallar et al., 1993, 1995) and healthy participants (Gallace et al., 2007; Pavlou et al., 2011), visuo-vestibular OKS can be effective in modulating thermoregulatory control in healthy participants. In particular, we tested the hypothesis that left, but not right OKS, could affect body temperature regulation. Specifically, with respect to the control condition, (i.e., static fixation to a non-moving background, which does not induce an optokinetic reflex), we expected a different pattern of temperature change during left OKS, but not during right OKS. Such a finding would strengthen the suggestion made in Study #4, about a relationship between bodily-spatial processes and body temperature. Moreover, OKS do not require body movements, thus we can assess the presence of an effect on temperature clear from a metabolic heat production resulting from a prolonged motor effort. Lastly, we assessed the occurrence of a bodily and spatial remapping respectively on the proprioceptive drift (performed before, and after the stimulations), and on a line bisection task (performed before, during, and after the stimulations).

2.3.2. Materials and methods

Participants

Forty-eight healthy right-handed (Oldfield, 1971) students, recruited in the Department of Psychology of the University of Milano-Bicocca, took part in the study (24 for each experiment; Experiment #1: 12 females, mean age: 26±2.40 years, range: 22-31; mean education: 16.96±1.65 years, range: 13-22; Experiment #2: 12 females, mean age: 26.67±3.12 years, range: 21-33; mean education: 17.42±1.79 years, range: 13-22). Participants had normal or corrected-to-normal vision, no history of diseases of the central or peripheral nervous system, epilepsy, migraine, ongoing flu, or other concurrent conditions that may alter body temperature (i.e., females were asked not to participate during the menstruation phase of their cycle).

The study was approved by the local Ethical Committee, and performed according to the ethical standards laid down in the 1991 Declaration of Helsinki. All participants gave informed consent, after a brief session that outlined the nature of the study. Students received credits for their participation.

Temperature measurement

Skin temperature was measured during the whole of the single session by means of two wireless digital thermometers (see Study #4 for further details). The thermometers sampled at a rate of 0.07 Hz (4 recordings per minute).

Optokinetic and neutral visual stimulations

In each experiment, two experimental conditions were presented in a counterbalanced order across participants: a visual optokinetic stimulation condition, and a no-movement control condition. Both visual stimulations were presented on a 22 in LCD screen under control of a custom Matlab (Mathworks, Natick, MA) script. Participant were aligned with the centre of the screen at a 40 cm distance. During the optokinetic stimulation, a series of black vertical bars (27 cm long and 2 mm thick) were superimposed on a white background, at a distance of 3 cm from each other, and moved at a constant speed of 10 cm s-1, toward the left in Experiment #1 (LOK) and toward the right in Experiment #2 (ROK). In the no-movement control condition a static white background was presented.

Both stimulations lasted 10 min (see Gallace, Auvray, & Spence, 2007, Experiment 2, for further details).

Line bisection task

A blue horizontal line (20 cm long, 2 mm wide) was presented aligned with the horizontal midline of the screen. A red bar (2 mm long, 1 mm wide) was superimposed on the left or on the right side of the blue line. The position of the red cursor along the blue line was controlled by pressing two keyboard buttons, one moving the cursor 1 mm toward the left and one toward the right. In each trial, participants were asked to position the cursor in the midpoint of the blue horizontal line, and then press the space bar. The distance of the cursor from the objective line midpoint was automatically registered, in mm. On each trial, the cursor could appear in a random position within the first 5 cm (on the left) or the last 5 cm (on the right) of the line, in a random order, 5 time on the left and 5 time on the right of the line, for a total of 10 trials. Participants repeated the line bisection task 5 times throughout the experiment: during the baseline, the control stimulation condition and the two post-stimulation phases, the blue line was presented over a plain white background; during the optokinetic stimulation, the bisection task was superimposed to the vertical black bars moving over the white background (Gallace et al., 2007).

Proprioceptive drift

Participant sat comfortably in front of the table, with their eyes closed. The *"target hand"* was placed palm down on a board 10 cm below the table surface, with the index finger positioned by the experimenter on a specific location mark. The "*pointing hand"* leant palm down on the table surface in a starting position, aligned with participant shoulder. On each trial, participants were asked to do a pointing movement with the index finger of the pointing hand on the table surface, in correspondence to the perceived position of the tip of the index finger of the target hand. The experimenter registered the position of the index pointing finger relative to the target index finger, and asked the participants to bring the pointing hand back at the starting position. Ten trials were executed, paced by the experimenter. On each experiment, half of the participants used their right hand as the pointing hand and the left as the target hand; the other half did the opposite. In order to calculate the deviation from the actual location of the target finger, the pointing index finger was slightly soaked with ink, and the pointing was done on a paper sheet, previously aligned with the target position. Every two pointing movements the experimenter changed the sheet. The coordinates of each pointing movement and its deviation along the X and Y axes from those of the target finger were then calculated, in cm.

Procedure

The experiments were conducted in a semi dark room. During the whole session participants sat, in a comfortable position, in front of the table, with the temperature of the room being recorded during each phase. The session lasted about 65 min and consisted of five phases: 1) thermometer stabilization and baseline, 2) stimulation 1, 3) post-stimulation 1, 4) stimulation 2, 5) post-stimulation 2. In each of these phases, the experimenter recorded the initial and the final time of each activity, using the computer clock, which was synchronized with the thermometers.

1) *Stabilization phase and baseline (15 min).* The thermometers were activated and applied to the back of each participants' hands. The proprioceptive drift and line bisection tasks were then assessed. Lastly, participants were asked to relax and keep the hands leaning on the table until the end of the 15 min period.
2) *Stimulation 1 (10 min).* According to the order of stimulation (optokinetic/neutral or neutral/optokinetic), which was balanced across participants, the first visual stimulation was delivered. After the first 5 min of

stimulation, during the ongoing stimulation, the line bisection task was presented. In this phase, two temperature measures were computed, by averaging the four temperature samplings during the first and the last minute of stimulation. At the end of the stimulation participants were instructed to close their eyes.

3) *Post-stimulation 1 (10 min).* Immediately after the stimulation, participant underwent the proprioceptive drift and then the line bisection task. Lastly, participants was asked to relax and keep the hands leaning on the table until the end of the 10 min period.
4) *Stimulation 2 (10 min).* According to the order of stimulation (optokinetic/neutral or neutral/optokinetic), which was balanced across participants, the second visual stimulation was delivered. As in the previous stimulation phase, after the first 5 min of stimulation, the line bisection task was presented and other two temperature measures were computed, by averaging the four temperature samples during the first and the last minute of stimulation. At the end of the stimulation participants were instructed to close their eyes.
5) *Post-stimulation 2 (10 min).* As in the previous post-stimulation phase, immediately after the stimulation, participant underwent the proprioceptive drift and then the line bisection task. Lastly, participants was asked to relax and keep the hands leaning on the table until the end of the 10 min period.

2.3.3. Statistical analysis

The statistical analyses were carried out with the software Statistica (StatSoft, Tulsa, OK, USA, version 6.0). In all ANOVAs, significant effects and interactions were investigated with Newman-Keuls test *post hoc* for multiple comparisons. Partial eta squared (η_p^2) of significant effects were also computed, in order to determine the effect sizes (Cohen, 1988). Significance was set at $\alpha = 0.05$.

Temperature

In order to assess the presence of differences in hand skin temperature due to the experimental visual stimulation, for each experiment, a repeated-measures ANOVA was performed on the average of the four temperature samplings in the first and the last minute of stimulation. The ANOVAs were performed with the within-subjects factors of “Stimulation” (Experiment #1: Left Optokinetic - LOK / Control stimulation - CS; Experiment #2: Right Optokinetic ROK / Control stimulation - CS), “Hand” (left/right), and “Time” (Beginning/ End).

Proprioceptive Drift

In order to establish the occurrence of a subjective perceptual deviation of the hand location, for each experiment, four repeated-measures ANOVAs were performed on the mean deviations of the pointing localization task from the actual location of the *"target hand"*, expressed as the difference between post-stimulation *minus* baseline performances, separately for the deviation on the X and the Y axes, and for the *"target hand"* left or right, with the within-subjects factor of "Condition" (Experiment #1: post-LOK / post-CS; Experiment #2: post-ROK / post-CS).

Line Bisection Task

In order to establish the occurrence of a shift in the line bisection task during and after the stimulation conditions, a repeated measure ANOVA, one for each experiment, was run on the mean deviation from the subjectively perceived midline, expressed as the difference from the baseline performance, positive values indicating a shift of the perceived midline toward the right, negative ones a leftward shift. The ANOVA was run with a within-subjects factor of "Condition" (Experiment #1: LOK / post-LOK / CS / post-CS; Experiment #2: ROK / post-ROK / CS / post-CS).

2.3.4. Results

Temperature

In Experiment #1, the repeated-measures ANOVA performed on average of the four temperature samplings in the first and the last minute of stimulations, showed a significant effect of Time [$F_{(1,23)} = 57.05$, $p < 0.001$, $\eta_p^2 = 0.71$], and of the interactions Stimulation by Time [$F_{(1,23)} = 4.42$, $p < 0.05$, $\eta_p^2 = 0.16$], and Hand by Time [$F_{(1,23)} = 7.57$, $p < 0.05$, $\eta_p^2 = 0.25$]. The main effects of Stimulation [$F_{(1,23)} = 0.12$, $p = 0.73$], and of Hand [$F_{(1,23)} = 3.65$, $p = 0.07$], and the interactions of Stimulation by Hand [$F_{(1,23)} = 0.01$, $p = 0.94$], and of Stimulation by Hand by Time [$F_{(1,23)} = 1.42$, $p = 0.25$] were not significant. The main effect of Time showed that, overall, hands temperature generally increased during both stimulation conditions (Beginning M±SD° = 32.87±1.47°, end = 33.37±1.33°). Multiple comparisons exploring the Hand by Time interaction showed that the hands temperature increased at the end of the stimulations compared to the beginning, with the left hand having overall a greater temperature compared to temperature values of the right hand (left hand beginning = 33.01±1.39°, end = 33.45±1.29°; right hand beginning = 32.72±1.59°, end = 33.29±1.44°, all *p-values* < 0.001). Multiple comparisons exploring the Stimulation by Time interaction showed that hands temperature increased after both stimulation conditions (LOK beginning = 32.82±1.53° vs. LOK end = 33.47±1.21°, $p < 0.001$; CS beginning = 32.91±1.57° vs. CS end = 33.26±1.54°, $p <$

0.01); more interestingly, when comparing the initial and the final temperature values between the two stimulation condition, multiple comparisons showed equal temperature values at the beginning of the stimulations (LOK beginning = 32.82±1.53° vs. CS beginning = 32.91±1.57°, $p = 0.38$), but different end temperature values, thus demonstrating a greater increase of hands temperature during LOK, rather than during the control stimulation (LOK end = 33.47±1.21° vs. CS end = 33.26±1.54°, $p < 0.05$), as shown in figure 20A (left panel).

In Experiment #2, the repeated-measures ANOVA performed on average of the four temperature samplings in the first and the last minute of stimulations, showed a significant effect of Time [$F_{(1,23)} = 49.13$, $p < 0.001$, $\eta_p^2 = 0.68$], and of the interaction Hand by Time [$F_{(1,23)} = 8.89$, $p < 0.01$, $\eta_p^2 = 0.28$]. The main effects of Stimulation [$F_{(1,23)} = 0.01$, $p = 0.93$], and of Hand [$F_{(1,23)} = 1.78$, $p = 0.19$], and the interactions of Stimulation by Hand [$F_{(1,23)} = 0.05$, $p = 0.82$], of Stimulation by Time [$F_{(1,23)} = 0.03$, $p = 0.87$], and of Stimulation by Hand by Time [$F_{(1,23)} = 0.63$, $p = 0.43$] were not significant. The main effect of Time showed that, overall, hands temperature generally increased during both stimulation conditions (Beginning = 33.15±1.20°, end = 33.69±1.20°). Multiple comparisons exploring the Hand by Time interaction showed that the hands temperature increased at the end of the stimulations compared to the beginning, with the left hand having overall a greater temperature compared to temperature values of the right hand (left hand beginning = 33.32±1.31°, end = 33.70±1.26°; right hand beginning = 33.07±1.24°, end = 33.68±1.17°, all *p-values* < 0.001), but at the end of the stimulation the temperature of the hands was equal (left hand end = 33.70±1.26° vs. right hand end = 33.68±1.17°, $p = 0.58$). Notably, in Experiment #2, no significant main effect of the factor Stimulation, or interactions involving it, were found, indicating that rightward optokinetic stimulation generated the same effect in hand temperature as the exposure to a neutral condition, as shown in figure 20B (right panel).

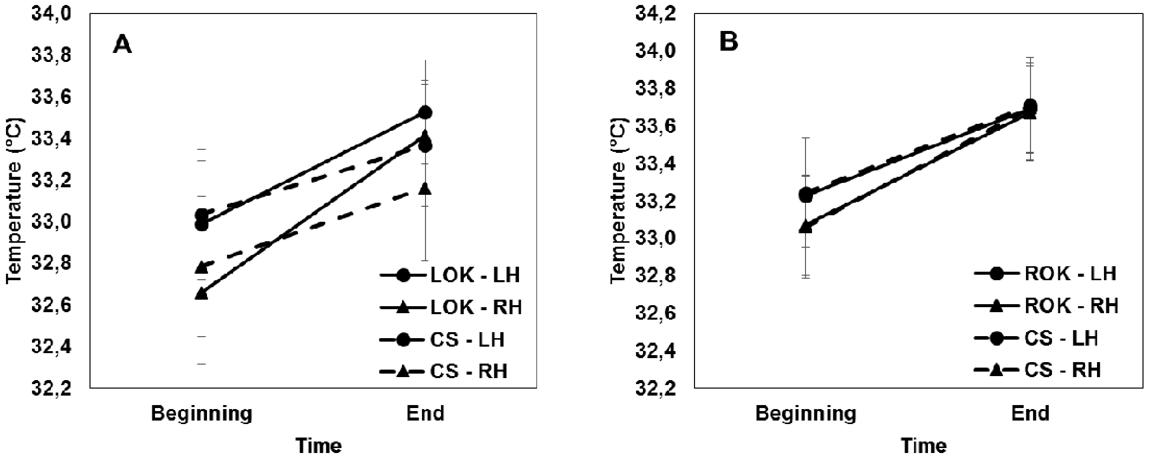

Figure 20. Mean (SE) skin temperature (°C) of the hands. Circles indicate temperature values for the left hand (LH), and triangles for the right hand (RH), at the beginning, and at the end of the visual stimulation conditions. Experiment #1 A: left optokinetic stimulation (LOK, solid line) and control stimulation (CS, dashed line). Experiment #2 B: right optokinetic stimulation (ROK, solid line) and control stimulation (CS, dashed line).

Proprioceptive Drift

The ANOVAs conducted on the mean deviations of the pointing localization task from the actual location of the *“right hand target"*, expressed as the difference between post-stimulation minus baseline performances, showed a significant effect of condition on the deviations on the X axis, just in Experiment #1, with the deviations from baseline being greater, and more shifted toward the midsagittal plane, after LOK with respect to the control stimulation [Experiment #1: drift on the X axis $F_{(1,11)} = 12.74$, $p < 0.01$, $\eta_p^2 = 0.54$, M±SDcm post-LOK = -2.25±2.36, post-CS = -1.06±1.92; Experiment #2: drift on the X axis $F_{(1,11)} = 0.01$, $p = 0.92$, post-ROK = -1.69±3.04, post-CS = -1.62±3.08]. Both ANOVAs on the deviations on the Y axes failed in showing significant effects of condition, in both experiments [Experiment #1: drift on the Y axis: $F_{(1,11)} = 0.06$, $p = 0.80$, post-LOK = -0.64±1.49, post-CS = -0.46±2.47; Experiment #2: drift on the Y axis: $F_{(1,11)}$

= 0.83, *p* = 0.38, post-ROK = -0.68±1.45, post-CS = -1.28±2.12] (figure 21, panel B for Experiment #1, and panel D for Experiment #2).

The ANOVAs conducted on the mean deviations of the pointing localization task from the actual location of the *"left hand target"*, expressed as the difference between post-stimulation minus baseline performances, failed in showing any significant effect of condition, in both experiments [Experiment #1: drift on the X axis $F_{(1,11)}$ = 0.10, *p* = 0.76, M±SDcm post-LOK = 1.36±2.53, post-CS = 1.52±2.48; drift on the Y axis: $F_{(1,11)}$ = 0.19, *p* = 0.89, post-LOK = -1.68±2.75, post-CS = -1.57±2.35; Experiment #2: drift on the X axis $F_{(1,11)}$ = 0.43, *p* = 0.52, post-ROK = 1.20±2.16, post-CS = 1.59±2.41; drift on the Y axis: $F_{(1,11)}$ = 0.94, *p* = 0.35, post-ROK = -0.76±1.49, post-CS = -1.28±2.78] (figure 21, panel A for Experiment #1, and panel C for Experiment #2).

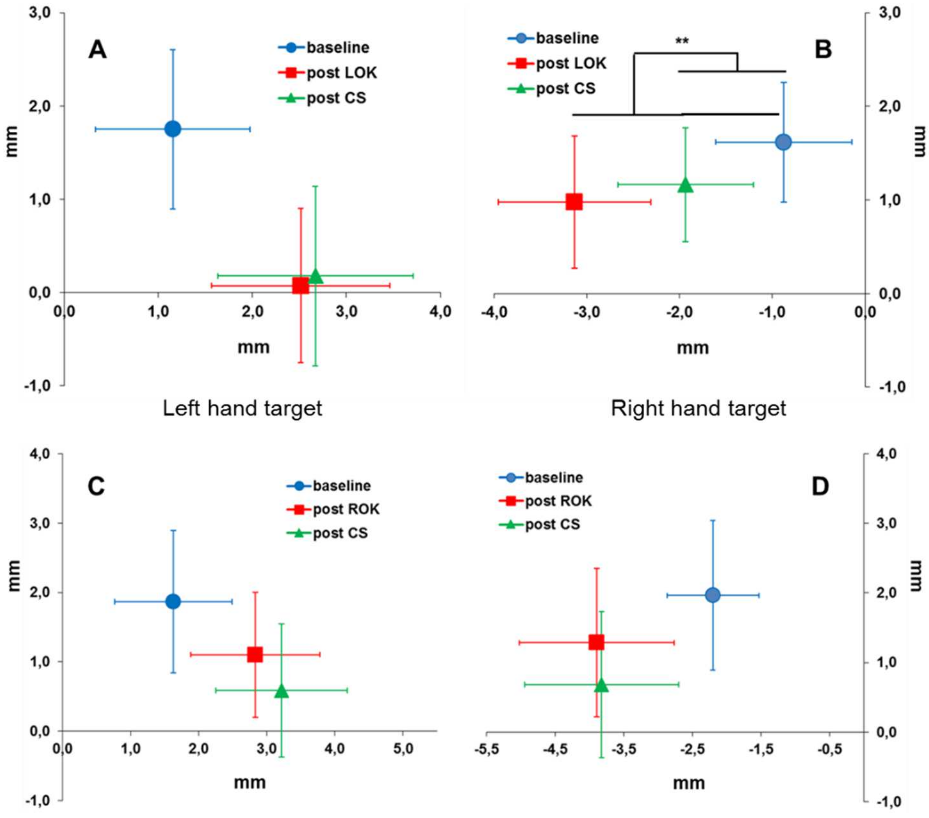

*Figure 21. Proprioceptive drift. Mean (SE, on both axes) pointing deviation (mm) from the target index finger, at the baseline (blue), post optokinetic stimulation (red), and post control stimulation (green). The origin of the axes corresponds to the actual location of the index finger. Experiment #1: A (left upper panel) left hand target; B (right upper panel) right hand target. Experiment #2: C (left lower panel) left hand target; D (right lower panel) right hand target. p < 0.001***, <0.01**, <0.05*.*

Line Bisection Task

In Experiment #1 (figure 22A), the repeated-measures ANOVA showed a significant effect of Condition [$F_{(3,69)} = 7.51$, $p < 0.001$, $\eta_p^2 = 0.25$]; multiple comparisons revealed that during LOK stimulation, participants perceived the line midline toward the left (M±SDmm = -0.81±3.94), compared to all the other conditions, in which participants bisected toward the right (vs. post-LOK = 1.76±2.51, $p < 0.001$; vs. CS = 0.40±2.38, and vs. post-CS = 0.66±2.32, both *p-values* < 0.05). Moreover, post-LOK differed from both CS and post-CS (both *p-value*s < 0.05). No difference was found between, CS and post-CS ($p = 0.63$).

In Experiment #2 (figure 22B), the repeated-measures ANOVA showed a significant effect of Condition [$F_{(3,69)} = 4.29$, $p < 0.01$, $\eta_p^2 = 0.16$]; multiple comparisons revealed that during ROK stimulation, participants perceived the line midline toward the right (M±SDmm = 0.28±2.50), compared to the post-ROK (-1.28±1.86, $p < 0.01$) and the CS (-0.80±1.57, $p < 0.05$) conditions, in which participants bisected toward the left. A trend over significance could be found also between ROK and post-CS (post-CS= -0.58±1.86, $p = 0.058$). As in Experiment #1, no difference was found between CS and post-CS ($p = 0.61$).

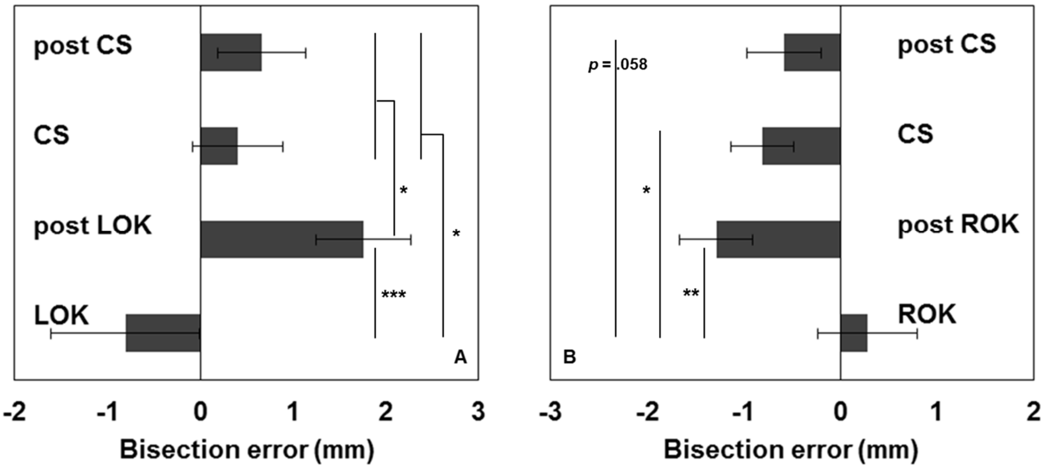

*Figure 22. Line bisection task. Mean (SE) bisection error (mm), expressed as difference from the baseline performance. Experiment #1 A: bisection error during (LOK) and after (post LOK) left optokinetic stimulation, and during (CS) and after (post CS) the control stimulation. Experiment #2 B: bisection error during (ROK) and after (post ROK) right optokinetic stimulation, and during (CS) and after (post CS) the control stimulation. p < 0.001***, <0.01**, <0.05*.*

2.3.5. Conclusion

This study assessed the hypothesis that visuo-vestibular OKS, and its directionally-specific effects on bodily spatial reference frames, can be effective in modulating thermoregulatory control in healthy participants. Hands' temperature was measured during an OKS with a movement inducing an optokinetic reflex with the slow phase toward the left (LOK, Experiment #1), and toward the right (ROK, Experiment #2), and during a control condition, where no optokinetic reflex was induced. All the conditions result into an increase of hands' temperature at the end of the stimulation. However, the hands' temperature increase during OKSs, as compared to that occurring during the control conditions, shows a difference related to the lateral direction of the OKS. Specifically, at the end of the left OKS, the temperature increase was greater compared to that occurring at the end of the control condition. By contrast, the hands' temperature increase during right OKS was just as in the control condition. Moreover, just after left OKS, but not right OKS, participants showed a drift in the localization of their right hand, in the same direction of the OKS (i.e., left) (Karnath, 1996). Whereas, in spite of both the different hands' temperature increase during left and right OKS, and the induction of a directional proprioceptive drift just after left OKS, we found a similar and symmetric pattern in the line bisection task, during and after both the left and the right OKSs. In fact, the moving background biased participants' performance toward the direction of the OKS, that is, a leftward bisection bias during left OKS, and a rightward bias during right OKS (Gallace et al., 2007; Pizzamiglio et al., 1990). Moreover, we found a novel evidence about a line bisection bias occurring after the end of the OKS, in the opposite direction of the previous OKS, in a similar fashion of negative aftereffects (Gibson, 1937). Namely: a rightward bisection bias after left OKS, and a leftward bias after right OKS.

2.4. Study #6: Visual attention orientation and thermoregulation (preliminary data)

2.4.1. Aim of the study

On the basis of the results of Study #4 and Study #5, which showed a directionally-specific effect of both visuo-motor adaptation to rightward displacing prisms and left OKS on thermoregulation, we run two experiments in order to assess the possible contribution of the sole visual spatial attention component, in temperature modulation. In particular, we tested the hypothesis that an implicit orientation of the visual attention toward the left hemispace, but not toward the right one, could affect body temperature regulation. To this aim, we made use of an adapted version of the classical paradigm of visual attention orientation (Posner, 1980), in order to orient implicitly participants' visual spatial attention toward the left (Experiment #1), and toward the right (Experiment #2) hemifield. In each experiment a control condition was included (i.e., visual attention was equally directed toward both hemifields). Specifically, with respect to the control condition, we expected a greater temperature increase during the implicit orientation of visual spatial attention toward the left, but not toward the right hemispace.

2.4.2. Materials and methods

Participants

Thirty-two healthy right-handed (Oldfield, 1971) students, recruited in the Department of Psychology of the University of Milano-Bicocca, took part in the study (16 for each experiment; Experiment #1: 8 females, mean age: 24.25±2.05 years, range: 21-29; mean education: 15.75±1.18 years, range: 13-18; Experiment #2: 8 females, mean age: 24.69±2.73 years, range: 21-31; mean education: 15.56±1.36 years, range: 13-18). Participants had normal or corrected-to-normal vision, no history of diseases of the central or peripheral nervous system, epilepsy, migraine, ongoing flu, or other concurrent conditions that may alter body temperature (i.e., females were asked not to participate during the menstruation phase of their cycle).

The study was approved by the local Ethical Committee, and performed according to the ethical standards laid down in the 1991 Declaration of Helsinki. All participants gave informed consent, after a brief session that outlined the nature of the study. Students received credits for their participation.

Temperature measurement

Skin temperature was measured during the whole of the single session by means of two wireless digital thermometers (see Studies 4 and 5 for further details). The thermometers sampled at a rate of 0.07 Hz (4 recordings per minute).

Implicit orientation of visual attention task

In each experiment, two experimental conditions were presented in a counterbalanced order across participants: a directional shift of visual attention toward an hemifield (left in Experiment #1, and right in Experiment #2), and a control condition. Both visual tasks were presented on a 22 in LCD screen by means of an ePrime software program. Participants were aligned with the centre of the screen at a 40 cm distance. On each trial, a dark grey fixation cross was presented in the centre of the white screen; after a random variable interval between 200 and 300ms, the target stimulus (a dark grey equilateral triangle, with an altitude of 1.5° of visual angle) appeared at 20° from the fixation cross, on the left or on the right, for 83ms. In half of the trials the triangle vertex opposite to the base pointed upward, in the other half downward. After the target disappearance, a visual mask was presented in the same target location for 1500ms (a 2° diameter circumference, filled with a grey scale random pattern) and participants had to give a verbal response, judging the direction of the vertex of the previous target stimulus, saying "up" or "down" in the microphone placed in front of them. Lastly, both the visual mask and the fixation cross disappeared and the blank white background remained on the screen for 400ms. In each session, 250 trials were presented. According to the experimental condition, the target stimuli could appear to the left or to the right of the fixation cross, with a specific probability of occurrence. Specifically, in the conditions of a lateral implicit shift of visual attention, the 80% of the trials appeared on one side of the screen and the remaining 20% on the other side (Experiment #1: 80% to the left, and 20% to the right of the fixation cross; Experiment #2: 20% to the left and 80% to the right of the fixation cross). In the control condition of both experiments the target appeared the 50% of the trials to the left, and the 50% to the right of the fixation cross. Within each condition, the stimuli appeared in a random order. It is worth noting that participants were asked to judge the direction of the vertex of the triangle, which pointed the 50% of the time upward and the 50% downward, in a random order. Also, participants were unaware of the manipulation of the target location. Thus the task was orthogonal to the crucial experimental manipulation, which consisted in the different proportion of the target location on the right or on the left of the screen, according to the experimental condition. For each trial, RT (time lapse between the target appearance and the verbal response) and accuracy (correct "up" or "down" response to target stimuli when the vertex pointed respectively upward or downward) were registered. In order to calculate the possible costs and benefits of the implicit shift of visual attention occurring in the lateral shift conditions compared to the control conditions, eight RTs means were calculated for each participant, in a 2x2x2 design: condition (cue vs. no-cue) x trial (valid vs. invalid) x task (up vs. down). Specifically:

- Condition (cue vs. no-cue): cue trials are all the trials of the experimental conditions where the proportion of the target spatial location has been manipulated, in order to have the 80% of the trials on one side and the remaining 20% on the other; in other words, is the condition where one side of the visual space has been implicitly "cued" by means of a greater target occurrence, compared to the other side. No-cue trials are all the trials of the control conditions, where the 50% of the trials occurred on one side and the remaining 50% on the other side, and thus, no portion of the visual space has been implicitly cued.

- Trial (valid vs. invalid): in the Attention Left (Experiment #1) and Right (Experiment #2) conditions, the valid trials correspond to those trials where the target appeared on the cued spatial location (80% of the total number of trials), and the invalid ones appeared on the not cued location (20% of the total number of trials). In the control conditions the number of valid and invalid trials is the same (50%); in the control condition of Experiment #1, valid trials are those with the target appearing on the left, and invalid on the right; in Experiment #2 the opposite.
- Task (up vs. down): the direction of the target vertex, which participants were asked to perform the judgement about.

Inaccurate trials, and those with RTs < 100ms were excluded from the calculation of the means. If an implicit shift of the visual spatial attention occurred in the cued conditions (with the proportion of 80-20 in Experiment #1, and of 20-80 in Experiment), one might expect faster RTs of valid trials, compared to RTs of invalid trials; whereas, in the no-cue conditions (with a proportion of 50-50 in both experiments), no difference between RTs of valid and invalid trials should occur. Also, no interaction with target vertex direction should be expected.

Procedure

The experiments were conducted in a semi dark room. During the whole session participants sat, in a comfortable position, in front of the table, with the temperature of the room being recorded during each phase. The session lasted about 60 min and consisted of five phases: 1) thermometer stabilization and baseline, 2) implicit orientation of visual attention task 1, 3) rest 1 4) implicit orientation of visual attention task 2, 5) rest 2. In each of these phases, the experimenter recorded the initial and the final time of each activity, using the computer clock, which was synchronized with the thermometers.

1) *Stabilization phase and baseline (13 min).* The thermometers were activated and applied to the back of each participants' hands, which were asked to relax and keep the hands leaning on the table until the end of the 13 min period.
2) *Implicit orientation of visual attention task 1 (10 min).* According to the order of the experimental condition (lateral shift of visual attention / control), which was balanced across participants, the first visual attention task was delivered. In this phase, two temperature measures were computed, by averaging the four temperature samplings registered during the first and the last minute of the attentional task.
3) *Rest 1 (10 min).* Participants was asked to relax and keep the hands leaning on the table until the end of the 10 min period.
4) *Implicit orientation of visual attention task 2 (10 min).* According to the order of the experimental condition, the second visual attention task was delivered. Two temperature measures were computed, by averaging the four temperature samples registered during the first and the last minute of the attentional task.
5) *Rest 2 (10 min).* Participants was asked to relax and keep the hands leaning on the table until the end of the 10 min period.

2.4.3. Statistical analysis

The statistical analyses were carried out with the software Statistica (StatSoft, Tulsa, OK, USA, version 6.0). In all ANOVAs, significant effects and interactions were investigated with Tukey's HSD (Honestly Significant Difference) test *post hoc* multiple comparisons. Partial eta squared (η_p^2) of significant effects were also computed, in order to determine the effect sizes (Cohen, 1988). Significance was set at $\alpha = 0.05$.

Temperature

In order to assess the presence of differences in hand skin temperature due to the experimental visual attention tasks, for each experiment, a repeated-measures ANOVA was performed on the average of the four temperature samplings in the last minute *minus* the average of the four temperature samplings during the first minute of the visual attention tasks. The ANOVAs were performed with the within-subjects factors of "Condition" (Experiment #1: Attention Left 80-20 / Control condition 50-50; Experiment #2: Attention Right 20-80 / Control condition 50-50), and of "Hand" (left / right).

Implicit orientation of visual attention task

In order to assess the presence of costs and benefits driven by the implicit direction of attention toward a hemifield, for each experiment, a repeated-measures ANOVA was performed on the mean RTs of the visual attention tasks. In Experiment #1, the ANOVA included the within-subjects factors of "Condition" (cue left 80-20 / no-cue 50-50), of "Trial" (valid / invalid), and of "Task" (up / down). In Experiment #2, the ANOVA included the within-subjects factors of "Condition" (cue right 20-80 / no-cue 50-50), of "Trial" (valid / invalid), and of "Task" (up / down).

2.4.5. Results

Temperature

In both experiments, the repeated-measures ANOVA performed on the difference between the four averaged temperature samplings in the last *minu*s the four sampling in the first minute of the attention tasks, failed in showing any significant effect or interaction [Experiment #1: Hand $F_{(1,15)} = 0.07$, $p = 0.80$, Condition $F_{(1,15)} = 1.68$, $p = 0.21$, Hand by Condition $F_{(1,15)} = 0.45$, $p = 0.51$; Experiment #2: Hand $F_{(1,15)} = 0.05$, $p = 0.82$, Condition $F_{(1,15)} = 0.07$, $p = 0.79$, Hand by Condition $F_{(1,15)} = 0.39$, $p = 0.54$], thus indicating that hand's temperature increase during the two conditions was equal, in both experiments (figure 23).

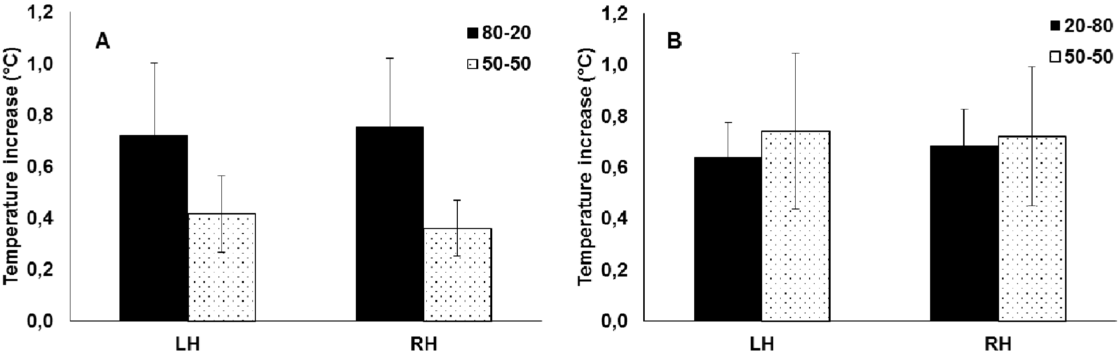

Figure 23. Mean (SE) skin temperature increase (°C) of the hands (expressed as difference from the baseline temperature). Experiment #1 A: temperature values for the left hand (LH) and the right hand (RH), during the visual task with attention shifted toward the left (80-20), and in the control condition (50-50). Experiment #2 B: temperature values for the left hand (LH) and the right hand (RH), during the visual task with attention shifted toward the right (20-80), and in the control condition (50-50).

Implicit orientation of visual attention task

In Experiment #1, the repeated-measures ANOVA showed a significant effect of Task [$F_{(1,15)} = 38.35$, $p < 0.001$, $\eta_p^2 = 0.72$], with RTs for stimuli pointing up been faster than those of the down targets (M±SDms up = 451.96±73.13, down = 487.42±73.15), and a significant Condition by Trial interaction [$F_{(1,15)} = 16.43$, $p = 0.001$, $\eta_p^2 = 0.52$]. Post hoc comparisons showed an advantage of 12.98ms for valid stimuli (i.e., left stimuli) compared to invalid ones (i.e., right stimuli) in the cue condition (i.e., 80% stimuli on the left and 20% on the right), but not in the no-cue condition (cue valid = 463.92±64.10 vs. cue invalid = 476.90±67.77, $p < 0.01$; no-cue valid = 472.28±84.16 vs. no-cue invalid = 465.67±86.78, $p = 0.26$; figure 24A). Moreover, RTs of the cue invalid trials were slower than the RTs of no-cue invalid trials ($p < 0.05$). The other main effects and interactions were not significant [Condition $F_{(1,15)} = 0.02$, $p = 0.90$; Trial $F_{(1,15)} = 0.83$, $p = 0.38$; Condition by Task $F_{(1,15)} = 1.48$, $p = 0.24$; Trial by Task $F_{(1,15)} = 0.00$, $p = 0.97$; Condition by Trial by Task $F_{(1,15)} = 1.78$, $p = 0.20$].

In Experiment #2, the repeated-measures ANOVA showed a significant effect of Task [$F_{(1,15)} = 5.42$, $p < 0.05$, $\eta_p^2 = 0.27$], with RTs for stimuli pointing up been faster than those of the down targets (M±SDms up = 488.60±66.03, down = 508.38±68.89), a significant effect of Trial [$F_{(1,15)} = 34.46$, $p < 0.001$, $\eta_p^2 = 0.70$], showing faster RTs of valid stimuli (i.e., on the right) compared to RTs of invalid stimuli (valid = 486.74±65.76, invalid = 510.24±65.82), and a significant Condition by Trial interaction [$F_{(1,15)} = 7.17$, $p < 0.05$, $\eta_p^2 = 0.32$]. Post hoc comparisons showed an advantage of 33.93ms for valid stimuli (i.e., right stimuli) compared to invalid ones (i.e., left stimuli) in the cue condition (i.e., 80% stimuli on the right and 20% on the left), but not in the no-cue condition (cue valid = 476.86±64.95 vs. cue invalid = 510.79±76.30, $p < 0.001$; no-cue valid = 496.63±77.95 vs. no-cue invalid = 509.68±68.83, $p = 0.13$; figure 24B). Moreover, RTs of the cue valid trials were faster than the RTs of both no-cue valid ($p < 0.05$) and no-cue invalid trials ($p < 0.001$). The other main effect and interactions were not significant [Condition $F_{(1,15)} = 0.42$, $p = 0.53$; Condition by Task $F_{(1,15)} = 0.97$, $p = 0.34$; Trial by Task $F_{(1,15)} = 0.88$, $p = 0.36$; Condition by Trial by Task $F_{(1,15)} = 0.36$, $p = 0.56$].

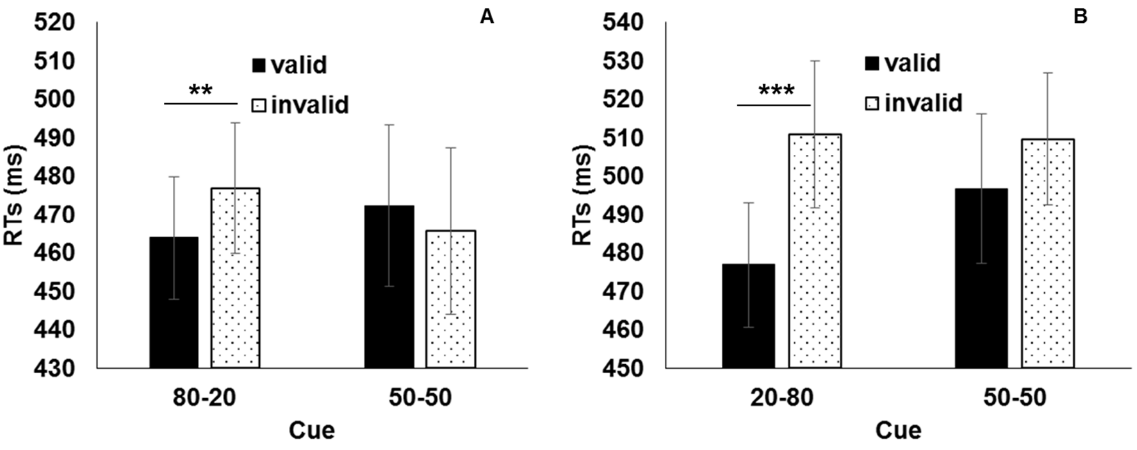

*Figure 24. Mean (SE) reaction time responses (ms). Experiment #1 A: RTs for valid (black bars) and invalid (dotted bars) trials, in the left spatial cue condition (80-20), and in the control condition (50-50). Experiment #2 B: RTs for valid (black bars) and invalid (dotted bars) trials, in the right spatial cue condition (20-80), and in the control condition (50-50). p < 0.001***, <0.01**, <0.05*.*

2.4.6. Conclusion

This study assessed the possible contribution of the implicit orientation of visual spatial attention component, in temperature modulation. Hands' temperature was measured during a visual task shifting implicitly participants' attention toward the left (Experiment #1), and toward the right (Experiment #2) hemispace, and during a control condition, where no spatial shift was induced. In each experiment, all the conditions result into an increase of hands' temperature at the end of the visual task, with no directionally-specific modulation occurring by means of the lateral shift of the attention. By contrast, participants showed an implicit shift of the attention toward the cued hemispace, in each experiment, as assessed by showing the classical advantage (i.e., faster RTs) in judging targets presented in the cued hemifield, in contrast to slower RTs for target presented in the not-cued hemispace.

In spite of the small sample size of these preliminary data, nonetheless results seem to suggest that the sole lateral shift of visual attention is not sufficient to induce a specific skin temperature modulation.

2.5. Discussion

In this chapter, I tried to investigate the processes underlying the relationship between representations of the body and the space around it, and homeostatic regulation, in healthy participants.

Study #4 demonstrated that hands' skin temperature can be altered, namely decreased, by means of visuo-motor adaptation to right shifting, but not left shifting, optical prisms, as compared to visuo-motor adaptation to a condition where no visual displacement occurred. Conversely, both the reduction of the pointing error and the sensorimotor AEs occurred with adaptation to both optical prisms.

Study #5 demonstrated a similar directional effect on skin temperature. That is: as compared to the temperature increase found during the fixation of a non-moving background, a greater temperature increase occurred during the fixation of a moving background inducing an optokinetic reflex with the smooth pursuit movement toward the left (left OKS), but not toward the right (right OKS). Moreover, whereas the expected bias in the line bisection task was evident during and after both OKSs, a mislocalization of the hand, as assessed by the proprioceptive drift task, was found only after left OKS.

Study #6 showed that the implicit lateral orientation of spatial attention toward one side of the space does not modulate temperature regulation, as compared to a condition where the attention was not directed toward a specific hemispace.

To date, the modulation of skin temperature in healthy participants has been investigated by means of perceptual illusions such as the Rubber Hand Illusion (Hohwy & Paton, 2010; Moseley et al., 2008), and different variations of the Full Body Illusion (Llobera et al., 2013; Macauda et al., 2015; Salomon et al., 2013). The drops in skin temperature reported in these studies were obtained applying conflicting multisensory inputs, such as visuo-tactile (Hohwy & Paton, 2010; Moseley et al., 2008; Salomon et al., 2013), visuo-vestibular (Macauda et al., 2015), and visuo-kinesthetic (Llobera et al., 2013) discordant information about the appearance and location of one's body. The processes enable to solve these multisensory conflicts are related to the phenomenon of embodiment (Longo, Schüür, Kammers, Tsakiris, & Haggard, 2008), which reflects the sense of bodily self-consciousness (Blanke et al., 2015) and is proposed to cause the drops in skin temperature reported in these studies. For instance, in order to explain the cooling of the participant's arm after the induction of the Rubber Hand Illusion, Moseley and colleagues (Moseley et al., 2008) suggest that such effect is likely to be caused by an autonomic thermoregulatory response to hand disembodiment. Somehow similarly, the drop of temperature observed after both a visuo-tactile (Salomon et al., 2013) and a visuo-vestibular (Macauda et al., 2015) Full Body Illusion has been related to an alteration of bodily self-consciousness, consequent to the induced self-identification and self-localization within, respectively, a virtual body and a mannequin.

In Studies #4 and #5, we demonstrate that temperature regulation can be modulated by means of two techniques, PA to rightward displacing prisms and left OKS, which affect bodily spatial representations of healthy participants, and are effective in the rehabilitation of right-brain-damaged patients. However, the pattern of results of our studies suggest that the action of these stimulations on thermoregulation is likely to be based on different neurocognitive mechanisms, as compared to those of the perceptual illusion previously described.

Prismatic lenses have been successfully used to reduce thermal manifestation of CRPS patients, by changing the perceived location of the hand relative to the body midline (Moseley et al., 2013). This evidence suggest that those cortical mechanisms implied in the processing of the perceived limb position in space, on the basis of visual and proprioceptive information, may also be involved in modulating temperature regulation.

The results of Study #4 corroborate Moseley et al. assumption, showing that the induction and the subsequent resolution of the sensorimotor discordance between visual and proprioceptive information induced by optical prisms displacing the visual scene to the right, causes a decrease of hands' temperature in healthy participants. Moreover, Study #5 indicates that those cortical mechanisms implied in the processing of the perceived limb position in space, on the basis of visuo-vestibular/optokinetic information, exert a modulation of temperature regulation (cf. Macauda et al., 2015 for thermoregulatory effects exerted by means of a visuo-vestibular conflict). In fact, left OKS brought about a greater hands' temperature increase during the stimulation, and a shift of the perceived location of the right hand toward the left, after the stimulation. It is worth noting that the proprioceptive drift was in the same direction of the previous left OKS, and this is in line with previous findings on neglect patients showing that the patients' horizontal rightward displacement of the midsagittal plane, as assessed by a straight-ahead task, was reduced by left OKS (shifted toward the left) and worsened by right OKS (shifted even more rightward) (Karnath, 1996).

Thus, from these observations, one might suggest that the effects found on temperature regulation after right PA and during left OKS may reflect a change in the sense of bodily self-consciousness (Blanke & Metzinger, 2009; Blanke et al., 2015; Blanke, 2012); specifically, the manipulation occurring during OKS might have affected the sense of self-location (Macauda et al., 2015), and PA might have affected both the senses of self-location and of agency. I refer you to our published paper for a more detailed discussion about the possible effect of PA on the sense of agency and about the possible factors underlying the asymmetrical effect on hands' temperature exerted by left- and right-displacing prisms (Calzolari, Gallace, Moseley, & Vallar, 2016).

Another relevant finding of our results concerns the asymmetrical effects on temperature. Critically, despite of the similarity and symmetry of the direct effects of sensorimotor adaptation and the aftereffects in the proprioceptive straight-ahead task with right-displacing and left-displacing prisms in Study #4, and of the effects in line bisection task during and after both left and right OKS in Study #5, the skin temperature changes found in the studies is asymmetrical and directional. In fact, in Study #4, temperature decreased only after adaptation to right displacing prisms, whereas no differences between the neutral condition and left displacing prisms were found. Similarly, In Study #5, temperature increased the most only after left OKS, whereas no difference between the neutral condition and right OKS was found. As far as the asymmetry of the effects found is concerned, evidence from brain-damaged patients regarding both sensorimotor adaptation to right-displacing and left-displacing prisms, and effects of left and right OKS, should be considered. Although there is no complete agreement upon hemispheric asymmetries in somatosensory processes (Dijkerman & de Haan, 2007), there is evidence from clinical populations that somatosensory and spatial processing deficits are more frequent after right brain damage (Bisiach & Vallar, 2000; Smania & Aglioti, 1995; Sterzi et al., 1993; Vallar, 1997). Moreover, disturbances in body representation and body ownership are more frequent after right brain damage (Gallace & Spence, 2014; Romano et al., 2014; Vallar & Ronchi, 2009). Studies in right brain-damaged patients affected by left spatial neglect show that adaptation to the rightward prismatic displacement of the visual scene, positively modulates higher-level spatial processing, ameliorating the main manifestations of this disorder (defective exploration of the left side of peri-personal space, as assessed by target cancellation and copy drawing tasks; rightward bias in line bisection), and results in a reduction of sensorimotor postural disturbances, deficits of tactile perception, and visual extinction to double simultaneous stimulation (Maravita et al., 2003; Nijboer, Olthoff, Van der Stigchel, & Visser-Meily, 2014; Rossetti et al., 1998; Tilikete et al., 2001). Conversely, adaptation to leftward prismatic deviation (Luauté et al., 2012) is ineffective in reducing the disproportionate rightward bias of right-brain-damaged patients with left neglect, and the other abovementioned manifestations of the syndrome, ameliorated by adaptation to rightward prismatic deviation (Rossetti et al., 1998).

Analogously, studies in left spatial neglect patients show that OKS modulates the subjective midpoint, as assessed by the displacement of line bisection in the direction of the movement during OKS (Pizzamiglio et al., 1990), and the position sense deficit, both vertical and horizontal (Vallar et al., 1995). Moreover, OKS stimulation with a leftward movement (contralateral to the side of the hemispheric lesion) improves both the position sense deficit (Vallar et al., 1993) and the patients' horizontal displacement of the midsagittal plane, as assessed by a straight-ahead task (Karnath, 1996), while stimulation with a rightward (ipsilateral) movement produces a worsening of the performance level of both the position sense deficit, and the straight ahead-task. Moreover, left OKS, as well as right PA, has been successfully used in the rehabilitation of neglect patients (Kerkhoff et al., 2006; Pizzamiglio et al., 2004). Such direction-specific effects of OKS on spatial tasks have been found also in healthy participants. In fact, the performance in haptic line bisection can be modulated in the direction of the OKS motion (Gallace et al., 2007), as well as occurs in postural control (Pavlou et al., 2011), and in the position sense (Post & Lott, 1990; Revol et al., 2009). Among other sensory stimulation (Chokron et al., 2007), left PA and right OKS are considered direction-specific stimulations capable to displace high-order, spatial (non-somatotopic) frames of reference in right brain-damaged patients with left hemineglect, reducing or increasing the extent of the patients' ipsilesional rightward directional error, and bringing about similar directional effects in healthy participants (Vallar, 1997). The computation of spatial frames of reference involves the continuous integration of signals from different sensory modalities (visual, vestibular, proprioceptive, tactile, and somatosensory) from the body and the space around it. The neural basis of these spatial frames includes the posterior parietal and the premotor frontal regions (Blanke et al., 2015; Sereno & Huang, 2014). Thus, we suggest that the directionally-specific effects found on hands' temperature (that is, temperature is modulated by right PA and left OKS only), may reflect a change in high-order, multisensory, spatial maps; moreover, cortical mechanisms implied in spatial processing, through the integration of visual, proprioceptive, tactile, and vestibular information, may also be involved in modulating temperature regulation.

As far as the results of Study #6 are concerned, an additional important consideration can be made. The study showed that orientating visual spatial attention toward one side of the space does not bring about a modulation of hands' skin temperature. One possible explanation may concern the nature of the task used (a typical unisensory visual attention task), as compared to other manipulations that bring about effects on temperature modulation. Even though the attention was directed toward one or the other side of the space, with respect of participants' body midline, there was a lack of incongruent and conflicting information about the location of the body, and no input was signalling a discordant location of the body (or of parts of it) in the space.

Moreover, the task did not require any reaching movement or interaction with the target, but only a verbal response. Thus, visual attention was confined and oriented toward an external object, located in extrapersonal space (even though within the reaching distance), rather than toward objects located in peri- and personal space, or even toward the body itself. It has been shown that the vision of the body, even when non-informative about stimulation, produces limb-specific modulation of thermal regulation (Sadibolova &

Longo, 2014). In particular, skin temperature of the left hand increased when participants had the illusion of directly seeing their hand through a mirror, but not during the illusion of seeing an object at the same location, or looking directly at their contralateral right hand. Moreover, temperature increased in the viewed hand but not the contralateral hand. The authors of the study suggested that during the vision of the body, an opposite (and complementary) process to that acting during the Rubber Hand and the Full Body Illusions, could result in an enhanced ownership over the seen limb, thus increasing temperature and homeostatic control (Sadibolova & Longo, 2014).

So far, the experimental manipulations that, have been shown to exert a high-order modulatory effect on thermoregulation comprise, to some extent, a "bodily component". Indeed, they usually encompass a combination of discordant inputs about location or appearance of the body, bringing about information about changes occurring in the personal and/or peri-personal space, such as visuo-tactile in the Rubber Hand Illusion and the Full Body Illusion (Hohwy & Paton, 2010; Moseley et al., 2008; Salomon et al., 2013), visuo-vestibular (Macauda et al., 2015), visuo-kinesthetic (Llobera et al., 2013). This kind of bodily information was present also in Study #4, (visuo-proprioceptive conflict) and Study #5 (visuo-optokinetic).

Moreover, these multisensory manipulation exerting a modulation of body temperature, such as the Rubber Hand Illusion and the Full Body Illusion, are typically associated with changes in the perception of the appearance and the location of the body, or body part, as assessed by both subjective (i.e., questionnaires used to investigate ownership, location and agency, as main subcomponents of embodiment) and objective measures of mislocalization of body parts (i.e., proprioceptive drift). In fact, both measures are necessary in order to assess the presence of embodiment over the fake hand, and disownership over the real one (Longo et al., 2008). Indeed, it has been shown that the temperature’s drop observed in the real ‘disowned’ hand during the induction of the Rubber Hand Illusion is positively correlated with the vividness of the illusion (Moseley et al., 2008). In line with this evidence, it is worth noting that in Study #5, only left OKS brought about a shift in the proprioceptive drift, whereas right OKS did not. Instead, both OKSs induced a symmetric and directional bias in the line bisection task, which involve a greater extrapersonal spatial component (Gamberini, Seraglia, & Priftis, 2008; Vallar et al., 1993), as compared to the proprioceptive drift.

On the basis of these observations, one might expect that by orienting the attention in other sensory modalities more linked to the body, such as, for instance, tactile attention, may to exert a modulation of temperature regulation, with a directional effect, such as those found in our study.

Finally, our results do not provide evidence of a hand-to-hand difference in the effect on temperature regulation. That is, in Study #4, adaptation to a rightward deviation of the visual field results in skin temperature reduction for both hands, and adaptation to a leftward deviation in skin temperature increase for both hands (cf. Gallace et al., 2014, where a temperature drop in both hands followed rTMS interference over the activity of the PPCs). Prism exposure brings about a uniform shift of the visual field, manipulating the body-space interface in egocentric coordinates (Girardi, McIntosh, Michel, Vallar, & Rossetti, 2004); thus, sensorimotor AEs reflect changes in the whole of the egocentric space, as indexed by the proprioceptive straight-ahead shift. Also in line with this view, after a PA session, the proprioceptive drift centered on the hand is in the same direction for both hands (Scarpina, Van der Stigchel, Nijboer, & Dijkerman, 2013), namely: after PA with the left hand to left deviating prisms, the felt position of both hands is shifted leftward. Thus, the process of spatial realignment within egocentric space, which occurs during sensorimotor adaptation to both rightward and leftward prism-induced displacement of the visual scene, may bring about a body-space remapping centered on the body midline. Accordingly, bodily space, including hands' position, is shifted coherently with the prism-induced displacement of the visual scene, but the relative position of the hands remains the same, with resulting bilateral symmetric effects, as far as the two hands are concerned. In this study, the lack of hands' specific effects indicates that the mechanisms involved in the prism-induced modulation of thermoregulation are likely to be related to the activity of higher-order, rather than more sensory-specific, brain networks. Similarly, the modulatory effects of direction-specific sensory stimulations, such as OKS, occur at the level of a spatial, non-somatotopic, egocentric representation of the body (Vallar et al., 1993; Vallar, 1997), as indexed by the bias in the line bisection task and the proprioceptive straight-ahead shift. This may explain the same lack of hand-to-hand difference in the effect on temperature regulation exerted by both left and right OKS in our study.

Thus, in the light of these observations, and on the basis of the novel findings presented in this Chapter, we may suggest that the directionally-specific effects that we found on hands' temperature, may reflect a change in high-order, multisensory maps, encoding and integrating information from different sensory modalities within personal and peri-personal space, in an egocentric reference frame (Blanke et al., 2015).

This proposal is line with the concept of a cortical 'body matrix' (Moseley, Gallace, & Spence, 2012), which will be outlined in the general discussion of this Thesis.

CHAPTER 3

The space on the body:
Tactile distance perception

In this Chapter we address the issue about how spatial relationship between objects that come in contact with the body are processed. In particular, we tried to answer the question: at which level of the somatosensory processing is the spatial distance between two simultaneous tactile events that passively occur on the skin elaborated? In other words, is tactile distance a basic attribute of touch perception?

3.1. Introduction

In order to estimate the metric properties of an object, like its shape and size, that passively touches the skin, we need to refer to the metric properties of the body part being touched, and thus to a representation of the bodily size (Longo et al., 2010). There are two intrinsic problems in using our body as a ruler for an object size estimation task. The first relates to the highly distorted topographic organization of somatosensory neurons in the brain, that provides a map of skin receptors density (Penfield & Boldrey, 1937). For instance, in the classic Weber's illusion, the perceived distance between two points touching the skin decrease as the tactile points are moved from a high receptor density skin region, such as the hand, to a low-density region, such as the forearm (Weber, 1996). Another example of the mental body representation distortions is the anisotropy of tactile distance perception on the hand: a tactile distance delivered along the width of the hand dorsum is systematically perceived bigger than the same distance delivered along the dorsum length (Longo & Haggard, 2011).

Secondly, in tactile processing, there is no evidence of direct afferent information that specify the actual size and shape of our body. Thus, in order to compute a tactile size estimation task, the tactile inputs must be rescaled into a pre-existent body representation. Some properties of touch can be evoked by stimulus parameters that activate selectively a particular set or sets of primary afferent fibers and are specified by a single firing of population of modality specific neurons (Doetsch, 2000). This is the case of those basic properties of touch, such as pressure, frequency, location and orientation (Bensmaia, Denchev, Dammann, Craig, & Hsiao, 2008; Chiu, Tommerdahl, Whitsel, & Favorov, 2005; Fitzgerald, Lane, Thakur, & Hsiao, 2004, 2006a, 2006b; Pruszynski & Johansson, 2014), which are coded at early stages of the somatosensory system. Some of these properties have been shown to be processed even at a subcortical level (Jörntell et al., 2014). Importantly, these basic tactile attributes are susceptible to sensory adaptation, i.e. the change of neural activity during sustained stimulation, which produces a change in the perception of a subsequent stimulus (Gescheider, Frisina, & Verrillo, 1979; Solomon & Kohn, 2014; Verrillo, 1985; Yang & O'Connor, 2014). Conversely, secondary tactile properties cannot be immediately encoded at this first level of somatosensory processing, and require an additional processing (Spitoni, Galati, Antonucci, Haggard, & Pizzamiglio, 2010). This is the case of the estimation of the spatial distance between two touches on the skin, which may require an additional computation, as individual sensory events must be integrated and referred to high-order mental body representations comprising the metric properties of the body part being touched (Mancini, Steinitz, Steckelmacher, Iannetti, & Haggard, 2015; Spitoni et al., 2010). Evidence in support of this view comes from studies showing that tactile distance perception is affected by higher-level alterations of the metric properties of the body. For instance, Taylor-Clarke and colleagues (Taylor-Clarke, Jacobsen, & Haggard, 2004) showed that modifying the visual experience of the body through visual magnification of the limb, alters the perception of tactile distances delivered on it. A study by de Vignemont and colleagues, showed a modulation of tactile distance perception on the finger during a proprioceptive illusion of elongation or shrinking of it (de Vignemont, Ehrsson, & Haggard, 2005). Specifically, tactile distances were perceived bigger when the touched body part felt elongated. Similarly, it has been shown that tactile distances were perceived bigger when the arm was illusorily felt elongated, by means of the manipulation of auditory feedback during an action with the limb (Tajadura-Jiménez et al., 2012). A distortion of tactile size perception occurs also during the vision of the body, even when non-informative about the stimulation (Longo & Sadibolova, 2013). Taken together, this evidence suggests that the brain attempts to preserve tactile size constancy by rescaling the primary, distorted somatosensory representation into a secondary, object-centered representation, which contains information on the perceived size and shape of body parts, according to the experience of the body. This entails that tactile perception of distance occurs at later stage of tactile processing, and that is mediated by secondary rather than primary somatosensory areas (de Vignemont, Ehrsson, et al., 2005; Medina & Coslett, 2010; Spitoni et al., 2010; Taylor-Clarke et al., 2004).

Size perception has been widely studied in other sensory modalities with adaptation paradigms. For instance, in vision it has been shown that after prolonged observation of a stripped pattern, when looking at a grid of the same orientation with narrower bars, these are perceived thinner than they are physically, and bars in a grid with broader bars, are perceived broader than they actually are (Blakemore & Sutton, 1969). These findings argue for the presence of neurons selectively sensitive to a circumscribed range of spatial frequencies, thus suggesting that spatial frequency is a basic attribute, coded centrally, at a low level of the visual system. Analogously, in a well-known haptic size-contrast illusion, participants are asked to simultaneously and repeatedly grasp two spheres of different size. After adaptation, a large perceptual aftereffect is experienced when the two spheres are replaced by spheres of identical size: the sphere placed in the hand previously adapted to the smallest one, is perceived as bigger relative to the other (Uznadze, 1966). Such adaptation-aftereffects paradigms have been extensively used, especially in the visual domain, because they can provide an opportunity in order to comprehend how information about different dimensions (such as movement, orientation, and size) is processed by specific neuronal population. Understanding how the brain adapts may provide insight into its computational goals, and the constraints on its functional organization. Adaptation is also of interest because it is widely used in human functional imaging and perceptual studies to infer the selectivity of neurons and brain areas, and to deduce the computations involved in sensory processing (Solomon & Kohn, 2014).

For instance, adaptation studies in the visual domain, showed that in the human visual system there are neuron selectively sensitive to the orientation (as well as the size) of the retinal image (Blakemore & Campbell, 1969; Maffei, Fiorentini, & Bisti, 1973). Moreover, adaptation to a specific size shows interocular transfer. That is, adaptation is effective in elicit an aftereffect, although weakened, when the adapter and test stimulus are presented to different eyes (Blakemore & Campbell, 1969). The orientation-specificity and interocular transfer of the aftereffect, suggest a cortical locus for the perceptual effect in primary visual cortex (V1), as orientation tuning and binocular responses first occur in V1 (Kohn, 2007). These and other characteristics of visual aftereffects, led to a distinction between low-level and high-level aftereffects, reflecting selective adaptation of neurons respectively in and beyond the earliest cortical visual areas, according to the size and the hierarchical organization of the receptive fields. In fact, cortical sensory processing is hierarchical (Felleman & Van Essen, 1991), with neurons in lower areas (like V1) having spatially smaller receptive fields and responding to simpler features of the stimulus than those in higher areas, with larger receptive fields. Another characteristic of low-level visual aftereffects is that they are coded in a retinotopic, rather than spatiotopic frame of reference. That is, the crucial factor in order to obtain these visual aftereffects, is the correspondence between the adaptation and test locations on the retina. For instance, the motion (Knapen, Rolfs, & Cavanagh, 2009), the direction (Wenderoth & Wiese, 2008), and tilt (Gibson & Radner, 1937; Hubel & Wiesel, 1968; Knapen, Rolfs, Wexler, & Cavanagh, 2010; Mathôt & Theeuwes, 2013) aftereffects have been shown to be retinotopic, thus suggesting that the adaptation occurs in V1, where receptive fields are small and retinotopically organized. On the other hand, high-level visual aftereffects related to latent proprieties of an object, such as its squishiness (Arnold, Petrie, Gallagher, & Yarrow, 2015), and shape (Suzuki, 2001), and visual aftereffects occurring during the perception of face's identity (Benton, Jennings, & Chatting, 2006; Leopold, O’Toole, Vetter, & Blanz, 2001; Melcher, 2005), and expression (Butler, Oruc, Fox, & Barton, 2008), rely more on non-retinotopic viewpoint dependent neural mechanisms, and are generally more robust to changes in size and even position between the adapting and test stimuli than low-level aftereffects (Benton et al., 2006).

3.2. Study #7: Tactile distance aftereffects. Aim of the study and experiment overview

This study explored how a prolonged experience (i.e., adaptation) to a tactile distance delivered on the dorsum of the hands affects the perception of subsequent distances (i.e., aftereffect). We implemented a new adaptation-aftereffect paradigm, adapted from the abovementioned haptic size-contrast illusion (Uznadze, 1966). In the haptic illusion participants adapt to a combination of tactile, proprioceptive and kinaesthetic afference. In the present task participants are passively touched on the dorsum of the hands, so that only tactile information is provided. Secondly, in the haptic illusion the stimuli are spheres, consisting in a continuous surface touching a region of the skin; instead in our study participants process a gap between two simultaneous but separated tactile events; thus, they are adapted to a spatial relationship between two points, namely to a distance.

In Experiment #1 (A and B) we examined if a passive tactile adaptation of the dorsum of both hands, to two stimuli different in distance, and consisting, respectively, of a larger and of a smaller distance, could induce a distance aftereffect, when a pair of subsequent stimuli are applied to the hands. That is, the relative size perception of a following couple of distances would be altered as a consequence of the previous adaptor size: we expected participants to perceive as larger the test stimulus applied on the hand previously adapted to the smallest distance, and vice versa.

In Experiment #2 we assessed whether the aftereffect found in the previous experiments is driven necessarily by a direct comparison between the distances delivered on the hands during the adaptation phase, or if it could be induced without the exposure to a contrast between distances during adaptation. To this end, in this experiment, only one hand was adapted, while the test stimuli were delivered on both hands.

In Experiment #3 the orientation specificity of the distance aftereffect was investigated. We tested the hypothesis that the adaptation to distances processed along a specific dimension of the hand (i.e., width) could not affect the subsequent processing of distance perception oriented along its orthogonal dimension (i.e., length). Thus, we expected a lack of distance aftereffect with test stimuli delivered with a 90° rotation compared to the adaptors orientation.

In Experiment #4 the location specificity of the distance tactile aftereffect was investigated. We tested the hypothesis that the distance aftereffect may be distinctive to the specific adapted region of the skin, analogously to the visual retinotopic aftereffects described above (Knapen et al., 2009, 2010; Wenderoth & Wiese, 2008). To this end, both the adaptors and the test stimuli were delivered over two different, but close regions of the same hand. Were adaptation location-specific, the induction of the distance aftereffect would have been the expected result.

In Experiment #5 we investigated the presence of intermanual transfer of the adaptation, assessing the occurrence of the aftereffect when adapting one hand and testing the other not-adapted hand. In order to test the bilateral transfer we made use of the anisotropy effect found by Longo and Haggard (2011): that is, distances delivered along the width of the dorsum of the hand are consistently perceived as larger than distances delivered along the length of the hand (the effect is absent on glabrous skin areas, such as the palm). After adapting the hand to a big stimulus along its width, we delivered the two test stimuli one along the width and one along the length of the hand: if a tactile distance aftereffect occurred, we expected a modulation (namely, a reduction) of the anisotropy effect, compared to a no-adaptation control condition where we expected the occurrence of the classic anisotropy effect. Crucially, the adaptor was delivered only on one hand, whereas the test stimuli were delivered both to the adapted and to not adapted hand, on different trials; so that, if a bilateral transfer of the adaptation occurred, we expected a reduction of the anisotropy effect even on the not adapted hand.

In Experiment #6 we investigated the frame of reference (somatotopic vs. external space) of the distance aftereffect. Specifically, we examined whether the adaptation to a tactile distance is coded in a skin frame of reference, or in the external space. As in Experiment #5, the hand was adapted to a big stimulus along its width, and then tested with two test stimuli one along the width and one along the length of the hand. Crucially during the test phase the hand orientation could vary: it could be oriented as during the adaptation phase (canonical), or rotated 90deg to the right (rotated). If the adaptation is somatotopically coded we expected a reduction of the anisotropy effect irregardless of the hand orientation during the test phase. Whereas, if the adaptation is coded in an external space frame of reference, we expected a reduction of the anisotropy effect only when, during the test phase, the hand is canonically orientated.

3.2.1. Materials and methods

Participants

Eighty four, healthy volunteers participated in the seven experiments: Experiment #1A (n=12; mean age=31 years; SD=6.7; 4 female), Experiment #1B (n=12; mean age=26.5 years; SD=5.9; 4 female), Experiment #2 (n=12; mean age=24.5 years; SD=5.9; 9 female), Experiment #3 (n=12; mean age=27 years; SD=6.5; 8 female), Experiment #4 (n=12; mean age=32 years; SD=7.7; 6 female), Experiment #5 (n=12; mean age=33 years; SD=9.2; 8 female), and Experiment #6 (n=12; mean age=26 years; SD=6.7; 6 female). Data from one participant in Experiment #1A, one participant in Experiment

#1B, one participant in Experiment #4, and two participants in Experiment #6 were excluded from analyses based on poor fit of the data ($R^2 < 0.5$ in one or more conditions). Remaining sample: Experiment #1A: n=11; mean age=30 years; SD=6.6; 4 female; Experiment #1B: n=11; mean age=26 years; SD=5.9; 4 female; Experiment #4: n=11; mean age=32 years; SD=7.9; 5 female; Experiment #6: n=10; mean age=24years; SD=4.3; 5 female. Overall, participants were right-handed, except one left-handed participant (handedness mean across groups = 85.56, range = -100 to 100), as assessed by the by the Edinburgh Inventory (Oldfield, 1971), with no history of tactile or somatosensory difficulties or of neurological or psychiatric illness. They gave written informed consent and were paid or given course credits for their participation. The study was approved by the local Ethics Committee.

Procedure

Since the procedure used in the seven experiments is quite similar, with only little variations, firstly we provide a general and common description of it, followed by a brief stimuli terminology section and by a concise description of the procedure of each experiment.

The tactile stimuli were pairs of pointed, wooden sticks, separated by 2, 3 or 4 cm, fixed to a foam board (Longo & Haggard, 2011). The tip of each post was rounded off (figure 25).

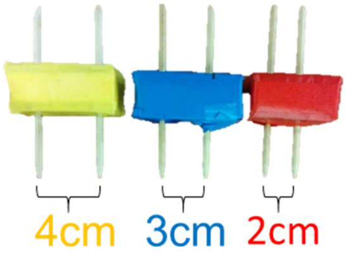

Figure 25. The stimuli used in Study #7. From left to right: the 4cm (yellow), the 3cm (blue) and the 2cm (red) distance between the two rod comprising each stimulus.

In all the experiments, participants were blindfolded and sat with their palms resting on the table, and their hands with the digits oriented toward the experimenter, which sat in front of them. On each trial they were exposed to an adaptation phase and a test phase. All the stimuli of both the adaptation and the test phases, were delivered manually by the experimenter. During the adaptation phase, participants were touched repeatedly and in succession, on the dorsum of the hands, with one or two tactile stimuli (depending on the experiment) comprising different distances. The duration of each touch, and the interval between stimuli, were approximately of one second. In all the experiments the adaptation phase was presented in two conditions. In each block, participants were adapted with one of the two adaptation conditions using an ABBA design (the starting condition was counterbalanced across participants, thus, half of the participants in each experiment adapted with the ABBA order of adaptation, the other half with the BAAB order). The adaptation period of the first trial of each condition lasted 60s, while the rest of trials consisted on 10s. Given that, after every 20 trials participants had a little rest, a long adaptation trial (60s) was repeated again after 20 trials, in order to reinforce the adaptation after the break. Importantly, during the adaptation phase, the stimuli were delivered along the whole length or width of the participant's hands (depending on the experiment), so that the stimulation was never applied systematically to the same bits of skin. In the test phase of each trial, two stimuli were always delivered, one time each only, in succession, with the same frequency of the adaptation phase (1 stimulus per second), one on each hand, or on different portions or different orientations of the same hand (depending on the experiment). For each test pair, immediately after the second touch, participants were asked to make untimed two-alternative forced choice verbal judgments about which of the two stimuli was perceived as having the two rods farther apart: the stimulus delivered first, or the second (figure 26).

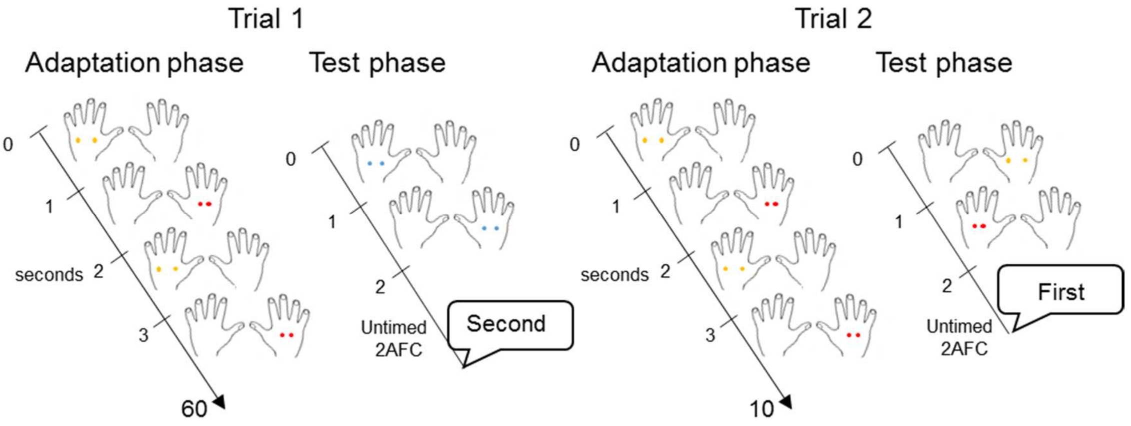

Figure 26. Schematic representation of the first two trials of each block of Experiment #1A.

The experimenter collected manually the responses. In each experiment, five pairs of tactile stimuli were used as the test stimuli (set 1: 2/4 cm, 2/3 cm, 3/3 cm, 3/2 cm, and 4/2 cm, used in Experiment #1A, #1B, #3, #5 and #6; set 2: 2/3 cm, 3/4 cm, 3/3 cm, 4/3 cm, and 3/2 cm, used in Experiment #2 and #4). The order of the pairs, and which stimulus was applied first, were randomised and balanced within blocks. In Experiments #1A, #1B, #2, #3 and #4, each pairs of test stimuli was delivered 16 times, for each condition of adaptation, for a total of 160 trials, divided in 4 blocks of 40 trials each. In Experiments #5 and #6, each pairs of test stimuli was delivered 12 times, for each condition of adaptation, and for each hand tested, for a total of 240 trials, divided in 4 blocks of 60 trials each.

We refer to an *across* stimulus, when the two rods are oriented along or parallel to the mediolateral axis of the hand, and to an *along* stimulus, when the two rods are oriented along or parallel to the proximodistal axis of the hand. Drawing an imaginary line from the adjacent surfaces of the thumb and index metacarpals to the lateral part of the dorsum of the hand, so that we can arbitrarily delimit the hand in two regions: distal and proximal to the wrist. A *distal* stimulus is an across stimulus delivered within this imaginary line and the metacarpophalangeal joints. A *proximal* stimulus is an across stimulus delivered within the line and the wrist (figure 27).

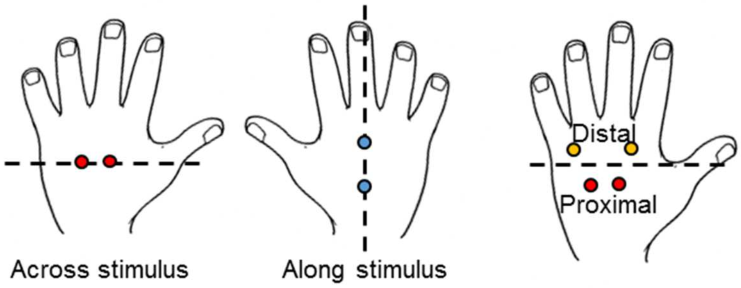

Figure 27. Schematic representation of a 2cm across, a 3cm along, a 4 cm distal, and a 2cm proximal stimuli.

Experiment #1A: Tactile distance aftereffect (across stimuli)

All the stimuli in both the adaptation and the test phases were across stimuli. In one condition of adaptation, the 2 and the 4 cm stimuli were delivered respectively to the right and to the left hand; in the other condition, the opposite pattern was applied: the right hand was touched with the 4 cm and the left hand with the 2 cm stimulus. The five test pairs of tactile stimuli, according to the length applied respectively to the right and to the left hand were: 2/4 cm, 2/3 cm, 3/3 cm, 3/2 cm and 4/2 cm (right/left hand stimulus) (figure 28, E1A).

Experiment #1B: Tactile distance aftereffect (along stimuli)

The procedure, the combination of stimuli used in the two adaptation conditions and the test stimuli pairs were identical to that used in Experiment #1A, with the exception of the orientation of the tactile stimuli during both the adaptation and the test phases, which in this experiment were applied along the proximodistal axis of the hands (along stimuli) (figure 28, E1B).

Experiment #2: One hand adapted

All the stimuli in both the adaptation and the test phases were across stimuli. In both conditions of adaptation only the left hand was adapted to a tactile stimulus (4 cm in the first condition, 2 cm in the second condition of adaptation), while the right hand was never adapted. In the test phase both hands were touched instead. The five test pairs of tactile stimuli, according to the length applied respectively to the right and to the left hand were: 2/3 cm, 3/4 cm, 3/3 cm, 4/3 cm, and 3/2 cm (right/left hand stimulus) (figure 28, E2).

Experiment #3: Orientation specificity

All the stimuli in the adaptation phase were across stimuli, and delivered in the same conditions of Experiment #1A (in one condition of adaptation, the 2 and the 4 cm stimuli were delivered respectively to the right and to the left hand; in the other condition, the opposite pattern was applied). All the stimuli in the test phase were along stimuli instead, and, according to the length applied respectively to the right and to the left hand were 2/4 cm, 2/3 cm, 3/3 cm, 3/2 cm and 4/2 cm (right/left hand stimulus) (figure 28, E3).

Experiment #4: Location specificity

All the stimuli in both the adaptation and the test phases were across stimuli, and were delivered to the left hand only, on two different regions: on the distal and on the proximal part of the hand. These two regions were identified and marked by the experimenter, who drew a line from the adjacent surfaces of the thumb and index metacarpals, to the lateral part of the dorsum of the hand; the distal surface was delimited by the line and the metacarpophalangeal joints, and the proximal hand skin surface was delimited by the line to the wrist (figure 27, third illustration). In one condition, the 2 and the 4 cm stimuli were delivered respectively to the distal and to the proximal surfaces of the left hand; in the other condition, the opposite occurred. The five test pairs of tactile stimuli, according to the length applied respectively to the distal and to the proximal part of the hand were: 2/3 cm, 3/4 cm, 3/3 cm, 4/3 cm, and 3/2 cm (distal/proximal stimulus) (figure 28, E4).

Experiment #5: Bilateral transfer

In the adaptation phase only the left hand was adapted. In one condition of adaptation participants were adapted to the 4 cm across stimulus; in the control condition, no stimulus was applied, so that no adaptation occurred. In the test phase, both of the two test stimuli were delivered, one across, one along, either to the left, or to the right hand. The order of the tested hand was counterbalanced and randomised within trials and blocks (figure 28, E5).

Experiment #6: Hand orientation

In both the adaptation and the test phase only the left hand was stimulated. During the adaptation the hand rested in the canonical orientation: palm down and digits toward the experimenter, who sat in front of the participant. In one condition of adaptation participants were adapted to the 4 cm across stimulus; in the other condition, any stimulus was applied, so that no adaptation occurred. In the test phase, both of the two test stimuli were delivered to the left hand, one in the across orientation, and one in the along, either with the hand oriented in the canonical position, or with the hand oriented rotated 90deg toward the right (digits toward the midsagittal plan) (figure 28, E6). The order of the hand orientation was counterbalanced and randomised within trials and blocks. In the rotated trials, after the adaptation phase, before the delivery of the test stimuli, participants were asked to rotate the left hand 90deg toward the right, and lean it on the table. At the end of the trial, after the response was given, participants were asked to bring back the hand in the canonical position, for the next trial. In the canonical trials, after the adaptation phase, before the delivery of the test stimuli, participants were first asked to rotate the left hand 90deg toward the right and bring it back to the canonical position, and then to lean it on the table. We took this precaution in order to avoid to have trials in which a movement was necessarily present and others where no movement occurred.

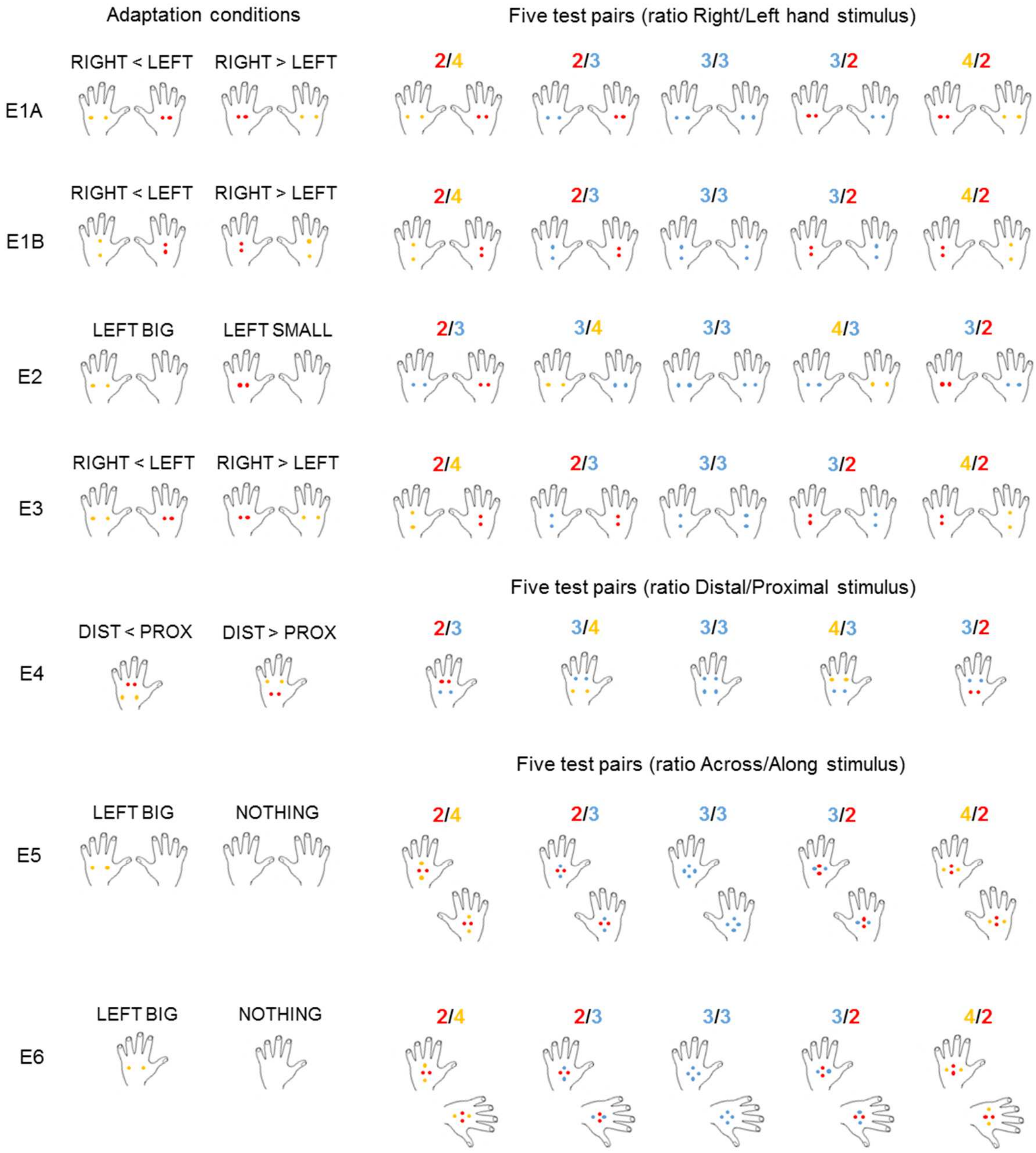

Figure 28. Schematic representation of the two adaptation conditions, and the five pairs of test stimuli, for each experiment. The red, blue and yellow couples of dots represent, respectively, the 2cm, the 3cm and the 4cm distance.

3.2.2. Statistical analysis

In Experiment #1A, #1B, #2, and #3, the proportion of trials in which the test stimulus delivered to the right hand was judged as having the two rods farther apart (bigger), was analysed as a function of the ratio of the length of the stimuli delivered to the right and to the left hand, for each adaptation condition. In Experiment #4, the proportion of responses in which the test stimulus delivered to the distal part of the left hand was judged as having the two rods farther apart was analysed as a function of the ratio of the length of the stimuli delivered to the distal and proximal portions of the hand, for each adaptation condition. In Experiment #5, the proportion of responses in which the across test stimulus was judged as having the two rods farther apart was analysed as a function of the ratio of the length of the across and along stimuli, for each adaptation condition, both for the left and the right hand test conditions. In Experiment #6, the proportion of responses in which the across test stimulus was judged as having the two rods farther apart was analysed as a function of the ratio of the length of the across and along stimuli, for each adaptation condition, both for the canonical and the rotated hand position condition. It is worth noting that participants responded to the order of the stimulus that was felt as having the two rods farther apart (i.e., the first or the second), and responses were therefore orthogonal to the right or left (Experiments #1A, #1B, #2, and #3), distal or proximal (Experiment #4), across or along (Experiments #5 and #6) dimension. Cumulative Gaussian functions were fit to each participant's data with least-squares regression, using MATLAB. Points-of-Subjective-Equality (PSEs), for each condition of adaptation, were calculated as the ratio of the length of the stimuli delivered to the right and left hand (Experiments #1A, #1B, #2, and #3), to the distal or proximal part of the hand (Experiment #4), in the across and along orientation, separately for the left and the right hand (Experiments #5), and in the across and along orientation, separately for each hand orientation (Experiment #6), at which the psychometric function crossed 50%. For statistical analysis the ratios were transformed logarithmically, in order to produce a symmetrical distribution around the point of actual equality. In Experiments #1A, #1B, #2, and #3, negative PSE values indicate a tendency to perceive a distance delivered on the right hand as smaller than those delivered on the left hand, while positive PSE values indicate the opposite. In Experiment #4, negative PSE values indicate a tendency to perceive a distance delivered on the distal part of the hand as smaller than those delivered on the proximal part of the hand, while positive PSE values indicate the opposite. In Experiments #5 and #6, negative PSE values indicate a tendency to perceive a distance delivered across as smaller than those delivered along the hand, while positive PSE values indicate the opposite. The slopes of the psychometric functions, for each condition of adaptation, were also computed (expressed in interquartile range). R-squared values were also calculated for each condition of adaptation; participants with R-squared < 0.5 in one or more conditions were excluded from the analyses. In Experiments #1A, #1B, #2, #3, and #4, the PSEs of the two adaptation conditions were compared against each other with a two-tailed paired-sample t-test. In Experiments #5, the PSEs of the two adaptation conditions, both of the left and the right hand, separately, were compared against each other with a two-tailed paired-sample t-test. In Experiments #6, the PSEs of the two adaptation conditions, both of the hand in the canonical and in the rotated orientation, separately, were compared against each other with a two-tailed paired-sample t-test. In addition to the analyses abovementioned, a mixed repeated measure ANOVA was performed on the mean PSEs values of Experiment #3 and Experiment #1B, with the within-subjects factor of “Adaptation condition” (1: right hand small/left hand big adaptor; 2: right hand big/left hand small adaptor) and the between-subjects factor of

"Adaptors orientation" (1: across - Experiment #3; 2: along - Experiment #1B), to directly compare the effect of the adaptors orientation on the possibility to induce an aftereffect.

3.2.3. Results

Experiment #1: Tactile distance aftereffect

In Experiment #1A, one participant was excluded due to low R-squared scores in the adaptation condition "right hand small adaptor/left hand big adaptor" (0.11). The remaining R-squared scores averaged across participants showed a good fit to the data (R^2=0.98 for both conditions of adaptation). As shown in figure 29, after participants were adapted with a small adaptor to the right and a big adaptor to the left hand, they perceived the test distance stimulus delivered on the right hand as bigger than the one delivered on the left hand (mean PSE = -.07; SD = .07). The opposite occurred after the adaptation condition where the right hand was adapted to a big adaptor and the left hand to a small one (mean PSE = .08; SD = .05). The mean PSEs between conditions were different ($t_{10} = 8.11$, $p < .0001$, Cohen's $d_z = 2.44$), thus indicating the presence of a different aftereffect in the two conditions.

In Experiment #1B, one participant was excluded due to low R-squared scores in the adaptation condition "right hand small adaptor/left hand big adaptor" (0.14). The remaining R-squared scores averaged across participants showed a good fit to the data ($R^2 > 0.93$ for both conditions of adaptation). The mean PSE for the two conditions were equal to -.11 (SD = .09) in the right hand small/left hand big adaptor, and equal to .04 (SD = .09) in the opposite condition, and were statistically different ($t_{10} = 5.27$, $p < .001$, $d_z = 1.59$), indicating that the two conditions of adaptation induced a different aftereffect (figure 30).

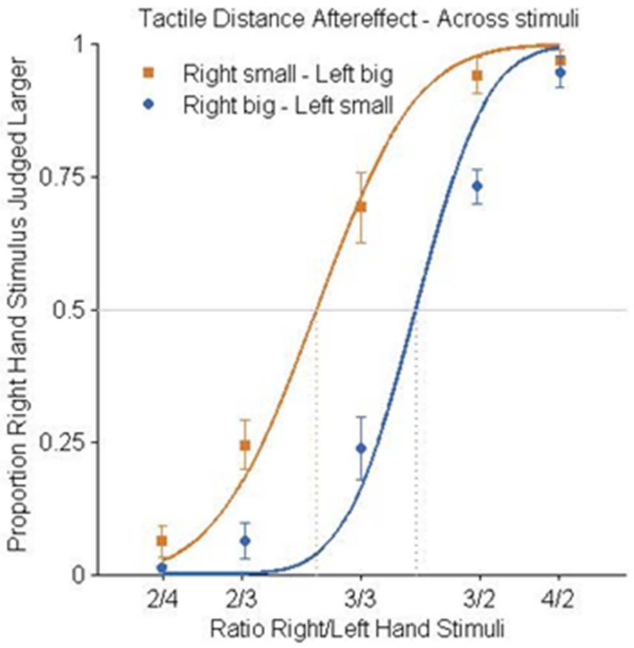

Figure 29. Experiment #1A. Tactile distance aftereffect - Across stimuli. Psychometric functions of each adaptation condition. The curves are cumulative Gaussian functions fit with least-squares regression. Error bars are standard error. The vertical lines represent the point of subjective equality for each condition (i.e., where the curve crosses 50%). In orange the adaptation condition with the 4cm stimulus delivered to the left and the 2cm to the right hand; in blue the adaptation condition with the 2cm stimulus delivered to the left and the 4cm to the right hand. The dots represent the proportion of judgments in which the test stimulus delivered on the right hand was perceived larger compared to the test stimulus delivered to the left hand, for each adaptation condition. On the abscissa are reported the 5 pairs of test stimuli delivered respectively to the right and left hand.

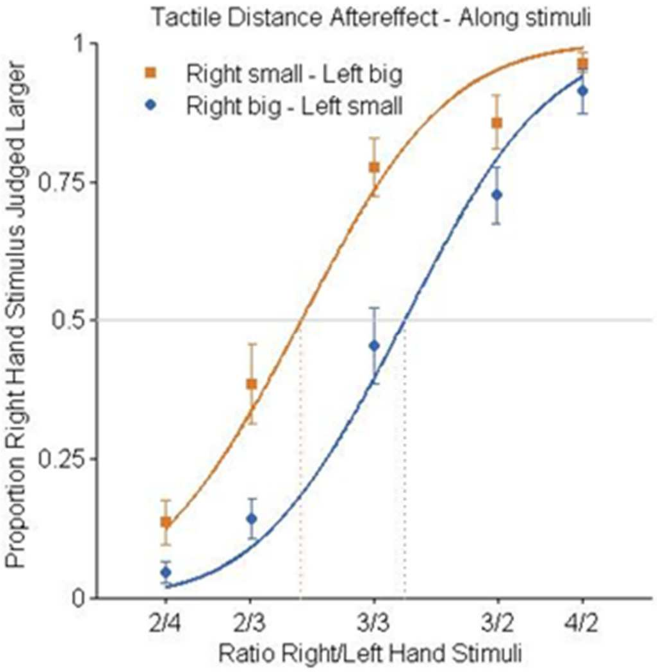

Figure 30. Tactile distance aftereffect - Along stimuli. In orange the adaptation condition with the 4cm stimulus delivered to the left and the 2cm to the right hand; in blue the adaptation condition with the 2cm stimulus delivered to the left and the 4cm to the right hand. The dots represent the proportion of judgments in which the test stimulus delivered on the right hand was perceived larger compared to the test stimulus delivered to the left hand, for each adaptation condition. On the abscissa are reported the 5 pairs of test stimuli delivered respectively to the right and left hand.

Experiment #2: One hand adapted

R-squared scores averaged across participants showed a good fit to the data (R^2>0.95 for both conditions of adaptation). The mean PSE for the two conditions were equal to -.07 (SD= .05) in the "big adaptor condition", and equal to .001 (SD= .03) in the "small adaptor condition", and were statistically different ($t_{11} = 7.79$, $p < .00001$, $d_z = 2.25$), indicating the presence of an opposite aftereffect in the two conditions. That is, when the left hand was previously adapted to the bigger distance, participants tended to perceive as larger the test stimulus delivered on the right compared to the one delivered to the left hand (figure 31).

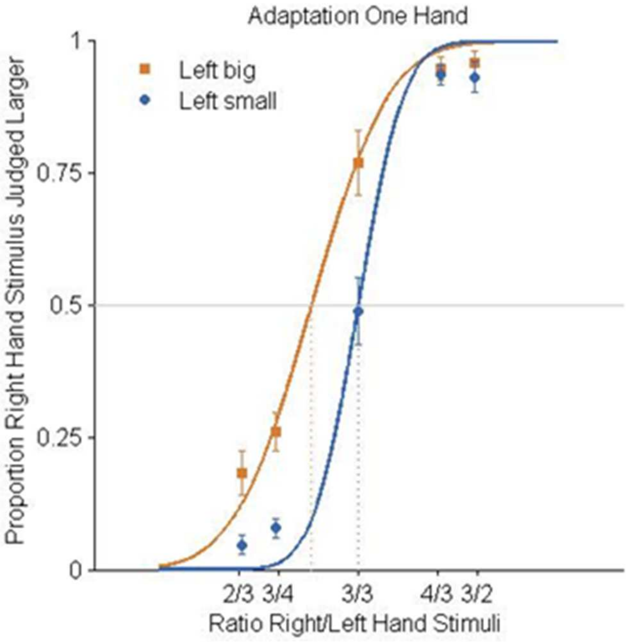

Figure 31. Experiment #2. One hand adapted. In orange the adaptation condition with the 4cm stimulus delivered to the left hand; in blue the adaptation condition with the 2cm stimulus delivered to the left hand. The right hand was never adapted. The dots represent the proportion of judgments in which the test stimulus delivered on the right hand was perceived larger compared to the test stimulus delivered to the left hand, for each adaptation condition. On the abscissa are reported the 5 pairs of test stimuli delivered respectively to the right and left hand.

Experiment #3: Orientation specificity

R-squared scores averaged across participants showed a good fit to the data ($R^2 > 0.87$ for both conditions of adaptation). The mean PSE for the two conditions were equal to -.03 (SD = .09) in the right hand small/left hand big adaptor, and equal to -.02 (SD = .09) in the opposite condition, and were not statistically different ($t_{11} = 0.30$, $p = .77$), indicating the absence of an opposite aftereffect in the two conditions (figure 32). That is, after adaptation to the across orientation, the perception of distances on the along orientation was not affected.

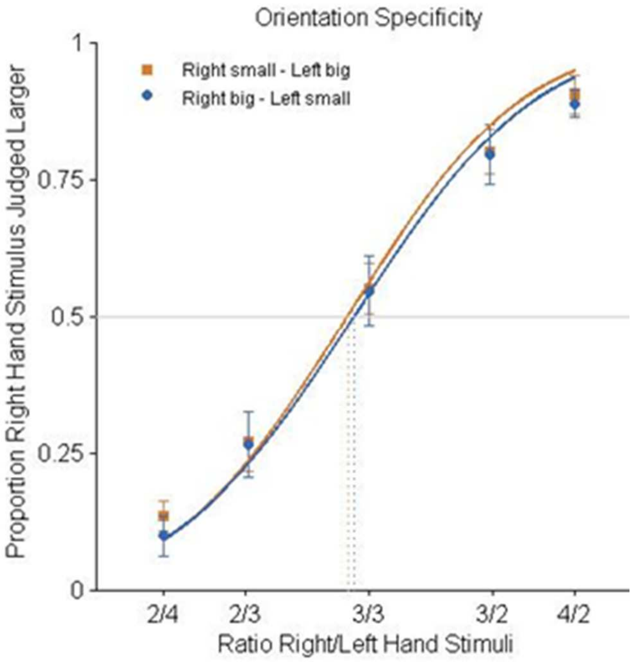

Figure 32. Experiment #3. Orientation specificity. In orange the adaptation condition with the across 4cm and 2cm stimuli delivered respectively to the left and to the right hand; in blue the adaptation condition with the across 4cm and 2cm stimuli delivered respectively to the right and to the left hand. The dots represent the proportion of judgments in which the along test stimulus delivered on the right hand was perceived larger compared to the along test stimulus delivered to the left hand, for each adaptation condition. On the abscissa are reported the 5 pairs of along test stimuli delivered respectively to the right and left hand.

Moreover, given the results of Experiment 1B, we can reasonably exclude the possibility that the lack of transfer in the opposite orientation could be explained by a general lack of aftereffect in the along orientation. Indeed, the ANOVA showed a significant effect of Adaptation condition [$F_{(1,21)} = 13.10$, $p = .002$, $\eta_p^2 = .38$], and of the interaction Adaptation condition by Adaptors orientation [$F_{(1,21)} = 10.02$, $p = .005$, $\eta_p^2 = .32$]. The effect of Adaptors orientation was not significant [$F_{(1,21)} = 0.24$, $p = .88$]. The inspection of the means of the interaction showed a significant difference between the PSEs in Experiment 1B ($p < .001$), confirming the presence of an opposite aftereffect in the two conditions, whereas no difference between the PSEs of Experiment 3 was found ($p = .75$). Overall, this analysis corroborates the finding that the aftereffect is orientation specific: ascertain that the distance aftereffect with stimuli delivered along the length of the hands does exist, as well as in the across orientation, if one is adapted to across stimuli, there is no distance aftereffect when the test stimuli are delivered in the along orientation.

Experiment #4: Location specificity

One participant was excluded due to low R-squared scores in the adaptation condition "distal small adaptor/proximal big adaptor" (0.45). The remaining R-squared scores averaged across participants showed a good fit to the data $R^2 > 0.87$ for both conditions of adaptation). The mean PSE for the two conditions were equal to -.02 (SD = .04) in the distal small/proximal big adaptor, and .05 (SD = .03) in the distal big/proximal small adaptor, and were statistically different ($t_{10} = 8.61$, $p < .00001$, $d_z = 2.60$), indicating the presence of an opposite aftereffect in the two conditions. That is, participants tended to perceive as larger the test stimulus delivered on the portion of the hand that was previously adapted to the smaller distance (figure 33).

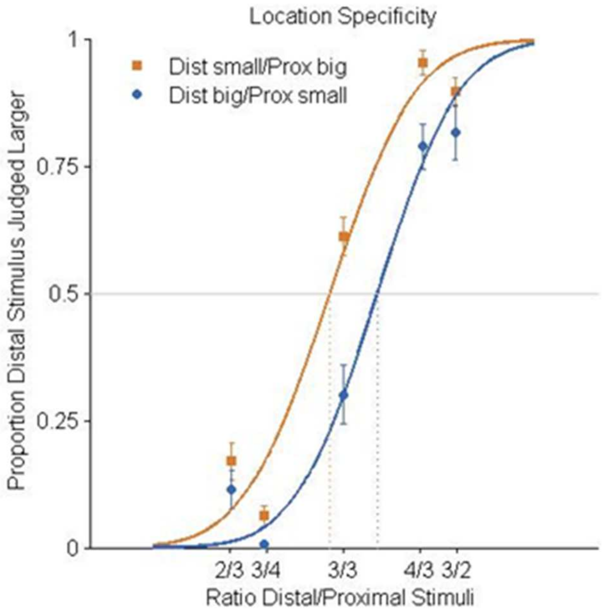

Figure 33. Experiment #4. Location specificity. In orange the adaptation condition with the 4cm and 2cm stimuli delivered respectively to the proximal and to the distal part of the left hand; in blue the adaptation condition with the 4cm and 2cm stimuli delivered respectively to the distal and to the proximal region of the hand. The dots represent the proportion of judgments in which the distal test stimulus was perceived larger compared to the proximal test stimulus, for each adaptation condition. On the abscissa are reported the 5 pairs of test stimuli delivered respectively to the distal and to the proximal part of the hand.

Experiment #5: Bilateral transfer

R-squared scores averaged across participants showed a good fit to the data ($R^2 > 0.89$ for all the four conditions). When testing the left (the one that could be adapted), the mean PSE in the non-adaptation condition was equal to -.10 (SD = .10), confirming the presence of the original anisotropy effect. In the big across adaptor condition, the mean PSE was equal to .03 (SD = .09). The mean PSEs of the two conditions were statistically different ($t_{11} = 3.54$, $p < .01$, $d_z = 1.02$), indicating the presence of an aftereffect in terms of a modulation (specifically, a reduction) of the anisotropy effect, when the hand was adapted to the big across stimulus, compared to the non-adaptation condition (figure 34, left panel). By contrast, when test stimuli were delivered to the right hand (never adapted), the mean PESs did not differ between the two conditions ($t_{11} = 0.43$, $p = .68$), and both showed the presence of the anisotropy effect (adaptation condition, mean PSE = -.14, SD = .09; non-adaptation condition, mean PSE = -.13, SD = .13; figure 34, right panel). This indicates that no bilateral transfer occurred.

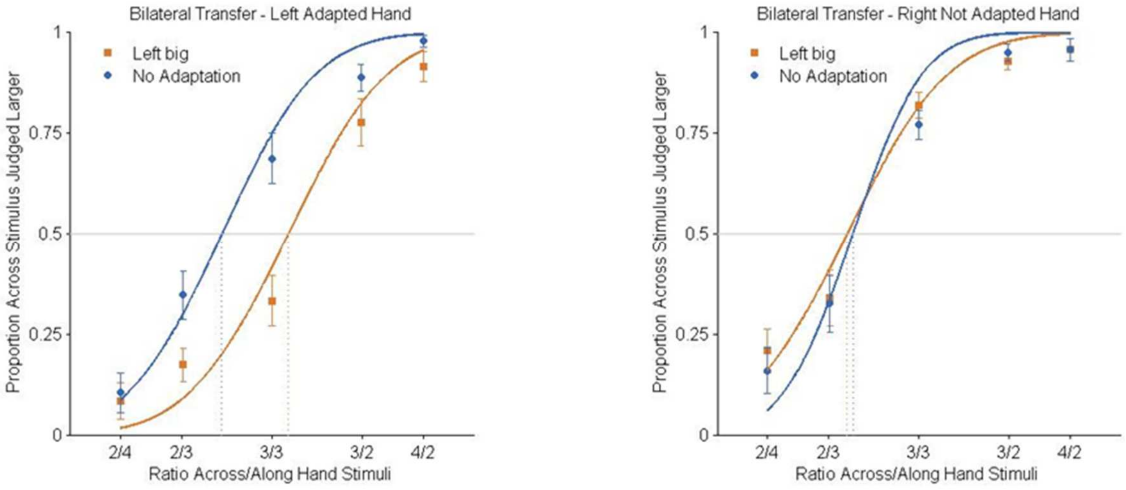

Figure 34. Experiment #5. Bilateral transfer. In orange the adaptation condition with the 4cm stimulus delivered to the left hand; in blue the control adaptation condition, when no stimulus were delivered. The right hand was never adapted. The dots represent the proportion of judgments in which the across test stimulus was perceived larger compared to the along test stimulus, for each adaptation condition, on each hand. Left panel: test stimuli delivered on the left hand. Right panel: test stimuli delivered on the right hand. On the abscissa are reported the 5 pairs of test stimuli delivered respectively across and along the hand.

Experiment #6: Hand orientation

Two participants were excluded due to low R-squared scores in three (0.06, 0.07 and 0.16) and all the four conditions (0.01, 0.42, 0.49 and 0.41).The remaining R-squared scores averaged across participants showed a good fit to the data R^2>0.92 for all the four conditions). When testing the left hand in the canonical position, the mean PSE in the non-adaptation condition was equal to -.10 (SD = .09), confirming the presence of the anisotropy effect(Longo & Haggard, 2011). In the big across adaptor condition, the mean PSE was equal to.-03 (SD = .09). The mean PSEs of the two conditions were statistically different (t_9 = 3.84, p < .01, d_z = 1.21), indicating the presence of an aftereffect and replicating the results of Experiment 5 (when testing the left hand). In fact, the same reduction of the anisotropy effect was found, when the hand was adapted to the big across stimulus, compared to the non-adaptation condition (figure 35, left panel). When test stimuli were delivered to the left hand rotated 90deg, the same pattern of results was found: the mean PSE in the non-adaptation condition was equal to -.14 (SD = .15), confirming the presence of the anisotropy effect, while in the big across adaptor condition the mean PSE was equal to .-02 (SD = .14). The mean PSEs of the two conditions were statistically different (t_9 = 4.81, p < .001, d_z = 1.52). Thus, indicating the presence of the same aftereffect even when the hand is rotated with respect to the adapting phase, and suggesting that the adaptation is somatotopically coded (figure 35, right panel).

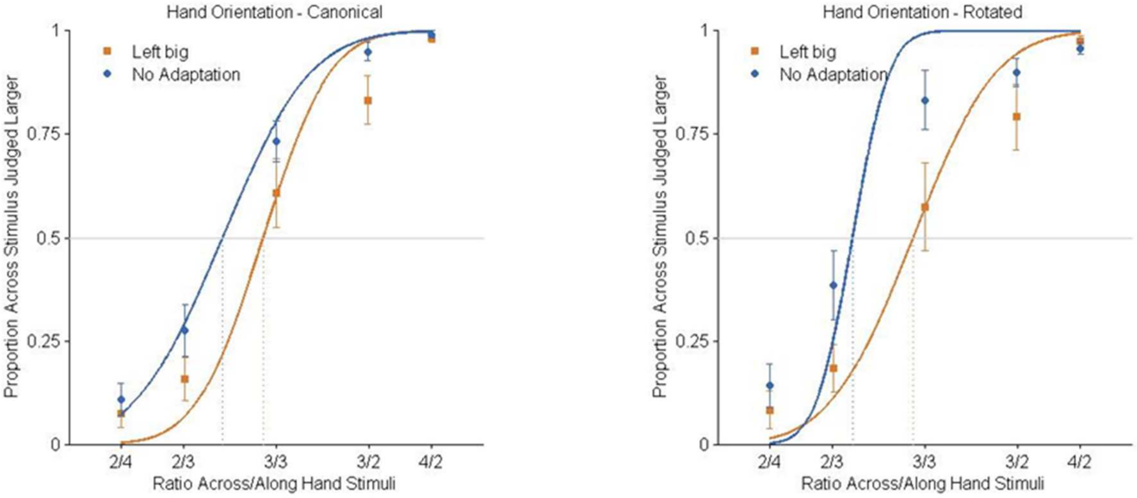

Figure 35. Experiment #6. Hand rotation. In orange the adaptation condition with the 4cm stimulus delivered to the left hand; in blue the control adaptation condition, when no stimulus were delivered. The right hand was never adapted or tested. The dots represent the proportion of judgments in which the across test stimulus was perceived larger compared to the along test stimulus, for each adaptation condition, for each orientation of the hand. Left panel: test stimuli delivered on the left hand in the canonical orientation. Right panel: test stimuli delivered on the left hand rotated 90°. On the abscissa are reported the 5 pairs of test stimuli delivered respectively across and along the hand.

3.3. Discussion

The results of Experiments #1A and #1B demonstrated that it is possible to induce a tactile distance aftereffect with passive touch on the dorsum of the hands, in the same way of the haptic size contrast illusion (Uznadze, 1966): after participants' hands were adapted to two different in size distances, they systematically perceived as bigger the subsequent stimulus delivered to the hand adapted to the smallest distance. The aftereffect is induced with tactile distances delivered both across (#1A) and along (#1B) the hand. This evidence suggest that the processing of spatial relationship between two simultaneous tactile events occurring passively on the skin, is an attribute of touch perception susceptible to sensory adaptation, which brings about negative aftereffects (i.e., a constant application of an appropriate stimulus will diminish the quality of that stimulus, and therewith the quality evoked by a subsequent stimulus for that dimension will be shifted temporarily toward the opposite quality; Gibson, 1937) in the perception of subsequent distances. The first novel finding of our results is that we induced a size aftereffect trough passive touch, so that only tactile information are available to participants. By contrast, in the haptic size aftereffects, in addition to tactile input, information about the position of the fingers and the joints, muscle tension and movement are available to participants, so that the nature of the adaptation could in this case be not only tactile, but also proprioceptive and kinaesthetic. A second important difference of our distance aftereffect with previous visual and haptic size aftereffects, is that participants adapted to two simultaneous but discrete touches on the skin; thus, they were adapted to a gap, rather than to a continuous object, and have to compute and estimate a judgment on a distance, rather than on a length.

Experiment #2 showed that the aftereffect is not driven by the adaptation to a contrast in distances. In fact, even if weaker, a distance aftereffect could be obtained by adapting one hand only (cf. in haptic, Walker, 1978).

Importantly, in Experiments #3 and #4, we demonstrated that the distance aftereffect is respectively orientation and location specific. Indeed, adapting the hand to a distance delivered along its width, did not affect the processing of subsequent distances delivered along its length. And moreover, delivering two adaptors different in size both along the same dimension (i.e., the width), but on different regions of the hand, brought about the distance aftereffect. Orientation specificity of size and length aftereffects can be found in vision (Blakemore & Campbell, 1969; Maffei et al., 1973) and in haptic (Walker, 1977).

In Experiment #5 we further investigated the distance aftereffect, showing that no intermanual transfer of the adaptation occurred. That is: the adaptation to a distance of one hand does not affect the processing of distances delivered on the other hand, suggesting that no interhemispheric transfer of tactile information occurred. In haptic, there is some evidence showing that size aftereffects do not transfer to the not adapted hand (Walker & Shea, 1974). However, another study (van der Horst et al., 2008) showed that the curvature aftereffect exhibit a partial, but significant, intramanual (i.e., transfer of adaptation between fingers of the same hand) and intermanual transfer (i.e., transfer of adaptation between fingers of both the hands). According to their findings, the Authors suggest that curvature information is not only represented at a level that is directly connected to the mechanoreceptors of individual fingers but is also represented at a stage in the somatosensory cortex shared by the fingers of both the hands. Thus, the lack of intermanual transfer of the distance aftereffect, suggests that spatial relation between touches is represented unilaterally in the somatosensory cortex.

Finally, in Experiment #6, we showed that tactile distances are coded in a somatotopic frame of reference, rather than in the external space. This evidence is similar to those found in the haptic domain, where it has been shown that kinesthetic figural aftereffects are localized in the hand itself, rather than referred to that part of phenomenal space in which the felt widths are located (Cameron & Wertheimer, 1965).

In vision, it has been shown that nearly all the levels of visual processing are affected by adaptation (for a review on visual adaptation see Solomon & Kohn, 2014), as well as different properties of visual stimuli, both basic and high-order, are susceptible to adaptation (cf. introduction low-level vs. high-level visual aftereffects, pp. 122-123). Thus, it might be important understand whether aftereffects observed in higher stages generated locally, or are affected by earlier stages of processing. A suggested method in order to disentangle this issue is to measure the spatial specificity of adaptation effects (Solomon & Kohn, 2014). In fact, the spatial size of receptive fields (RFs) increases along the visual hierarchy; thus, if an adapter confined to one sub-region of a receptive field does not influence responses to stimuli presented to another sub-region, this might suggest that the effects are induced at an earlier stage of the visual hierarchy, where receptive fields are smaller.

Analogously, we can apply the concept of receptive field to touch and to the somatosensory system. Tactile RFs are hierarchically defined within the somatosensory stream. Indeed, neurons in the primary somatosensory cortex (SI) show relatively small RFs and are tuned for the orientation of static stimuli (DiCarlo, Johnson, & Hsiao, 1998; DiCarlo & Johnson, 2000; Hsiao, Lane, & Fitzgerald, 2002; Mountcastle, 1997), and they seem comparable with neurons in V1 (Hubel & Wiesel, 1977). Neurons in the secondary somatosensory cortex (SII) have larger, even bilateral, RFs (Iwamura, 2000), and receive inputs directly from SI (Disbrow, Litinas, Recanzone, Padberg, & Krubitzer, 2003;

Friedman, Jones, & Burton, 1980; Pons, Garraghty, Friedman, & Mishkin, 1987). These properties of SII RFs suggest that this brain area might underlie integration of information from multiple skin locations. This suggestion is supported by evidence in primates showing that many SII neurons responded to stimuli administered on several finger pads, thus indicating that SII RFs extend to multiple skin locations (Fitzgerald et al., 2006a). Moreover, they showed that the RF location often formed a line across multiple digits and finger pads, and when neurons had multiple pads showing tuning for particular stimulus orientations, the preferred orientation was similar across different tuned pads (Fitzgerald et al., 2006b). Taken together, these findings suggest that SII neurons have the potential both to integrate information from different skin locations and to represent larger-scale spatial features of tactile stimuli with common stimulus properties across skin locations. On the basis of this evidence, it has been suggested that the secondary somatosensory cortex may provide the neural mechanism responsible for integrating and structuring multiple stimuli in passive touch (Serino, Giovagnoli, de Vignemont, & Haggard, 2008). Importantly, the Authors proposed that SI could provide conscious detection and localization for single tactile stimuli, whereas SII might be the first representation of a tactile field underpinning spatial organization of tactile events. An analogous suggestion comes from a study by Haggard & Giovagnoli (2011), which investigated the existence of a tactile field supporting computation of spatial relations between discrete stimulus locations. In four experiments they have studied the perception of large-scale spatial patterns (i.e., stimulus patterns extending over skin regions larger than the degree of local receptive field overlap) delivered on different parts of the body (the hand, arm and back). Importantly, one of those experiments explored the nature of the spatial representation underlying the tactile fields, showing that tactile pattern perception makes reference to structural representations of the body, such as body parts separated by joints, and that tactile field may depend on a mental representation of large-scale body structure, as well as on the spatial information provided by tactile receptors in each skin region. (Haggard & Giovagnoli, 2011). It has been proposed that, whereas the skin constitutes a continuous receptor surface covering the body, at a cognitive level, body representations segment the body into discrete parts, on the basis of their structural, motor, and physical characteristics, so that the body part structure itself constrains a categorical perception of tactile processing (de Vignemont, Tsakiris, & Haggard, 2005). For instance, a tactile distance is overestimated when the two touches occurs in two structurally separated body parts (one on the hand, and one on the forearm, crossing the wrist), relative to the same distance delivered within the same segment (both touches on the hand or on the forearm), with joints being the landmarks which segregate the body into distinct parts (de Vignemont, Majid, Jola, & Haggard, 2009). Consistent with this view of a categorical distortion of tactile space across body part boundaries, are the results by Knight and colleagues (2014), who showed a reduction of the anisotropy effect (Longo & Haggard, 2011) at the wrist. This evidence, rather than reflecting a sole increase in acuity in the vicinity of anatomical landmarks such as the wrist (Cholewiak & Collins, 2003; Cody, Garside, Lloyd, & Poliakoff, 2008; Weber, 1996), seems to reflect a perceptual segmentation of the body, with the joints forming the boundaries of body-part categories (Knight et al., 2014). It is worth noting that, in our study, tactile distances were delivered always within the same body part (i.e., the dorsum of the hand, specifically a region delimited by the wrist and the metacarpophalangeal joints), thus, presumably involving the body representation of a specific body-part category.

Taylor-Clarke and colleagues (2004) showed that altering the visual experience of the body alters perceived tactile distances. Specifically, after a training in which participant received a visual magnification of a low receptor density body part (the forearm) and a concomitant visual miniaturization of a high receptor density (the hand), the classic Weber's illusion was reduced. Thus, Authors suggested that judging a tactile distance requires a rescaling of neural signals, from a distorted, primary representation based on receptor density, to an object-centered space. Secondly, they suggested that this rescaling process requires a representation of the physical size of the stimulated body part. Finally, they postulate that size estimation imply an involvement of secondary, interpretative brain regions of the parietal cortex (Taylor-Clarke et al., 2004).

The neural basis of what Haggard & Giovagnoli (2011) called large-scale tactile judgement has rarely been studied. However, Spitoni and colleagues (Spitoni et al., 2010) reported a brain region specialized for representing the distance between two tactile stimuli. They found that a region in the right angular gyrus was more activated when participants judged whether a tactile distance presented to the right arm was greater or smaller than another distance presented to the right thigh, relative to judgements comparing the intensity of the same stimuli. Moreover, in a recent tDCS study (Spitoni et al., 2013), they reported that right but not left angular gyrus modulates the metric component of the mental body representation.

However, on the basis of the results of our study, it might be worth to reconsider some aspects of the tactile distance processing, such as the nature and the extent of the body representations comprising the metric properties of the body part touched and the concept of tactile receptive field. Firstly, the orientation and location specificity of the aftereffect reveal that in order to process a tactile distance delivered on the dorsum of the hand, we do not need a representation comprising the metric properties of the entire hand as a whole. From Experiment #1A (across stimuli) and #1B (along stimuli) we demonstrated that it is possible to adapt both the dimensions of the hand that we have taken into account (the mediolateral and proximodistal axes of the dorsum). If we assume that the presence of the negative aftereffect reflects the perceptual consequences of an alteration (or of a rescaling, using the terminology by Taylor-Clarke et al. 2004) of the mental body representation, by means of the previous sensory adaptation to a certain distance, we can reasonably say that both the mental representations of the width (Experiment #1A), and of the length (Experiment #1B) of the dorsum of the hand can be altered (or rescaled) by the adaptation. Now, if we presume that the rescaling process occurs through a sophisticated bodily map, which takes into account all the metric properties of the object-hand comprised between joints, as a whole, we might have expected that the adaptation to a distance delivered along one dimension of the hand could affect the perception of distances delivered along the other dimension. Instead, as shown by the orientation specificity of the adaptation (Experiment #3), the mental ruler we use for the distance judgement is highly contingent to the dimension of the hand that has been adapted. In other words, rescaling the width of the hand's dorsum does not produce a corresponding rescaling of its length. And even more surprisingly, we found that it is possible to adapt specific sub-regions of the dorsum, along the same dimension (Experiment #4). So that, the rescaling is specific not only for a particular dimension of the body part, but, even more, it is specific to sub-portions of the body part that are not distinctly enclosed by defined body boundaries or joints. Moreover, the results of the control Experiments #5 and #6 corroborate the evidence of a low-level effect, since the lack of interhemispheric transfer and the somatotopic frame of reference of the adaptation.

Thus, we first suggest that the estimation of spatial relation between two tactile events on the skin does not require to refer, at first, to a mental body representation comprising the metric properties of the body part as a whole, as a discrete object. On the basis of our results, it seems unlikely that tactile distance processing relies at first instance on high-level and multisensory representations sustained by high-order parietal areas, where other sensory information (proprioceptive, visual, auditory, etc.) are integrated with tactile input in order to build elaborated and multimodal representation of the body (Ehrsson, Kito, Sadato, Passingham, & Naito, 2005; Longo et al., 2010; Medina & Coslett, 2010). Rather, it is likely to occur at earlier stages of the somatosensory system, where more basic properties of touch are elaborated and eventually integrated in tactile patterns.

The second aspect that is worth taking into account at the light of our results, which is strictly linked to the conclusion above mentioned, is the concept of tactile receptive field (Haggard & Giovagnoli, 2011; Serino et al., 2008). Drawing a parallel with the visual RFs hierarchy mentioned above (Solomon & Kohn, 2014), given the spatial and orientation specificity of the aftereffect, we might argue that the adaptation occurs at a low-level along the tactile hierarchy, where receptive fields are small. It has been suggested that the key information for computing tactile distance may be the number of receptive fields between the two stimulated locations (Longo & Haggard, 2011). The Authors proposed a model of how RFs geometry could shape the body representation used for tactile size and distance perception: the “pixel model”. The model takes into account several aspects of somatosensation, such as receptor density (i.e., the number of receptors per unit area in the skin), tactile acuity (i.e., spatial resolution of touch perception), cortical magnification (i.e., the relative proportion of cortical territory coding a specific skin surface) and RF size, and made use of the anisotropy effect (i.e., across distances are perceived systematically larger than along ones; the effect is present only when stimuli are delivered on hairy skin regions, as the hand dorsum, but not on the palm) for addressing the relative contribution of each of these factor in producing Weber’s Illusion. Particularly, they underlined that, whereas cortical magnification and receptor density are fundamentally areal measures, which, by definition, cannot be anisotropic, the geometry of RFs is anisotropic. In fact, RFs on the hairy skin of the limbs are generally oval-shaped, with the long axis running proximo-distally, both in the spinal cord (Brown, Fuchs, & Tapper, 1975) and in SI (Alloway, Rosenthal, & Burton, 1989; Brown et al., 1975), while RFs on the glabrous skin are generally smaller and more circular (Powell & Mountcastle, 1959). Moreover, the pattern of anisotropy of RFs on the hand reflected the anisotropy effect found in the tactile distance judgements. Thus, Authors suggest that the Weber's illusion between different orientations on a single skin surface may arise as a consequence of RF geometry, and specifically, the size of objects touching the skin would be inversely proportional to the size of RFs along the orientation of the stimulus. And also, given that RF size is inversely correlated with tactile acuity (Paul, Brown, Koerber, & Millecchia, 2004), this could be an explanation for the classical Weber's illusion. Importantly, the Authors proposed that, given the lack of direct afference that specifies RFs geometry, the somatosensory system could assume the RFs to be uniform, rather than anisotropic, and then represented into a body mental map as uniform and isotropic shaped. The body representation may then be composed of distinct "pixels", each one corresponding to a single RF location on the skin, and the pixel would be erroneously represented as uniform, even if they might have an anisotropic form. So that, during a tactile distance judgement, counting the number of "pixel" without regard to their actual shape, could bring about the anisotropy effect when stimuli are delivered in the two different dimension of the hand dorsum (which has oval-shaped RFs, with the long axis running proximodistally), but not when stimuli are delivered on the palm (where the RFs are more circular and smaller).

In our study we demonstrated that it is possible to modulate the anisotropy effect on the dorsum of the hand (specifically by reducing the anisotropy in judgments between across and along stimuli) after adaptation to a tactile distance (Experiments #5 and #6). Thus, we might argue that the adaptation operates at the level of this mosaic representation of body surface, presumably altering the RFs mental body shape of SI.

GENERAL DISCUSSION

This Thesis includes several studies aimed to explore different body mental representations, such as those involved in the processing of body orientation and location in the external space, and those that represent a model about the metric properties of the body. I believe that this work, although not as comprehensive as the many facets of body representations, brings some novel findings and indications for future research to each corresponding debate.

In the first Chapter I have studied the processes involved in the remapping of bodily and spatial representations occurring during prism adaptation, the factors that may affect these processes, and the neural correlates of spatial remapping of proprioceptive maps occurring during PA.

Overall the results suggest that some bodily and spatial representations are susceptible to multisensory stimulations, especially those underpinning the sense of location of the body, sustained by high-order, multisensory areas in the posterior parietal cortex. In particular, the main findings are the following:

- The spatial remapping among sensorimotor systems implied in PA is affected by multisensory conflicts, in a somehow different extent and manner, according to the visuomotor exposure condition employed.

- The ecological PA procedure is more effective in a complete concurrent condition, where the limb and the movement are visible during the entire action; this may be caused by the nature of the procedure itself, which might imply a greater involvement of more complex internal models of the predicted action. Results confirm previous findings that the repeated pointings PA procedure is more effective in a terminal condition, where the hand and the movement are available at the end of the pointing only.
- PA processes are sustained by multisensory spatial maps that integrate proprioceptive, visual and acoustic information about the location of the body in the space, as assessed by novel findings showing that the recalibration of the pointing error is enhanced by the multisensory integration of inputs in different modalities during the pointing toward visuo-acoustic targets; and visuo-motor adaptation is obtained and sensorimotor AEs are induced when pointing to an acoustic stimulus, although its localization appears more erratic;
- The integrity of the left parieto-cerebellar circuit is required for an appropriate spatial remapping of proprioceptive maps to occur, and that the modulation through transcranial Direct Current Stimulation of these cortical areas temporarily restores the aftereffects. Indeed, the spatial realignment of proprioceptive maps may be impaired by unilateral cerebellar lesion; the directionally altered proprioceptive AEs may be restored by the excitatory tDCS delivered over the spread left posterior parietal cortex, and improved by anodal tDCS over the left damaged cerebellum.

Other studies should be encouraged to better clarify the factors influencing PA and its underlying processes in the remapping of sensorimotor bodily and spatial representations.

Also, more work is needed to further evaluate the optimal conditions for the application of prism adaptation in the rehabilitation of right-brain-damaged patients with left spatial neglect (Jacquin-Courtois et al., 2013; Newport & Schenk, 2012). Some implications to these purposes come from the findings of the first Chapter. A study by Fortis et al. (2013) evaluated the level of satisfaction in performing the repeated pointing and the ecological adaptation procedures, and the possible difficulties participants had encountered in executing them, showing that participants rated the ecological procedure as more pleasant, less monotonous, and more sustainable than the pointing procedure. This finding has an important implication for rehabilitation purpose. In fact, increasing the patients' compliance to the therapy may allow a higher number of brain-damaged patients to go through the whole training, as a result of a greater and active participation in the activities aimed at inducing adaptation and aftereffects. One might suggest that reducing the duration of the repeated pointing procedure may result in a more sustainable and less tedious procedure, increasing patient's compliance to the treatment. Our results showed that participants were more accurate in the pointing, and fewer trials were needed in order to point correctly to visuo-acoustic stimuli, suggesting that the number of trials of a single training session may be reduced by the employment of the bimodal visuo-acoustic PA procedure.

Moreover, the results of the third study suggest that tDCS may be a possible therapeutic adjuvant to the PA treatment of spatial neglect in right-brain-damaged patients. Anodal tDCS over the PPC of the right hemisphere during PA could up-regulate the activity of the right hemispheric side of the parieto-cerebellar network underlying the PA process of spatial realignment, as well as decreasing the imbalance of neural activity with the left hemispheric side of the network (Rossi & Rossini, 2004), resulting in an increase of the beneficial effects of visuo-motor PA on left spatial neglect.

In the second Chapter, I have investigated the relationship between bodily spatial representations and homeostatic regulation. In three studies we examined if and how a change in spatial bodily maps affects skin temperature regulation in unimpaired participants, by means of different techniques, inducing direction-specific and lateralized effects: prims adaptation, optokinetic stimulation and shift of visual attention. Results showed that temperature regulation of healthy participants can be modulated by means of adaptation to rightward displacing prisms and left OKS, two techniques which show directional-specific effects on bodily spatial representations of healthy participants, and are effective in the rehabilitation of right-brain-damaged patients (Chokron et al., 2007).

Overall the results suggest that the directionally-specific effects that we found on hands' temperature, may reflect a change in high-order, multisensory maps, encoding and integrating information from different sensory modalities (such as visual, proprioceptive and vestibular inputs) within personal and peri-personal space, in an egocentric reference frame (Blanke et al., 2015).

So far, in the studies investigating the modulation of skin temperature (Hohwy & Paton, 2010; Llobera et al., 2013; Moseley et al., 2012; Sadibolova & Longo, 2014), results have been explained in the light of the “body matrix”. This neuro-functional model, proposed by Moseley, Gallace and Spence (2012) is a multisensory representation of peri-personal space, and, in particular, of the space directly around the body. This representation comprises a network of brain regions that receive and combines information from vision, proprioception, and touch. Interestingly, Moseley and colleagues suggest that a peculiar characteristic of the body matrix, which differentiates it from other representations of peri-personal space, is that it is aligned with a body-centered frame of reference, rather than being centered over specific body parts. Moseley and colleagues propose that the main function of the body matrix is to maintain the psychological and homeostatic integrity of the body. The body matrix also accommodates for changes in a person’s body structure and orientation, by integrating multisensory inputs. By incorporating regulatory functions such as temperature control and the processing of proprioceptive, visual and tactile inputs, the body matrix is proposed to be the substrate that directly inter-relates cognitive representations such as ownership over a body part and homeostatic function such as thermoregulation. Moreover, they suggest that that many cortical representations contribute to this interrelationship. One fundamental role is given to the connections between the PPC, which elaborates peri-personal and body-centered spatial information (Blanke et al., 2015; Sereno & Huang, 2014), and the autonomic centers in the insular cortex and their projections to the brainstem, that might be the possible neural substrate by which body-centered spatial representations can modulate limb-specific blood flow, and, thus, thermoregulation. In fact, thermoregulation is strongly mediated by the insula (Diwadkar, Murphy, & Freedman, 2014), which generally is involved in interoceptive signalling (Craig, 2002, 2009; Critchley et al., 2004). Interestingly, vestibular and interoceptive systems have strong neuroanatomical and functional links, based on shared representation in the insula (see Balaban, 1999 for a review). Thus, it is possible that the vestibular system may play a role on thermoregulation (Macauda et al., 2015).

Following on from the body matrix, the suggestion can be made that the remapping of the spatial frames of reference occurring during PA to rightward displacing lenses and visuo-vestibular left OKS, signals and exerts some changes in this multisensory body-centered cortical representation of the body, resulting in alterations of homeostatic control.

Moseley and colleagues (Moseley, Gallace, & Spence, 2012) also propose that this body-centered multisensory representation might be altered by abnormal feedback from other brain areas, as it occurs after brain damage. For example, a malfunctioning in the part of this representation responsible for mapping one side of the space around the body might, be caused by altered input from the side of the body that more often occupies that part of space. Thus, we suggest that this physiological parameter may be employed as an implicit index of modifications of the body representations in those pathological conditions showing an altered sense of body ownership (Romano et al., 2014), as well as in patients with directional-specific and egocentric-centered deficits, predominantly caused by unilateral cerebral lesions, such as left hemineglect patients. For instance, the modulation of skin temperature can be taken as an addition index of the effectiveness of a rehabilitation treatment.

Finally, in the third Chapter I have explored another type of mental body representations, in particular those providing information about the metric properties of body parts, which are used as a ruler in order to process the spatial relationship between tactile events on the skin.

We implemented a new adaptation-aftereffect paradigm, adapted from a haptic size-contrast illusion (Uznadze, 1966), and we applied it, for the first time to passive touch, in order to study how a sustained exposure to a certain distance between two touches could affect the perception of a subsequent one.

Our results support the existence of tactile distance aftereffect with passive touch, i.e., independent of proprioceptive and kinaesthetic information from the hands. Unlike previous haptic aftereffects in the modality of touch, where the stimulus consisted in a continuous surface, we induced the aftereffect using two simultaneous, but separated points touching the skin. This demonstrates that size aftereffects are also induced through the calculation of distance between two edges of a single object. And more interestingly, we provide some novel evidence that this tactile distance aftereffect shares numerous characteristics with the lower-level visual and haptic aftereffects, such as orientation and location specificity, lack of bilateral transfer, and it is coded in somatotopic coordinates, rather than in the external space. Thus suggesting that, although being susceptible to higher-order body representation modulations (de Vignemont, Ehrsson, et al., 2005; Tajadura-Jiménez et al., 2012; Taylor-Clarke et al., 2004) the perception of tactile distance is a more basic property of touch than suggested by previous evidence. Moreover, our results suggest that a possible cortical site of the body representation underlying tactile distance processing might be the found in SI. Indeed, the characteristics of our tactile distance aftereffect, and particularly the orientation and location specificity of the adaptation, and the modulation of the anisotropy effect (Longo & Haggard, 2011), provide further evidence that the mental body representations underlying tactile distance processing, retain anisotropies of the geometry of SI receptive fields (Alloway et al., 1989; Brown et al., 1975), adding new converging evidence in support of a model of Weber’s illusion, which links tactile distance perception to low-level properties of SI, the “pixel model” (Longo & Haggard, 2011).

However, further studies are needed to evaluate the pixel model, and to investigate the brain regions sustaining tactile distance perception. According to the pixel model, some predictions can be made about the distance aftereffect when adapting other body parts or other regions of the skin (i.e., glabrous versus hairy skin) that present a different geometry of their RFs. Finally, it would be worth to implement our tactile distance aftereffect paradigm in an electrophysiological study, in order to investigate the neural substrate of the adaptation, and at which level of the somatosensory processing the computation of tactile distance occurs.

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Acknowledgments

I wish to express my heartfelt thanks and deepest gratitude to my supervisor, Prof. Giuseppe Vallar, who guided and supported me throughout my educational path and academic career, trusting my capacities and improving my independence as a researcher. He has always been a mentor to me, present and available for good advices and stimulating discussions with his expertise and knowledge.

My sincere appreciation goes to my co-supervisor, Dr. Alberto Gallace, for his endless help and support at all the stages of my research.

A special thanks goes to Prof. Matthew Longo and his incredible collaborators, Eamonn, Elena, Luigi, Eleonora, Renata and Klaudia, for embracing me in the BodyLab during my visiting period at Birkbeck, University of London; it has been a very inspiring experience, which remarkably contributed to my professional, as well as personal, development.

A huge thanks to Roberta and Paola for their precious encouragement and support from the very beginning of my path.

Many thanks to the great team and collaborators of the Neuropsychology Laboratory of the Istituto Auxologico Italiano, Elisabetta, Carlotta, Angela, and Nadia, for their unceasing work, great organization and help in recruiting participants for the researches.

I would like to thanks the apprentices and (ex-) students who helped me in the data collection and other stages of my research, with remarkable scrupulousness and enthusiasm, Luca, Irene, Martina, Elena, Federica, and Daniele.

Thank you to the members of my beloved band, the PhDevils, Daniele, Alberto, Carlotta and Giulio, great scientists and real friends.

I also wish to thank all my friends and colleagues in Milan and London, for their support and affection, and for sharing with me these four unforgettable years of science and many beers: Anna, Giulia, Silvia, Irene, Carola, Ciro, Francesco, Leonor, Elena, Emanuela, Luca Panca, Luca Rino, Nea and Manu, Rossella, Milena, Ermanno, Pietro, Carlo, Natalie, Manu and many others.

A special thanks to my Beefs, Laura (a.k.a. the Caterpillar of Angel) and Elena (a.k.a. the Rhino of Harringay), the London experience would have not been the same without you.

Thank you to all the incredible people who took part in my studies, I would not be here without your participation.

My deepest gratitude goes to my beloved mum and dad, for their unconditional trust, love and support.

To Fabio, thank you for have been suffering and cheering with me through all these years.