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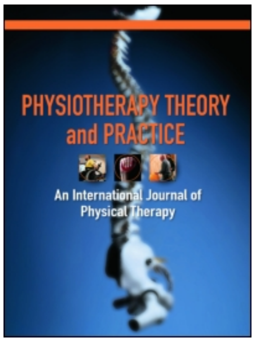

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Unisensory and multisensory Self-referential stimulation of the lower limb: An exploratory fMRI study on healthy subjects

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ABSTRACT

Background: The holistic view of the person is the essence of the physiotherapy. Knowledge of approaches that develop the whole person promotes better patient outcomes. Multisensory Self-referential stimulation, more than a unisensory one, seems to produce a holistic experience of the Self ("Core-Self"). ***Objectives***: (1) To analyze the somatotopic brain activation during unisensory and multisensorial Self-referential stimulus; and (2) to understand if the areas activated by multi-sensorial Self-referential stimulation are the ones responsible for the "Core-Self." ***Methods***: An exploratory functional magnetic resonance imaging (fMRI) study was performed with 10 healthy subjects, under the stimulation of the lower limbs with three Self-referential stimuli: unisensory auditory-verbal, unisensory tactile-manual, and multisensory, applying the unisensory stimuli simultaneously. ***Results***: Unisensory stimulation elicits bilateral activations of the temporoparietal junction (TPJ), of the primary somatosensory cortex (S1), of the primary motor cortex (BA4), of the premotor cortex (BA6) and of BA44; multisensory stimulation also elicits activity in TPJ, BA4, and BA6, and when compared with unisensory stimuli, activations were found in: (1) Cortical and subcortical midline structures—BA7 (precuneus), BA9 (medial prefrontal cortex), BA30 (posterior cingulated), superior colliculum and posterior cerebellum; and (2) Posterior lateral cortex—TPJ, posterior BA13 (insula), BA19, and BA37. Bilateral TPJ is the one that showed the biggest activation volume. ***Conclusion***: This specific multisensory stimulation produces a brain activation map in regions that are responsible for multisensory Self-processing and may represent the Core-Self. We recommend the use of this specific multisensory stimulation as a physiotherapy intervention strategy that might promote the Self-reorganization.

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Introduction

The phenomenon of consciousness and identity, known as the Self (Damásio 2010; Northoff and Bermpohl 2004; Northoff et al. 2006), is influenced by an individual's life experiences and is relatively stable. One of the life experiences that may constitute a threat to the stability of the Self is the presence of a health condition. The sensation that is generated is that of loss of emotional consciousness and loss of bodily-consciousness. This holistic view means that we are interested in engaging and developing the whole person and may provide a novel insight for the clinical reasoning in physiotherapy.

In recent years, there has been a major concern among philosophers, psychologists, and neuroscientists about the Self. Many authors have categorized different perceptions and distinct concepts of the Self (e.g., Physical-Self, Mental-Self, Spiritual-Self, Proto-Self, Autobiographical-Self, and Bodily Self-consciousness) (Damásio 1999, 2003, 2010; Gallagher 2000; Panksepp and Northoff 2009). In physiotherapy, alongside Mental-Self and Autobiographical-Self, the most important concept is the Bodily Self-consciousness. The latest research assumed that Bodily Self-consciousness is comprised of at least four different feelings: (1) Experience of owning a body (body-ownership); (2) experience of being a body in relation to external references (Self-location); (3) my own position experience (first person perspective); and (4) sense of agency (Blanke 2012; Serino et al. 2013).

Despite the existence of all these concepts of the Self, Damásio (1999) conceived the "Core-Self" as a continuous conjunction of interoceptive and exteroceptive

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stimuli leading to the continuous representation of the experience of the Self as a unit. However, in order to achieve a continuous Self representation as a whole, the internal and external stimuli should be Self-referential. Self-referential stimuli are experienced by the individual himself and are strongly related to one's own person (Northoff and Bermpohl 2004; Northoff et al. 2006).

If the stimuli are Self-referential, the Self-referential processing in the brain is common to different components of the Self and in different cognitive and sensory domains (Gillihan and Farah 2005; Lloyd 2002; Northoff et al. 2006; Yaoi et al. 2009). Some authors claimed that the "Core-Self" is where Self-referential processing takes place in the brain (Northoff and Bermpohl 2004) and is essential to create a model of the Self. This theory is supported by other researchers (Damásio 1999, 2003, 2010; LeDoux 2003; Panksepp 2005) that established a relationship between sensory inputs and Self-referential processing. They claim that this relationship takes place in specific brain regions during Self-referential cognitive, motor, imagery, and unisensory tasks: (1) Cortical midline structures (CMS)—in medial prefrontal cortex and in the precuneus. The neural activity, particularly in the anterior region, is essential for transforming simple sensory information into more complex Self-referential processing (Mahy et al. 2014; Northoff et al. 2006); (2) lateral prefrontal cortex (LPFC) a higher-order processing occurs, in relation to the autobiographical, emotional, spatial, and verbal Selves; and (3) lateral parietal cortex, bilateral temporal poles, insula, temporoparietal junction (TPJ), and subcortical midline structures, including thalamus (Ward 2013), posterior cingulate cortex, and right cerebellum (Yaoi et al. 2009). These brain areas also seem to have an important role in Self-consciousness and in tasks that involve thinking about the mental states of other persons (Schurz et al. 2014).

However, many of the studies related with Self-referential stimulation are focused on single sensory modalities alone (frequently vision) (Beauchamp 2005a; Gutchess et al. 2010) and according to the opinion of some investigators (Tsakiris, Costantini, and Haggard 2008; De Vignemont 2006), the unisensory stimulation may not be sufficient to invoke the perception of a holistic Self. In fact, everyday life perceptual activities often appear in multiple sensory modalities at once, and our brain is prepared and has the ability to integrate multisensory information related to the body into a unique and coherent perception (Freiherr et al. 2013; Shams and Seitz 2008).

The studies that reference multisensory stimulation highlight some brain regions that are responsible for the structure of the Self: (1) Activity in the prefrontal cortex suggests a whole-body percept through the integration of multisensory information across multiple body segments (Bekrater-Bodmann et al. 2011; Ehrsson et al. 2004; Gentile et al. 2015; Lopez et al. 2008; Rizzolatti et al. 2002; Tsakiris et al. 2007a); (2) posterior insula and frontal cortex related to Self-consciousness, specifically without motor action (Blanke and Arzy 2005; Tsakiris et al. 2007a); (3) posterior cingulated that plays an important role in the construction of subjective feeling of the Self (Guterstam et al. 2015; Lopez et al. 2008; Vogeley et al. 2004; Yaoi et al. 2009); (4) TPJ as an important multisensory area capable of integrating inputs from different modalities (Blanke 2012) and containing an internal model of the body that enables the brain to maintain a consistent representation of one's body (Arzy et al. 2006; Blanke and Arzy 2005; Tsakiris, Costantini, and Haggard 2008). Activation of the TPJ has also been identified in a variety of Theory of Mind studies[1] (Aichhorn et al. 2009); and (5) a brain network comprising medial prefrontal cortex (BA9), precuneus (BA7), posterior cingulate gyrus (BA30), and TPJ (Ciavarro et al. 2012; Ruby and Legrand 2007).

On a global basis, the TPJ is characterized as a region between the temporal and parietal lobes surrounding the ends of the sylvian fissure. TPJ is also referred to as the superior temporal gyrus, posterior inferior parietal lobe, ventral parietal cortex, and angular gyrus. TPJ is the region that includes BA 22, 37, 39, 40, 42 (Geng and Vossel 2013; Matsuhashi et al. 2004; Schurz et al. 2014).

Literature is extensive with respect to the role of multisensory integration across exteroceptive perception (e.g., vision and audition), and action. However, Seth (2013) argues in favor of a predictive model of Core-Self. This model must necessarily contain a combination of subjective feelings involving the body and interoceptive and exteroceptive signs/stimuli. For the clinical practice of physiotherapy, it is important to know which brain regions are activated with specific strategies of sensory stimulation used in different areas of intervention. Therefore, we propose three types of specific stimulation that have never been performed in any study of brain activity and in particular their application in the lower limbs, a tactile-manual and auditory-verbal stimulation (requesting to feel some body parts) and a multisensory stimulation applying the two previously stated stimuli simultaneously.

[1]Theory of Mind is the cognitive capacity to attribute mental states to *Self* and others (Premack and Woodruff 1978) and more recently (Goldman 2012).

These stimuli were also selected because: (1) of the need to understand their effect in brain activity, with the purpose of a suitable therapeutic decision-making; (2) they originally define Physiotherapy (alongside with Motion); (3) they are rarely used in Physiotherapy clinical practice and we would like to know its importance for future recommendation of its use; and (4) they can be considered a Self-referential stimuli because they are directly related to the person's own body (Northoff et al. 2006).

As a matter of fact, the unisensory stimulation strategies that have been most used and studied in neurological Physiotherapy are pressure stimulation with objects, thermal stimulation for recovery of sensation, intermittent pneumatic compression intervention for improving tactile and kinesthetic sensation, electrical stimulation, magnetic stimulation, tensive mobilizations of the peripheral nerves, acupuncture and stimulation with cotton, soft brush, or with different textures (Chen and Shaw 2014; Flor and Diers 2009; Johansson 2012). Nevertheless, they cannot be considered as Self-referential stimulus. Moreover, the most commonly used multisensory strategies are motor imagery, action observation, music therapy, and training with a mirror or in a virtual environment. These multisensory stimulation strategies are more focused on movement than on body perception and consciousness (Johansson 2012).

Our exploratory whole-brain functional magnetic resonance imaging (fMRI) study is based on the brain activity of lower limbs during three Self-referential stimuli on healthy older subjects: (1) a unisensory Self-referential stimulus that involves an auditory-verbal stimulus requesting to feel specific body parts (hip, thigh, and knee); (2) a unisensory Self-referential stimulus with tactile-manual stimulation of the same body parts, according to the Haptonomie science (also known as the science of affectivity) (Veldman 2001); and (3) a third Self-referential stimulus, applied according to the principles of multisensory stimulation (Freiherr et al. 2013) and comprising the two previous stimuli applied simultaneously.

The selection of the lower limb is due to the fact that there is extensive research on brain activity during sensory stimulation of the upper limbs but not on lower limbs, especially in their proximal segments. Lower limb activation patterns during sensorial stimulation are still not well understood. More recently, attention has turned to the role of the lower limb proximal structures and current evidence shows that these core muscles are essential in controlling hip abduction and internal rotation of the femur, thereby promoting a more functional distal movement. On the other hand, core instability leads to the development of lower extremity injury (Chuter 2012).

Two main goals have been elected for the study: (1) To analyze the somatotopic activation during auditory-verbal and tactile-manual unisensory Self-referential stimuli and multisensorial Self-referential stimulus, comprising the two previous stimuli, applied simultaneously; and (2) to understand if the areas activated by multisensorial Self-referential stimulation are the ones that are described in literature as responsible for multisensorial Self- processing.

We have established two hypotheses: (1) considering that the stimuli under study are self-referential, we hope that the activated brain regions are the same as defined in the literature, as responsible for the self-referential processing, found in other studies using other sensory modalities such as cortical midline structures (primary somatosensory cortex and prefrontal cortex), midline subcortical structures (thalamus, posterior cingulate cortex, and cerebellum), TPJ, and insula; and (2) multisensory Self-referential stimulation compared with unisensory Self-referential stimulation elicits brain activity in regions responsible for multisensory Self-referential processing, and for that reason, these regions could form the Core-Self.

Methods

Participants

Our study is based on a sample of normal older subjects because: (1) the knowledge of normal brain activity during several stimulations allows us to understand the normal and abnormal behavior. It also allows us to provide more appropriate forms of intervention in aging and in neurological disorders (Kolb and Whishaw 1998); and (2) little is known about the processing of multisensory Self-referential stimuli in older adults.

As we can see in Table 1, ten healthy subjects (five male/five female), between 52 and 84 years old (average age of 60.3 ± 9.1 years), were recruited to the study and were given a written informed consent to sign in accordance with the Declaration of Helsinki. All the experimental procedures conducted in this study and described below were approved by the Ethical Committee of Health Sciences Institute at the Portuguese Catholic University.

All subjects were screened to ensure that they were in compliance with fMRI safety requirements. All participants were right-handed and right-footed, assessed with the Waterloo Handedness Questionnaire-Revised (WHQ-R), and the Waterloo Footedness Questionnaire-Revised (WFQ-R) (Elias et al. 1998). Inclusion criteria included

Table 1. Subjects characteristics.

Subjects	Age	Gender	Handedness and footedness	QMI - auditory and kinesthetic domains	STAI Y1	SLUMS	STQ
1	84	F	Right	24	34	25	23
2	57	M	Right	18	28	26	24
3	60	M	Right	17	32	30	14
4	63	F	Right	24	26	28	18
5	56	F	Right	20	28	25	19
6	55	M	Right	10	25	30	9
7	52	F	Right	21	43	25	15
8	64	F	Right	24	34	27	14
9	56	M	Right	16	25	30	17
10	56	M	Right	20	41	30	20
Average	60.3	–	–	19.4	31.6	27.6	17.3

QMI: auditory and kinesthetic domains (min. 10; max. 70); STAI Y1: State-Trait Anxiety Inventory (min. 20; max. 80); SLUMS: Saint Louis University Mental Status (min 1; max. 30); STQ: Social Touch Questionnaire (min. 0; max. 80);

non-brain lesioned subjects, not having psychiatric, motor-sensorial or cognitive disorders or touch avoidance behavior, and all participants had to be Portuguese native speakers. Anxiety indicators were assessed according to the State Trait Anxiety Inventory (STAI) scale (Kvaal et al. 2005); cognitive disorders were assessed according to Portuguese version of the Saint Louis University Mental Status scale (SLUMS) (Tariq et al. 2006); touch avoidance was assessed according to the Social Touch Questionnaire (STQ) (Wilhelm et al. 2001; Vieira et al.2016); and clarity and vividness of the ability of mental imagery was assessed applying the Questionnaire upon mental imagery (QMI—auditory and kinesthetic domains) (Sheehan 1967) (Table 1).

Procedures for brain activity acquisition

Functional images, based on a whole-brain approach, were acquired with a three Tesla Scan Siemens Magnetom Trio at the Portuguese Brain Imaging Network Grid. The experiment started with one 3D anatomical T1-weighted MPRAGE sequence, voxel size 1 × 1 × 1, repetition time (TR): 2.530 ms, echo time (TE): 3.42 ms, field of view (FOV): 256 × 256 mm, and a matrix size of 256 × 256. The anatomical sequence was composed of 176 slices. The fMRI experiment was acquired in 2 functional runs: RUN 1—right lower limb and RUN 2—left lower limb, in the same session, sensitive to BOLD signal sequences, a TR: 2500 ms, TE: 30 ms, voxel size 3 × 3 × 3 mm, FOV: 256 × 256, and a matrix size of 86 × 86. For each run, 200 volumes were acquired with 45 slices.

Experimental paradigms

Before stepping into the fMRI machine, the subjects were informed that they would be required to lie down in the scanner with their eyes closed and should experience the various stimulations passively. Headphones were placed on subjects in order to protect them from scanner noise and to hear the verbal commands more clearly.

All subjects were submitted to a single session which included one structural scan and one functional scan with two runs. Each run consisted of three stimulation blocks and one fixation block (Table 2). For the three stimulation blocks the goal was to create a somatotopic activity map according to:

- **Block 1: Auditory-Verbal Stimulus Requesting to Feel Specific Body Parts**—*"feel your hip, feel your thigh, feel your knee"*—recorded with a sound recorder using a female voice and translated into Windows media audio (wma) format. It should be noted that, up to this moment, in embodied cognition studies[2] simulation tasks and action words related to the body have only been used, much like imagining body movements or the use of tools (Esopenko et al.

Table 2. Experimental paradigm.

	495 seconds per RUN (990 seconds per subject)				
	Fixation Block Baseline 1	Block 1 	Block 2 	Block 3 	Fixation Block Baseline 2
RUN 1: Right Lower Limb Stimulation	330 seconds	Pseudo-randomized sequence, with 5 repetitions of each block (7 seconds of stimuli per repetition) and 15 seconds of rest, in between each repetition.			330 seconds
RUN 2: Left Lower Limb Stimulation	330 seconds	Pseudo-randomized sequence, with 5 repetitions of each block (7 seconds of stimuli per repetition) and 15 seconds of rest, in between each repetition			330 seconds

[2]The theory is that many of the dimensions of cognition (language, memory, attention, and reasoning) are embodied, i.e., they are dependent and are influenced by characteristics of the body, how that body collects the information of the environment, the way the body interacts with the brain, and how the brain processes this information and raises awareness (Anderson 2003; Hauk and Tschentscher 2013).

2008; Gabbard 2012; Hauk et al. 2008; Kemmerer and Gonzalez-Castillo 2010; Pulvermüller et al. 2009; Rueschemeyer et al. 2010; Van Dam et al. 2010).

- **Block 2: Tactile-Manual Stimulus** based on Haptonomy (Veldman 2001) performed by a specialized physiotherapist. This particular form of touch was applied with both hands simultaneously around the subject´s relevant body part. Once the hands were in complete contact with the subject's skin, a slight pressure was exerted and then both hands were gently removed. The choice of type of tactile stimulus was due to the fact that there is limited information about how the brain responds to skin-to-skin contact in a pleasant way (Essick et al. 2010; Guest et al. 2009; Lindgren et al. 2012; Löken et al. 2011; McCabe et al. 2008; Olausson et al. 2010; Sliz et al. 2012).
- **Block 3: Multisensory Simultaneous Stimulus** involving auditory-verbal and tactile-manual stimulation. For this block, multisensory integration principles (Freiherr et al. 2013) were considered: (1) unimodal sensory stimuli have to be applied within a certain temporal sequence; (2) sensory stimuli of different modalities have to match in time and space (i.e., stimuli must be delivered in a synchronous manner); (3) contextual and semantic congruency is fundamental; and (4) multisensory integration is most effective when less ambiguous individual stimuli are applied. When the conditions set out in the principles are satisfied, the sensory stimuli seem to come from the same object and one can achieve optimal integration results. The synchrony of the stimuli was assured by intensive training of the person who applied them, by the visual and auditory feedback received during the experiment so that the stimuli were applied simultaneously and by the presence of an external evaluator that oversaw and validated the congruence of multisensory stimulation.

Each stimulation block (three per run) included five trials lasting 7 seconds each, with 15 seconds of rest time between each trial (totaling 105 seconds of stimulation per run). The fixation blocks lasted 30 seconds, and were applied before the first stimulation trial and after the last stimulation trial per run (two runs total as described above). The total time for each run came to 495 seconds. The overall functional acquisition lasted 990 seconds for each subject.

The fixation blocks were used for baseline purposes, and the participants were asked to lay at rest and not to make any intentional movement. Carey (2012) states that in order to obtain a brain map of sensory responses, it is sufficient to compare de bold signal measured during the stimulation with a baseline "rest." However, some authors claim that when cognitive tasks are performed, a different design may be required with the purpose of isolating the specific cognitive process. In fact, the auditory-verbal stimulus used in this study could be considered a cognitive task because it requires proper phonological and semantic processing. Also, the areas responsible for this processing are very similar to the human brain "default network." This network is active during the conscious resting state and many studies demonstrate that these areas are deactivated during cognitive tasks and therefore authors should not make comparisons between cognitive tasks and the baseline "rest."

At first glance, this could be observed out as a methodological weakness in this study. However, deactivation only occurs when the stimulus (or task) makes little or no demands to the semantic system. When the stimulus (or task) itself engages the semantic system, deactivation does not occur (i.e., words with meaning (not pseudo-words) do not deactivate the "default network" when compared to the baseline "rest") (Binder et al. 2009).

The functional acquisition started with the right lower limb, and the sequence of the following stimulation blocks was the same for all subjects. This sequence was previously randomized on Matlab R2013a (Mathworks). Three different image codes were displayed on a computer screen regarding each block, with visibility accessible only to the physiotherapist. This procedure allowed the physiotherapist to identify the different blocks and to assess their duration.

In order to evaluate the perception of the stimuli, at the end of the experiment the participants were presented with a questionnaire built specifically for this study and adapted from "Questionnaire Upon Mental Imagery" (Sheehan 1967) composed of three statements: (1) How vivid and clear was the feeling of your hip, thigh, and knee when you heard the body parts names; (2) how vivid and clear was the feeling of your hip, thigh, and knee when you felt the touch on your body; and (3) how vivid and clear was the feeling of your hip, thigh, and knee when you heard the body parts names and felt the touch at the same time, rated on a 7-point Likert scale: (1) Very vivid and clear; (2) vivid and almost as clear; (3) generally clear and vivid; (4) not so clear and vivid but still recognizable; (5) vague and unclear; (6) very vague and hardly recognizable; (7) I think of it, but do not have an image before me (Table 3).

Table 3. Stimuli perception assessment.

Statements	Average (n = 10)
1.How vivid and clear was the feeling of your hip, thigh, and knee when you heard the body parts names	2.2
2.How vivid and clear was the feeling of your hip, thigh, and knee when you felt the touch on your body	1.7
3.How vivid and clear was the feeling of your hip, thigh, and knee when you heard the body parts names and felt the touch at the same time	1.3

For each statement: min. = 1 (More clear and vivid); max. = 7 (Less clear and vivid)

Image Processing and Data Analysis

BrainVoyager^{TM} QX version 2.3 software (Brain Innovation B.V., The Netherlands; http://www.brainvoyager.com) was used to process images and analyze data. The anatomical images were reoriented into a space where the anterior and the posterior commissures were aligned in the same plane (AC-PC) and were then mapped using the Talairach reference system.

Functional images were intensity-adjusted and all slice scans were time- and 3D motion-corrected, temporal-filtered, and subsequently co-registered to the structural image. In order to attain signal equilibrium, the first three functional volumes were discarded. The effects of stimulation blocks versus baseline were determined by performing, for each functional run, a one-way repeated ANOVA measure to identify significant clusters for each contrast. A whole-brain mask was included in order to eliminate voxels located outside of the boundaries of the brain. We considered the presence of significant clusters at the 0.05 threshold, corrected for multiple comparisons using a cluster threshold estimator (based on Monte Carlo simulations [1,000 interactions]). The cluster-size thresholding allowed us to define multi-subject volumes of interest (VOIs), according to the clusters' center of mass (CoM), and to measure their activation volumes. We also examined the surrounding areas that were included in the identified clusters using the Brain Voyager-Brain Tutor atlas.

These areas were properly identified according to the location of their CoM and peak voxel, but no activation volume was recorded due to the intrinsic limitations of using a brain atlas in order to segment those areas. The VOIs were obtained using particular contrasts. The contrast of separate auditory-verbal, tactile-manual, and simultaneous auditory-verbal and tactile-manual stimulus with the baseline was used to provide a Self-referential processing map for each type of stimulation.

In literature, we can find different criteria for detecting brain areas responsible for multisensory processing (e.g., super-additivity, max criterion, and mean criterion). However, this degree of sensitivity is dependent on the sensory modality of the stimuli or on the type of tasks involved in sensory stimulation. As such, certain limitations have been identified in these criteria and so far a suitable consensus has not been reached yet (Beauchamp 2005b; Doehrmann and Naumer 2008; Goebel and van Atteveldt 2009).

For example, if there is the involvement of an auditory stimulus and the appropriate semantic processing, Doehrmann and Naumer (2008) suggest an alternative analysis that allows for the identification of multisensory processing areas. However, they still refer the need of the stimuli involved to be significant and for their implementation to be congruent in time and space. In this analysis, two conditions are contrasted (congruent vs. incongruent), eliminating the contrast with the unisensory condition.

Taking into account: (1) the limitations on the criteria identified in literature; (2) that there is an increasing recommendation for the use of more liberal criteria fitted to the topic at study; (3) the fact that this is an exploratory study that uses for the first time an audio-verbal stimulus combined with tactile-manual stimulation; (4) the interest is not to eliminate the contrast with the unisensory stimuli, but the comparison between stimuli applied simultaneously with each one individually, because they embodied three distinct intervention strategies used in physiotherapy; and (5) that the experimental protocol was built on the principles of multisensory stimulation, in which one of the requirements is the semantic and spatial-temporal coherence of stimuli; we make the option to perform the following contrasts: (1) Multisensory stimulation (Unisensory Tactile-Manual + Unisensory Auditory-Verbal) > Unisensory auditory-verbal stimulus; and (2) Multisensory stimulation (Unisensory Tactile-Manual + Unisensory Auditory-Verbal) > Tactile-manual stimulus, in order to understand if the brain regions activated are the ones described in the literature as responsible for multisensorial Self- processing.

Results

The participants did not reveal high levels of anxiety, cognitive impairment, and touch avoidance, which could affect the study results. They also revealed very good mental imagery ability in the sensory modalities addressed in the study, assessed before the experiment and also in the specific stimulations applied, assessed after the experiment (Tables 1 and 3).

Unisensory auditory-verbal stimulation versus baseline

For both lower limbs, auditory-verbal stimulation elicits a statistically significant (RFX, $p = 0.05$, corrected) cortical and subcortical activation, especially in the bilateral sensorimotor areas (S1, primary motor cortex (M1)-BA4, and premotor cortex-BA6), left BA44, bilateral thalamus, and bilateral anterior and posterior cerebellum.

For the right lower limb, two of the seven clusters found, stand out due to the high activation volume, both at the right and left TPJ (Figure 1a, Table 4). Cluster 1 has its CoM and Peak Voxel level at BA22 (No. voxels = 22477; t (36) = 8.03; $p < 0.000001$ for the right hemisphere) and includes BA 39, 40, and 41. Cluster 7 has its CoM and Peak Voxel level at BA42 (No. voxels = 33197; t (36) = 7.81; $p < 0.000001$ for the right hemisphere) and includes BA22, 39, 40, and 41.

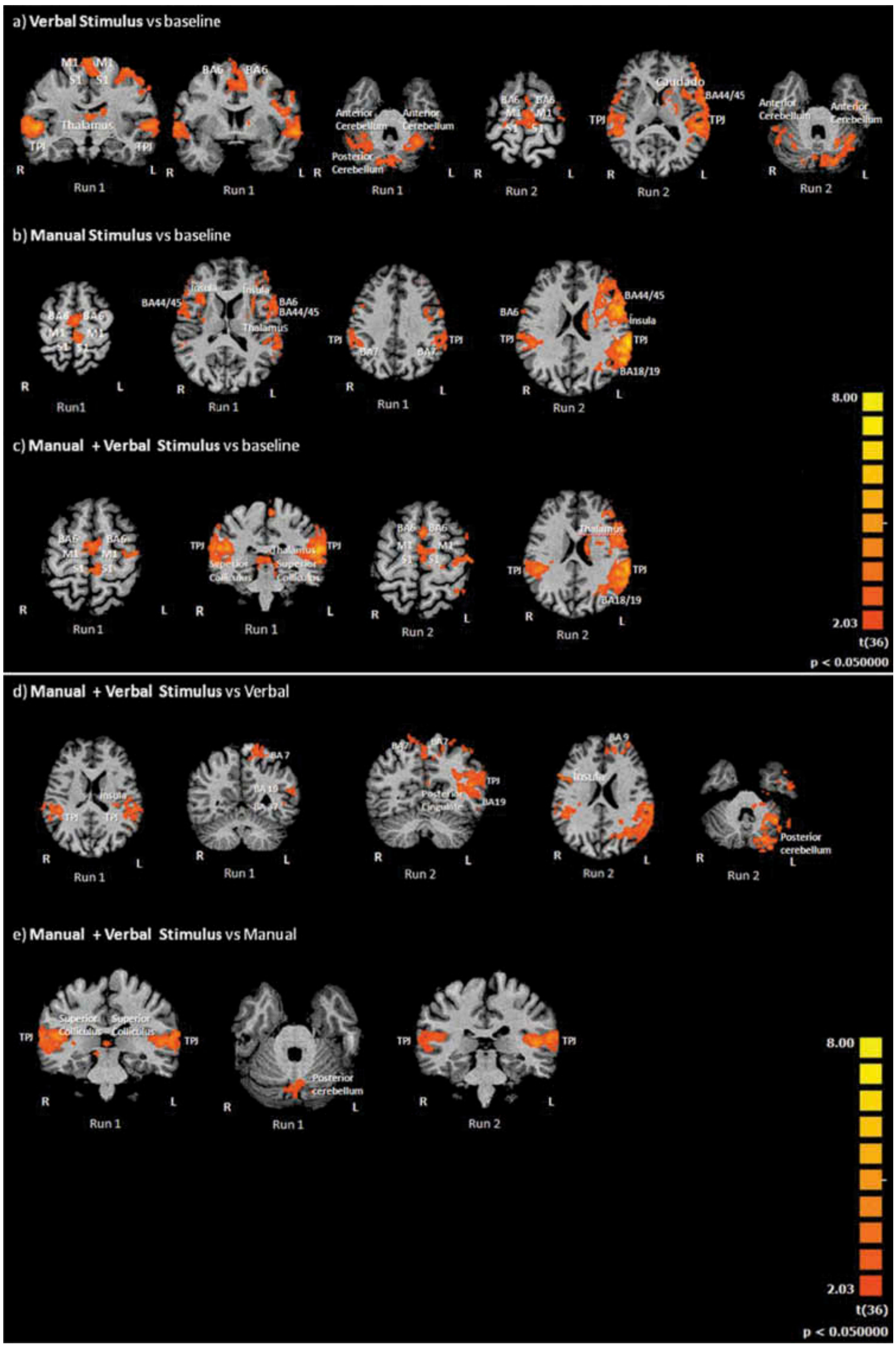

Figure 1. Statistical maps of activation for lower-limb stimulation.
BA: Brodmann area; R: right hemisphere; L: left hemisphere; Run 1: right leg; Run 2: left leg.

Table 4. Clusters of activations.

			Center of mass*					Peak Voxel*								
Contrast	Run	Cluster	x	Y	z	Region area	BA	x	y	Z	Region area	BA	Other BA included in the cluster	Nº Voxels	t-test	p-value
Auditory-verbal	Right	1	52.13	−7.25	4.22	R. Superior Temporal Gyrus-Temporoparietal Junction	R 22	50	−17	6	R. Superior Temporal Gyrus-Temporoparietal Junction	R 22	R 39,40,41	22477	8.03	P < 0. 000001
vs		2	37.23	−53.17	−28.12	R. Cerebellum – Anterior lobe – Culmen (IV&V)	–	32	−44	−27	R. Cerebellum – Anterior Lobe – Culmen (IV&V)	-	-	5825	6.11	P < 0.000001
Baseline		3	3.44	−78.30	−24.66	R. Cerebellum – Posterior Lobe – Pyramis (VIII)	–	17	−80	−30	R. Cerebellum – Posterior Lobe –Pyramis (VIII)	-	-	3623	4.15	P < 0.000193
		4	0.08	−5.37	56.31	L. Medial Frontal Gyrus	L 4	2	−5	57	R. Medial Frontal Gyrus	R 4	R&L S1 R& L 6	7089	5.59	P < 0.000003
		5	−0.10	−19.21	9.08	L. Thalamus – Medial Dorsal Nucleus	–	2	−11	12	R. Thalamus – Medial Dorsal Nucleus	-	-	3621	4.28	P < 0.000130
		6	−36.48	−53.19	−27.76	L. Cerebellum – Anterior lobe – Culmen (IV&V)	–	−31	−53	−30	L. Cerebellum – Anterior lobe – Culmen (IV&V)	-	-	4332	6.03	P < 0.000002
		7	−53.33	−11.91	13.13	L. Superior Temporal Gyrus-Temporoparietal Junction	L 42	−58	−29	12	L. Superior Temporal Gyrus-Temporoparietal Junction	L 42	L 22,39,40,41	33197	7.81	P < 0.000001
	Left	1	51.74	−14.23	4.90	R. Superior Temporal Gyrus – Temporoparietal Junction	R 22	44	−26	−3	R. Superior Temporal Gyrus-Temporoparietal Junction	R 22	R 39,40,41,42	12249	5.14	P < 0.000011
		2	38.98	−46.91	−27.51	R. Cerebellum–Anterior lobe-Culmen	–	50	−38	−30	R. Cerebellum – Anterior lobe - Culmen	-	-	2575	4.52	P < 0.000065
		3	−18.67	−62.19	−26.62	L. Cerebellum-Anterior Lobe-Culmen (IV&V)	–	−34	−50	−30	L. Cerebellum-Anterior Lobe-Culmen (IV&V)	-	-	7098	5.52	P < 0.000004
		4	−2.55	−7.07	57.15	L. Medial Frontal Gyrus	L 4	−1	−17	66	L. Medial Frontal Gyrus	L 4	R&L S1 R 4 R&L 6	5643	5.42	P < 0.000005
		5	−14.34	−2.16	12.67	L. Thalamus-Anterior Ventral Nucleus		−13	−8	21	L. Caudado	-	-	2883	5.05	P < 0.000014
		6	−51.09	−9.63	15.09	L. Inferior Frontal Gyrus	L44	−52	10	24	L. Inferior Frontal Gyrus	L44	L 45,46, L. Ínsula L TPJ	62346	6.64	P < 0.000001
Tactile-manual vs baseline	Right	1	52.13	−33.32	27.21	R. Inferior Parietal Lobule-Temporoparietal Junction	R 40	56	−26	18	R. Parietal Postcentral Gyrus- Temporoparietal Junction	R 40	R 7, 39	6425	4.81	P < 0.000028
		2	43.74	11.85	14.22	R. Ínsula	R 13	50	25	12	R. Inferior Frontal Gyrus	R 45	R. 44	8976	4.75	P < 0.000032
		3	−2.90	−8.26	55.66	L. Medial Frontal Gyrus	L 4	−4	−2	60	L. Medial Frontal Gyrus	L 4	L&R S1 R 4 L&R 6	6269	4.6	P < 0.000051
		4	−9.89	−19.25	10.74	L. Thalamus-Medial Dorsal Nucleus	–	−16	−17	15	L. Thalamus-Ventral Lateral Nucleus	-	-	1678	4.22	P < 0.000155
		5	−48.60	11.95	14.03	L. Inferior Frontal Gyrus	L 44	−58	1	30	L. Frontal Precentral Gyrus	L 6	L Anterior Ínsula	14594	5.69	P < 0.000003
		6	−55.40	−36.48	26.33	L. Inferior Parietal Lobule-Temporoparietal Junction	L 40	−55	−38	33	L Supramarginal Gyrus-Temporoparietal Junction	L 40	L 7, 39	10490	4.84	P < 0.000025
	Left	1	51.88	−29.74	23.61	R. Inferior Parietal Lobule-Temporoparietal Junction	R 40	50	−32	24	R. Inferior Parietal Lobule-Temporoparietal Junction	R 40	R 39,41,42	2986	4.42	P < 0.000088
		2	48.33	7.21	28.52	R. Inferior Frontal Gyrus	R 44	45	−5	51	R. Frontal Precentral Gyrus	R 6	-	3163	4.55	P < 0.000059
		3	−37.52	−19.48	15.59	L. Posterior Ínsula	L13	−64	−32	21	L. Superior Temporal Gyrus-Temporoparietal Junction	L 40	L 18, 19,22,39,41,42,44,45, 46	152836	8.77	P < 0.000001

(*Continued*)

Table 4. (Continued).

Center of mass*								Peak Voxel*								
Contrast	Run	Cluster	x	Y	z	Region area	BA	x	y	Z	Region area	BA	Other BA included in the cluster	Nº Voxels	t-test	p-value
(Tactile-manual + auditory-verbal) vs baseline	Right	1	52.49	−17.44	9.56	R. Superior Temporal Gyrus- Temporoparietal Junction	R 41	53	−20	12	R. Superior Temporal Gyrus- Temporoparietal Junction	R 22	R 39,40, 41,42	29815	8.76	P < 0.000001
		2	−2.00	−13.46	60,56	L.Medial Frontal Gyrus	L 4	2	−5	57	R.Medial Frontal Gyrus	R 4	R & L S1 R & L 6	6600	4.85	P < 0.000025
		3	−5.60	−23.80	2.98	L. Thalamus	-	−16	−17	15	L. Thalamus-Ventral Lateral Nucleus	-	L & R Superior Colliculus	2753	5.25	P < 0.000008
		4	−52.75	−20.28	14.19	L. Superior Temporal Gyrus- Temporoparietal Junction	L 41	−58	−29	12	L. Superior Temporal Gyrus- Temporoparietal Junction	L 22	L 39,40,41,42	44650	9.41	P < 0.000001
	Left	1	52.07	−21.74	12.09	R. Superior Temporal Gyrus – Temporoparietal Junction	R 41	50	−11	6	R. Superior Temporal Gyrus- Temporoparietal Junction	R 22	R 39,40	13158	5.97	P < 0.000002
		2	−1.26	−9.09	58.45	L Medial Frontal Gyrus	L 4	−1	−17	66	L Medial Frontal Gyrus	L4	R & L S1 R&L 6 R & L 4	4914	5.3	P < 0.000007
		3	−15.13	−7.06	11.15	L. Thalamus-Ventral Lateral Nucleus	–	−13	−14	3	L. Thalamus-Ventral Lateral Nucleus	-	-	4363	4.9	P < 0.000021
		4	−47.66	−24.72	12.45	L Superior Temporal Gyrus - Temporoparietal Junction	L 41	−58	−29	12	L. Superior Temporal Gyrus- Temporoparietal Junction	L 22	L 18,19,39,40,41,42	98687	8.93	P < 0.000001
(Tactile-manual + auditory-verbal) vs	Right	1	51.16	−30.72	20.22	R. Ínsula	R 13	53	−20	12	R. Superior Temporal Gyrus- Temporoparietal Junction	R 22	R 39, 40,41,42	3782	4.47	P < 0.000075
auditory-verbal		2	−15.64	−49.25	58.41	L. Superior Parietal Lobe	L 7	−16	−47	57	L. Parietal Lobe-Precuneus	L 7	-	1428	5.69	P < 0.000003
		3	−38.86	−12.24	4.13	L. Ínsula	L 13	−37	−17	0	L. Ínsula	L 13	-	1491	4.48	P < 0.000074
		4	−54.86	−35.88	19.47	L. Ínsula	L 13	−58	−29	15	L. Superior Temporal Gyrus- Temporoparietal Junction	L 22	L 39, 40,41,42	4965	4.22	P < 0.000157
		5	−50.88	−61.51	−6.13	L. Middle Occipital Gyrus	L 19	−52	−65	−12	L. Temporal Fusiform Gyrus	L 19	L 37	1535	4.13	P < 0.000202
	Left	1	46,91	−29.61	19.48	R. Ínsula	R 13	47	−35	21	R. Ínsula	R 13	-	2156	4.02	P < 0.000278
		2	1.65	−49.35	57.52	R. Medial Parietal Lobe-Precuneus	R 7	20	−50	66	R. Parietal Postcentral Gyrus-Precuneus	R 7	L 7	3342	6.33	P < 0.000001
		3	−9.55	49.94	26.61	L. Medial Prefrontal Cortex	L 9	−4	52	30	L. Medial Prefrontal Cortex	L 9	-	4000	4.24	P < 0.000148
		4	−12.25	−95.32	−14.79	L. Occipital Lingual Gyrus	L 17	−13	−95	−21	L. Cerebellum Posterior Lobe-Uvula (IX)	-	-	1934	4.42	P < 0.000087
		5	−2.50	−49.17	5.80	L. Posterior Cingulate	L 30	−1	−47	15	L. Posterior Cingulate	L 30	-	1409	4.4	P < 0.000093
		6	−48.36	−40.37	17.89	L. Superior Temporal Gyrus- Temporoparietal Junction	L 39	−46	−56	12	L. Middle Temporal Gyrus- Temporoparietal Junction	L 39	L 18,19,22,40,42	41592	5.28	P < 0.000007
		7	−25.20	−74.01	−33.82	L. Cerebellum Posterior Lobe-Pyramis (VIII)	–	−28	−65	−42	L. Cerebellum-Posterior/ Inferior - Semi-Lunar Lobe (HVII)	-	-	3241	4.5	P < 0.000068

(*Continued*)

Table 4. (Continued).

			Center of mass*					Peak Voxel*								
Contrast	Run	Cluster	x	Y	z	Region area	BA	x	y	Z	Region area	BA	Other BA included in the cluster	Nº Voxels	t-test	p-value
(Tactile-manual + auditory-verbal) vs tactile-manual	Right	1	53.61	−16.26	4.93	R. Superior Temporal Gyrus-Temporoparietal Junction	R 41	53	−14	3	R. Superior Temporal Gyrus-Temporoparietal Junction	R 22	R 38,39,40	16221	8.63	P < 0.000001
		2	2.17	−35.05	−2.32	R. Midbrain-Superior Colliculum	–	8	−29	0	R. Midbrain- Superior Colliculum	L Superior Colliculum	-	1572	4.06	P < 0.000247
		3	−1.06	−71.94	−24.15	L. Cerebellum-Posterior Lobe-Vermis - Pyramis (VIII)	–	−1	−74	−30	L. Cerebellum-Posterior Lobe- Vermis - Pyramis (VIII)	-	-	2074	3.62	P < 0.000899
		4	−56.52	−22.84	5.53	L. Superior Temporal Gyrus-Temporoparietal Junction	L 41	−58	−29	12	L. Superior Temporal Gyrus-Temporoparietal Junction	L 22	L 38,39,40	16035	7.15	P < 0.000001
	Left	1	54.27	−19.29	7.15	R. Superior Temporal Gyrus-Temporoparietal Junction	R 41	47	−14	6	R. Superior Temporal Gyrus-Temporoparietal Junction	R 22	R 39.42	7679	5.11	P < 0.000012
		2	−55.59	−24.13	5.86	L. Superior Temporal Gyrus-Temporoparietal Junction	L 41	−46	−23	3	L. Superior Temporal Gyrus-Temporoparietal Junction	L 22	L 39.42	16369	7.55	P < 0.000001

*Talairach coordinates; BA: Brodmann area; R: right hemisphere; L: left hemisphere; S1: primary somatosensory cortex.

For the left lower limb, two of the six clusters also revealed a high activation volume (Figure 1a, Table 4).

The cluster with the greatest volume is the number 6 and has both its CoM and Peak Voxel level at left BA44 (No. voxels = 62346; t (36) = 6.64; $p < 0.000001$ for left hemisphere) and includes left TPJ, left insula, and left BA45 and 46. The other one (number 1) corresponds to the activation of the right TPJ and has both its CoM and Peak Voxel level at BA22 (No. voxels = 12249; t (36) = 5.14; $p < 0.000011$) and extends to right BA39, 40, 41, 42 (Figure 1a, Table 4).

S1 and M1 activations are located in the lower-limb representation (sensorimotor homunculus).

Unisensory tactile-manual stimulation versus baseline

For the right lower limb, tactile-manual stimulation elicits a statistically significant (RFX, $p = 0.05$, corrected) activation in bilateral TPJ, thalamus, contralateral BA4 (extending to hipsilateral BA4, bilateral S1, and bilateral BA6, located in the lower-limb sensorimotor representation), and BA44 and BA6 (near Broca's area). Cluster 5 is the one with the greatest volume of activation has its CoM at left BA44 and Peak Voxel level at left BA6 (No. voxels = 14594; t (36) = 5.69; $p < 0.000003$) and includes the left BA13—anterior insula (Figure 1b, Table 4).

For the left lower limb, tactile-manual stimulation elicits a statistically significant (RFX, $p = 0.05$, corrected) bilateral TPJ, and contralateral BA6. The cluster with the greatest activation volume is the number 3 and was detected in left TPJ, with the CoM in left BA13—posterior insula and Peak Voxel at left BA40 (No. voxels = 152836; t (36) = 8.77; $p < 0.000001$) and includes left BA18, 19, 22, 39, 41, 42, 44, 45, 46 (Figure 1b, Table 4).

Multisensory stimulation (unisensory tactilemanual + unisensory auditory-verbal) versus baseline

For the right lower limb, multisensory stimulation with tactile-manual and auditory-verbal stimulus elicits a statistically significant (RFX, $p = 0.05$, corrected) activation in bilateral TPJ, contralateral thalamus (extending to bilateral superior colliculus) and bilateral S1, M1-BA4, and BA6 (located in the lower-limb sensorimotor representation). The two clusters with the greatest activation volume (number 1 and 4) were found in the TPJ and have their CoM at BA41 and Peak Voxel at BA22 (No. voxels = 29815; t (36) = 8.76; $p < 0.000001$ for the right hemisphere and No. voxels = 44650; t (36) = 9.41; $p < 0.000001$ for the left hemisphere). Those clusters also include bilateral BA39, 40, 41, and 42 activations (Figure 1c, Table 4).

For the left lower limb, we have detected activations in bilateral TPJ, ipsilateral Thalamus and bilateral S1, M1 M1–BA4, and BA6 (located in the lower-limb sensorimotor representation). The two clusters with the greatest activation volume (number 1 and 4) were found in the TPJ and have their CoM at BA41 and Peak Voxel at BA22 (No. voxels = 13158; t (36) = 5.97; $p < 0.000002$ for the right hemisphere and No. voxels = 98687; t (36) = 8.93; $p < 0.000001$ for the left hemisphere). Those clusters also include, respectively, right BA39, 40, and left BA18, 19, 39, 40, 41, 42 (Figure 1c, Table 4).

Multisensory stimulation versus unisensory auditory-verbal stimulation

Compared with auditory-verbal stimulus, multisensory stimulation for the right lower limb elicits a statistically significant (RFX, $p = 0.05$, corrected) activation in bilateral TPJ and contralateral BA7 (precuneus), BA13 (insula), and BA19 (extending to BA37). The two clusters with the greatest activation volume (number 1 and 4) were found in the TPJ.

Cluster 1 has its CoM at BA13 and Peak Voxel level at BA22 (No. voxels = 3782; t (36) = 4.47; $p < 0.000075$ for the right hemisphere) and includes BA 39, 40, 41, and 42. Cluster 4 has its CoM at BA13 and Peak Voxel level at BA22 (No. voxels = 4965; t (36) = 4.22; $p < 0.000157$ for the left hemisphere) and includes BA22, 39, 40, 41, and 42 (Figure 1d, Table 4).

For the left lower limb elicits a statistically significant (RFX, $p = 0.05$, corrected) activation in ipsilateral TPJ, BA9, BA30 (posterior cingulate), posterior cerebellum, contralateral BA13 (insula), and bilateral BA7 (precuneus) (Figure 1d, Table 4). Cluster 1 is the one with the greatest activation volume and has both CoM and Peak Voxel level at BA39 (No. voxels = 41592; t (36) = 5.28; $p < 0.000007$ for the left hemisphere) and includes BA 18, 19, 22, 40, and 42 (Figure 1d, Table 4).

Multisensory stimulation versus unisensory tactile-manual stimulation

Compared with tactile-manual stimulus, multisensory stimulation for the right and left lower limb elicits a statistically significant (RFX, $p = 0.05$, corrected) activations at bilateral TPJ. Specifically, for the right lower limb, we detected activation at bilateral superior colliculus, and contralateral posterior cerebellum (Figure 1e, Table 4).

For the right lower limb, we detect four clusters and the two clusters with the greatest activation volume (number 1 and 4) were found in the TPJ. Cluster 1 has its CoM at BA41 and Peak Voxel level at BA22 (No. voxels = 16221; t (36) = 8.63; $p < 0.000001$ for the right hemisphere) and includes BA 38, 39, and 40. Cluster 4 has its CoM at BA41 and Peak Voxel level at BA22 (No. voxels = 16035; t (36) = 7.15; $p < 0.000001$ for the left hemisphere) and includes BA38, 39, and 40.

For the left lower limb, we detect two clusters with the greatest activation volume in the TPJ. Cluster 1 has its CoM at BA41 and Peak Voxel level at BA22 (No. voxels = 7.679; t (36) = 5.11; $p < 0.000012$ for the right hemisphere) and includes BA39 and 42. Cluster 2 has its CoM at BA41 and Peak Voxel level at BA22 (No. voxels = 16.369; t (36) = 7.55; $p < 0.000001$ for the left hemisphere) and includes BA39 and 42 (Figure 1e, Table 4).

Discussion

Brain map for unisensory Self-referential stimulation

As we can infer from our results the first hypothesis was corroborated, because alongside with activity in TPJ, ínsula and BA44, cortical (S1, BA4, and BA6), and subcortical (thalamus and cerebellum) midline structures were activated by the tactile-manual and auditory-verbal unisensory stimuli provided. This fact is supported by other studies (LeDoux 2003; Northoff et al. 2006) that also claim that if Self-referential processing is supported by sensory processing and linked to it, we should observe activations in both subcortical and cortical midline regions.

There is a predominance of activations in the left cerebral hemisphere. Literature points out some reasons for this such as: (1) the left-hemisphere lateralization for the phonological and semantic processing (Binder et al. 2009); and (2) the right handedness and footedness of the subjects (Jirak et al. 2010). In the case of this study, all subjects are right handed and right footed.

Unisensory Self-referential stimulation trigger bilateral activation of sensorimotor areas (S1, BA4, and BA6) located in the lower-limb sensorimotor representation. All investigations agree that the S1 area has a prominent contralateral response. Nevertheless, recent evidence (Tamè et al. 2012) revealed that S1 contributes to the spatial coding of touch by discriminating between different body parts and integrates the somatosensory input coming from the two sides of the body. These findings also corroborate the fact that body parts are not perceived per se, but they imply a sense of the whole body system (Borghi and Cimatti 2010). Several studies (Bao et al. 2012; Davis et al. 1998; Fabri et al. 2005; Tamè et al. 2012) also demonstrated that unilateral stimulation of the human lower limb can elicit activations in bilateral S2, and in a recent study (Almeida et al. 2015), activations were detected in bilateral S1, BA4, and BA6 for the lower limb movement with tactile-manual and auditory-verbal stimulation.

One of the reasons that explains bilateral activations in S1 and S2 is that there are direct projections from somatosensory inputs to ipsilateral S1 (besides contralateral projections) and also that thalamic projections and contralateral S1 and S2 information are sent through the corpus callosum to ipsilateral S1 and S2 (Blankenburg et al. 2008; Tamè et al. 2012). Another reason linked specifically with lower limbs and supported by literature (Selzer et al. 2006) could be related to the central pattern generators (i.e., gait is the lower limbs´ main function and the rhythmic movement between the two legs is managed by a central pattern generator that corrects imperfect sensory feedback and adapts central input to the peripheral input).

Movement is critical for developing the sense of our own body. Nevertheless, the sense of body is previously grounded in sensations rather than in agency. Literature about embodied cognition is only focused on action and less on Self-sensing the body (Borghi and Cimatti 2010) and unfortunately, according to the most radical interpretation of embodied cognition theory, action is the core of embodied cognition.

The most significant embodied theory of cognition is the mirror neuron theory, which claims that the motor system is automatically activated when conceptual and perceptual tasks are performed (i.e., when processing auditory-verbal stimuli (action verbs); when observing another person's body performing actions or manipulating objects (Mahon and Caramazza 2008); and also when performing tasks that comprise words or verbs related to the body parts (Jirak et al. 2010).

However, the motor system (BA4 and BA6) is also engaged in mental operation tasks that do not involve any movement (Georgopoulos 2000; Hanakawa et al. 2002). These areas are considered the key to associate symbolic cues and responses in both motor and non-motor behaviors, such as deciphering the meaning of words, introspection, and thoughts (Clark 2006; Hanakawa et al. 2002). In fact, thinking allows us to have Self-consciousness, and this is linked to Self-representation (i.e., we observe our physical or mental state, thus obtaining an internal image of ourselves) (Legrand 2007). Other authors (Rochat and Striano 2000; Ruby and Legrand 2007) claim that sensory stimulation related to the body is crucial to explain our intuitive perception of being located where the body is felt.

The most important dimension of the Self is the feeling of one's body. The interconnections of different modalities of sensory information with proprioception and with the motor system provide a solid and lasting signature of the Self. In particular, sensorimotor cortices code for some abstract and global representation of the boundary between the Self and the external world (Ruby and Legrand 2007; Tsakiris 2010).

The unisensory tactile-manual and auditory-verbal stimulus related to feeling the body elicits strong activation in BA44. The most recent literature confirms the interaction between semantic knowledge and sensorimotor processes. Embodied cognition theory also proposes that in order to understand a sentence, we simulate the perceptual processes that sustained the task meaning (Caramazza et al. 2014). In fact, BA44 is involved in nonverbal functions, such as working memory, attention in speech, mirror neuron system, and object manipulation, but also in a variety of language tasks, including production, comprehension, processing, syntactic information as well as word and sentence processing (Bedny et al. 2007; Bookheimer 2002; Embick et al. 2000)

BA 44 also seems to be responsible for the congruence of the words related to the body and respective movement (Josse et al. 2012) because some aspects of semantic knowledge about words are stored in the form of motor representations (Caramazza et al. 2014) and body schema is reflected in lexical–semantic representations (Rueschemeyer et al. 2010). Findings from other studies (Borghi and Cimatti 2010; Gianelli et al. 2013; Goldman and De Vignemont 2009; Schaefer et al. 2012) suggest that the body is always an acting body, and that language is also a form of action.

Bernal et al. (2015) also confirmed that the BA44 is part of a language functions network, along with anterior insula, BA6 and BA4, with connections to cerebellum. In fact, for auditory-verbal stimulus we observed the involvement of the anterior and posterior cerebellum, and for the tactile-manual stimulus, the activation of the anterior insula. Unisensory auditory-verbal Self-referential stimulation and unisensory tactile-manual Self-referential stimulation elicits strong and significant activation of bilateral TPJ.

Studies relating unisensory stimuli, similar to those applied in this investigation, with the Self, concluded that: (1) in touch experiences, the differentiation between Self and other is based on a network of brain regions that supports a sense of the Bodily-Self, comprising TPJ, precentral gyrus and posterior parietal cortex (Ebisch et al. 2011); (2) faced with a tactile stimulus, TPJ, alongside with other structures, helps to promote the consciousness of this stimulus (Gallace and Spence 2008); (3) there is a convergence of somatosensory, auditory and visual responses in this region (Matsuhashi et al. 2004); and (4) unisensory processing of Self-referential stimulation provide an input to the multisensory processes in TPJ (Gallace and Spence 2008; Serino et al. 2013).

In fact, TPJ is responsible for multisensory processing. Several functional imaging studies, performed with normal subjects and patients with perceptive problems, reported the involvement of this region in multisensory stimulation, in cognitive and behavioral tasks related to the Self. They conclude that TPJ: (1) is essential for Self-location, for maintaining a coherent sense of one's body, and for visuospatial perspective, because it receives visual, tactile, auditive, proprioceptive, and vestibular signals of the body orientation within the environment (Serino et al. 2013); (2) encodes a map of auditory information crucial for articulatory representations, kept in premotor cortex (Josse et al. 2012); (3) possess an internal model of the body that is capable of determining whether sensory events belong to one's own body (Orlov et al. 2010); (4) is involved in the attention process, responding to significant stimuli or tasks (Geng and Vossel 2013); (5) is activated during mental state reasoning in adults, in Theory of Mind, and in mental imagery of one's own body (Blanke et al. 2005); (6) is involved in vestibular processing and in the perception of human bodies or body parts (Blanke and Arzy 2005); and (7) is a crucial region for conscious experience of the normal Self (Blanke et al. 2005).

Brain map for multisensory Self-referential stimulation

Due to lack of consensus in literature of the most appropriate criteria for the detection of regions of multisensory integration, Goebel and van Atteveldt (2009) recommend that whatever the options, the results should all be presented, described, and analyzed in the greatest detail possible.

Multisensory Self-referential stimulation elicits bilateral activations of the TPJ, of the primary somatosensory cortex (S1), of the primary motor cortex (BA4), and of the premotor cortex (BA6).

Compared with tactile-manual unisensory Self-referential stimulation, multisensory Self-referential stimulation showed activity in the: (1) bilateral TPJ; (2) bilateral superior colliculum; and (3) left posterior cerebellum. Literature shows that the left cerebellar hemisphere is engaged in language processing (Jirak et al. 2010) and that the posterior lobe is involved in higher-level tasks with an important role in language, spatial, and cognitive functions (implicated in prefrontal-cerebellar loops), and in emotional processing associated with the cerebellar-limbic circuit (Stoodley et al. 2012). The cerebellum is also an interface between motor and sensory events, and the sensory inputs from different modalities reach the cerebellum through the superior colliculum (Glickstein et al. 2011; Manni and Petrosini 2004). The posterior cerebellum is also responsible for the homunculus representation of the lower limb in the posterior lobe (Manni and Petrosini 2004).

Compared with auditory-verbal unisensory Self-referential stimulation, multisensory Self-referential stimulation elicits activity: (1) in cortical and subcortical midline structures—BA7 (precuneus), left BA9 (medial prefrontal cortex), left BA30 (posterior cingulated), and left posterior cerebellum. BA7, BA9, and BA30 are regions that are repeatedly activated in studies related to the Self. Northoff et al. (2006) demonstrated that there is a consistent activity in the cortical-subcortical midline system that underlies the human Self. They have also pointed out that Self-referential processing in those regions constitutes the Core of our Self and their activation is observed in Self-referential tasks across all domains and sensory modalities; and (2) in posterior lateral cortex (such as bilateral TPJ, bilateral posterior BA13 (insula), left BA19, and left BA37). Regarding all these structures, bilateral TPJ is the one that showed the biggest activation volume. Posterior bilateral insula activations were also detected in multisensory Self-referential stimulation compared with unisensory auditory-verbal stimulation. This result is in line with previous studies (Tsakiris et al, 2007a) that claim that the posterior insula is responsible for attribution of body parts to oneself in the absence of motor action, thus insular activity may reflect body-ownership rather than reflecting agency. The posterior insula also belongs to a sensorimotor network for body-ownership, transforming sensory inputs into feelings (Craig 2003; Ferri et al. 2012; Tsakiris 2010). Björnsdotter et al. (2009) state that gentle touch is processed in the posterior insular cortex, and one of the stimuli used in multisensory stimulation is based on gentle touch. Regarding the activation of left BA19 and BA37 with multisensory Self-referential stimulation compared to baseline and compared with unisensory auditory-verbal stimulation, some researchers (Dehaene et al. 2002; Gardini et al. 2005; Olivetti Belardinelli et al. 2009) suggest that these areas are involved in sensory mental imagery experiences, supported by different brain networks, depending on the type of image that needs to be generated, which involves also the frontal (BA9), parietal (BA13), and temporal regions (mostly BA40).

As regards the activation produced in our study, during multisensory stimulation, many researchers (Ebisch et al. 2011; Ferri et al. 2012; Fu et al. 2006; Jirak et al. 2010; Kuehn et al. 2012; Northoff and Bermpohl 2004; Ruby and Legrand 2007; Sperduti et al. 2011; Suzuki et al. 2013; Tamè et al. 2012; Tsakiris et al. 2010; Yaoi et al. 2009) who investigated the cerebral correlations of a common and unique Self, link all the abovementioned structures to several dimensions of the Self.

Some authors support the existence of a brain network comprising a few of the regions also found in our experience such as the medial prefrontal cortex (BA9), precuneus (BA7), posterior cingulate gyrus (BA30), and TPJ (Ciavarro et al. 2012; Ruby and Legrand 2007). Nevertheless, Ruby and Legrand (2007) stated that these brain network cannot be considered Self-specific because the activation of the regions that form the network could be explained also by the reasoning involved in the evaluation of the sensory inputs using the information stored in memory. They also argued that sensorimotor integration may also play an important role in the construction of the Self.

Our experiment seems to indicate that Self-referential multisensory inputs related to the body, more than unisensory ones, produce an activation map in regions that are responsible for multisensory Self-processing, thus confirming the second hypothesis. Actually, we live in a multisensory environment, and the interaction between our genetic heritage and this environment defines and reorganizes our brains at every moment. Our brain has a large capacity for automatic and simultaneous integration and processing of multisensory information (Johansson 2012).

For these reasons, in order to achieve a Self adjusted to reality, there has to be a constant updating of sensory and motor representations (Tsakiris et al. 2007b). Recent research in older adults (Freiherr et al. 2013) has shown that there is a stabilization or an increase of brain multisensory processing, despite the decline in unisensory systems during aging, and our sample seems to demonstrate the integrity of multisensory processing. It is important to highlight that this process is very important for body perception, for the processing of emotions, and for the stability of the aging Self (Coleman et al. 1999).

Sensory stimuli (visual, auditive, tactile, and proprioceptive) are perceived through sensory organs distributed on the body surface. Nevertheless, the body is perceived as a unique entity and not as a set of fragmented parts (Gentile et al. 2015; Tessari et al. 2010). When the stimuli are addressed to a particular body part, sensory information is processed in sensorimotor brain areas related to that body part. However, there is a process that transforms sensation of the body parts in a single and unique body perception. Some facts support this process: (1) throughout our body, there are neurons with large visual, auditory, tactile, and proprioceptive receptive fields; (2) there is a multisensory interplay in low level cortical structures, considered until recently as unisensory areas (primary sensory cortices); and (3) neuronal populations exist in specific high level multisensory brain areas that process multisensory information provided by the body (Cappe et al. 2009; Driver and Noesselt 2008; Gazzola et al. 2012; Keysers et al. 2010; Petkova et al. 2011; Schroeder and Foxe 2005).

Implications for physiotherapy practice

The results of this study may guide new clinical reasoning because, if we apply the multisensory Self-referential stimulation with tactile-manual and auditory-verbal stimuli (appealing to feel body parts), we can contribute to the Self-Consciousness and Identity, helping to maintain the stability of the Self or its reorganization (Tajadura-Jiménez et al. 2012). Furthermore, the results may represent an effective strategy for promoting better perceptual learning. In fact, perceptual learning allows a cerebral reorganization and has an important impact in different dimensions, such as cognitive and motor dimensions (Cuppini et al. 2011; Shimojo and Shams 2001).

We also highlight the need for the use of meaningful stimuli for the subject because some brain areas responsible for the multisensory processing are activated strongly in response to meaningful stimuli (Beauchamp 2005a; Doehrmann and Naumer 2008). Also, it is essential to take into account the principles of multisensory stimulation (Freiherr et al. 2013), particularly the principle of congruence. In addition to the parameters of time and space, multisensory integration can also be influenced by the semantic congruence of the stimuli (Calvert and Thesen 2004).

It is important to notice that the unisensory stimuli applied in this study provide a direct relationship between the physiotherapist and the subject, through touch and speech. This statement needs to be considered thoroughly because not all stimuli promote a therapeutic relationship, which is a very important factor for the success of each health-related intervention. And because the way we talk and how we touch may have a negative or positive influence on the emotional condition of the individuals, the physiotherapist, when planning research studies or in clinical context, should be trained in voice projection and in affective touch. On the other hand, we have to be aware that multisensory experiences shared between ourselves and others can change the mental representation of our own identity (Tajadura-Jiménez et al. 2012).

Research implications

It is recommended to continue to study the impact of multisensory Self-referential stimulation with unisensory stimuli performed in this study on other body parts and on different outcomes (e.g., body Self-consciousness, postural control, upper and lower limb motor control, sensorial system, quality of life, gait, emotions, and cognitive function) both on healthy and non-healthy subjects, on young adults and children, as well as with larger samples. It is advisable also to use other analysis criteria to validate the brain map found, as responsible for the multisensory processing related with the Self, and in particular the Congruent versus Incongruent.

For future reference, fMRI research studies, using the same type of stimuli that was used for the current experiment, should set the procedures for functional sequences in the same run to minimize instrumental bias in order to allow for direct comparisons between right and left stimulation and to consolidate the validity of the results.

Due to the small number of subjects in the sample, this study should be considered as preliminary. In that sense it is recommended that the study should be replicated using a more robust sample size.

Conclusions

Taking into account the objectives of this study and the formulated hypothesis, we conclude that the somatotopic map of activation for unisensory auditory-verbal, for tactile-manual Self-referential stimulation, related to body parts of the lower limb in healthy subjects, elicits bilateral activations of sensorimotor areas (S1, BA4, BA6), of BA44 and of the TPJ. Specific for auditory-verbal stimulus, we found significant activation on left thalamus and on bilateral anterior and posterior cerebellum, and specific to tactile-manual stimulus, we detect significant activation in bilateral BA13 (insula) and bilateral BA44.

Moreover, the results of the multisensory Self-referential stimulation presented in our experiment offer a contribution to both the theory that Self-referential multisensory processing is the core of the Self and to the Damásio theory of a unique Self. In fact, besides the TPJ, already defined as a region of multisensorial processing related to the Self, some of the structures that belong to the cortical and subcortical midline structures also seem to be responsible for the multisensorial processing of this particular multisensorial Self-referential stimulus. This multisensory processing is supported by sensorimotor integration.

These findings seem to indicate that multisensory Self-referential processing of multisensorial Self-referential stimuli is mediated by (1) sensorimotor areas; (2) TPJ; (3) cortical and subcortical midline structures. This processing in these structures may represent the Self-Core.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the article.

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References

Aichhorn M, Perner J, Weiss B, Kronbichler M, Staffen W, Ladurner G. 2009. Temporo-parietal junction activity in theory-of-mind tasks: Falseness, beliefs or attention. J Cogn Neurosci. 21:1179–92. doi:10.1162/jocn.2009.21082.

Almeida P, Vieira AI, Canário N, Castelo-Branco M, Castro Caldas A. 2015. Brain activity during lower-limb movement with manual facilitation: An fMRI Study. Neurol Res Int. 2015:1–14. doi:10.1155/2015/701452.

Anderson ML. 2003. Embodied cognition: A field guide. Artif Intell. 149:91–130. doi:10.1016/S0004-3702(03)00054-7.

Arzy S, Thut G, Mohr C, Michel CM, Blanke O. 2006. Neural basis of embodiment: Distinct contributions of temporoparietal junction and extrastriate body area. J Neurosci. 26:8074–81. doi:10.1523/JNEUROSCI.0745-06.2006.

Bao R, Wei P, Li K, Lu J, Zhao C, Wang Y, Zhang T. 2012. Within-limb somatotopic organization in human SI and parietal operculum for the leg: an fMRI study. Brain Res. 1445:30–39. doi:10.1016/j.brainres.2012.01.029.

Beauchamp MS. 2005a. See me, hear me, touch me: Multisensory integration in lateral occipital-temporal cortex. Curr Opin Neurobiol. 15:145–53. doi:10.1016/j.conb.2005.03.011.

Beauchamp MS. 2005b. Statistical criteria in FMRI studies of multisensory integration. Neuroinformatics. 3:093–114. doi:10.1385/NI:3:2.

Bedny M, Hulbert JC, Thompson-Schill SL. 2007. Understanding words in context: The role of Broca's area in word comprehension. Brain Res. 1146:101–14. doi:10.1016/j.brainres.2006.10.012.

Bekrater-Bodmann R, Foell J, Kamping S. 2011. The importance of ventral premotor cortex for body ownership processing. J Neurosci. 31:9443–44. doi:10.1523/JNEUROSCI.2302-11.2011.

Bernal B, Ardila A, Rosselli M. 2015. Broca's area network in language function: A pooling-data connectivity study. Front Psychol. 6:687. doi:10.3389/fpsyg.2015.00687.

Binder JR, Desai RH, Graves WW, Conant LL. 2009. Where is the semantic system? A critical review and meta-analysis of 120 functional neuroimaging studies. Cereb Cortex. 19:2767–96. doi:10.1093/cercor/bhp055.

Björnsdotter M, Löken L, Olausson H, Vallbo A, Wessberg J. 2009. Somatotopic organization of gentle touch processing in the posterior insular cortex. J Neurosci. 29:9314–20. doi:10.1523/JNEUROSCI.0400-09.2009.

Blanke O. 2012. Multisensory brain mechanisms of bodily self-consciousness. Nat Rev Neurosci. 13:556–71.

Blanke O, Arzy S. 2005. The out-of-body experience: Disturbed self-processing at the temporo-parietal junction. Neuroscientist. 11:16–24. doi:10.1177/1073858404270885.

Blanke O, Mohr C, Michel CM, Pascual-Leone A, Brugger P, Seeck M, Landis T, Thut G. 2005. Linking out-of-body experience and self processing to mental own-body imagery at the temporoparietal junction. J Neurosci. 25:550–57. doi:10.1523/JNEUROSCI.2612-04.2005.

Blankenburg F, Ruff CC, Bestmann S, Bjoertomt O, Eshel N, Josephs O, Weiskopf N, Driver J. 2008. Interhemispheric effect of parietal TMS on somatosensory response confirmed directly with concurrent TMS-fMRI. J Neurosci. 28:13202–08. doi:10.1523/JNEUROSCI.3043-08.2008.

Bookheimer S. 2002. Functional MRI of language: New approaches to understanding the cortical organization of semantic processing. Annu Rev Neurosci. 25:151–88. doi:10.1146/annurev.neuro.25.112701.142946.

Borghi AM, Cimatti F. 2010. Embodied cognition and beyond: Acting and sensing the body. Neuropsychologia. 48:763–73. doi:10.1016/j.neuropsychologia.2009.10.029.

Calvert GA, Thesen T. 2004. Multisensory integration: Methodological approaches and emerging principles in the human brain. J Physiol. 98:191–205.

Cappe C, Rouiller EM, Barone P. 2009. Multisensory anatomical pathways. Hear Res. 258:28–36. doi:10.1016/j.heares.2009.04.017.

Caramazza A, Anzellotti S, Strnad L, Lingau A. 2014. Embodied cognition and mirror neurons: A critical assessment. Annu Rev Neurosci. 37:1–15. doi:10.1146/annurev-neuro-071013-013950.

Carey LM. 2012. Stroke rehabilitation: insights from neuroscience and imaging. New York: Oxford University Press.

Chen JC, Shaw FZ. 2014. Progress in sensorimotor rehabilitative physical therapy programs for stroke patients. World J Clin Cases. 2:316–26. doi:10.12998/wjcc.v2.i8.316.

Chuter VH. 2012. Janse de Jonge XA 2012 Proximal and distal contributions to lower extremity injury: A review of the literature. Gait and Posture. 36:7–15. doi:10.1016/j.gaitpost.2012.02.001.

Ciavarro M, Ambrosini E, Tosoni A, Committeri G, Fattori P, Galletti C. 2012. A meta-analysis of functional neuroimaging studies of self and other judgments reveals a spatial gradient for mentalizing in medial prefrontal cortex. J Cogn Neurosci. 24:1742–52. doi:10.1162/jocn_a_00233.

Clark A. 2006. Language, embodiment and the cognitive niche. Trends Cogn Sci. 10:370–74. doi:10.1016/j.tics.2006.06.012.

Coleman PG, Ivani-Chalian C, Robinson M. 1999. Self and identity in advanced old age: Validation of theory through longitudinal case analysis. J Pers. 67:819–49. doi:10.1111/1467-6494.00074.

Craig AD. 2003. Interoception: the sense of the physiological condition of the body. Curr Opin Neurobiol. 13:500–05. doi:10.1016/S0959-4388(03)00090-4.

Cuppini C, Magosso E, Ursino M. 2011. Organization, maturation, and plasticity of multisensory integration: Insights from computational modeling studies. Front Psychol. 2:77. doi:10.3389/fpsyg.2011.00077.

Damásio A. 1999. The feeling of what happens: Body and emotion in the making of consciousness. In: Brace H, editor (1st ed.). New York: Houghton Mifflin Harcourt.

Damásio A. 2003. Mental self: The person within. Nature. 423(6937):227. doi:10.1038/423227a.

Damásio A. 2010. Self comes to mind: Constructing the conscious brain. In: Heinemann W, editors. New York: Pantheon Books.

Davis K, Kwan C, Crawley A, Mikulis D. 1998. Functional MRI study of thalamic and cortical activations evoked by cutaneous heat, cold and tactile stimuli. J Neurophysiol. 80:1533–46.

De Vignemont F. 2006. A review of Shaun Gallagher, How the body shapes the mind. Psyche. 12:1–7.

Dehaene S, Le Clec'H G, Poline J, Le Bihan D, Cohen L. 2002. The visual word form area: A prelexical representation of visual words in the fusiform gyrus. Brain Imag. 13:321–25.

Doehrmann O, Naumer MJ. 2008. Semantics and the multisensory brain: How meaning modulates processes of audio-visual integration. Brain Res. 1242:136–50. doi:10.1016/j.brainres.2008.03.071.

Driver J, Noesselt T. 2008. Multisensory interplay reveals crossmodal influences on "sensory-specific" brain regions, neural responses, and judgments. Neuron. 57:11–23. doi:10.1016/j.neuron.2007.12.013.

Ebisch SJ, Ferri F, Salone A, Perrucci MG, D'Amico L, Ferro FM, Romani GL, Gallese V. 2011. Differential involvement of somatosensory and interoceptive cortices during the observation of affective touch. J Cogn Neurosci. 23:1808–22. doi:10.1162/jocn.2010.21551.

Ehrsson HH, Ehrsson HH, Spence C, Passingham RE. 2004. That's my hand! Activity in premotor cortex reflects feeling of ownership of a limb. Science. 305:875–77. doi:10.1126/science.1097011.

Elias LJ, Bryden MP, Bulman-Fleming MB. 1998. Footedness is a better predictor than is handedness of emotional lateralization. Neuropsychologia. 36:37–43. doi:10.1016/S0028-3932(97)00107-3.

Embick D, Marantz A, Miyashita Y, O'Neil W, Sakai KL. 2000. A syntactic specialization for Broca's area. Proc Natl Acad Sci USA. 97:6150–54. doi:10.1073/pnas.100098897.

Esopenko C, Borowsky R, Cummine J, Sarty G. 2008. Mapping the semantic homunculus: A functional and behavioural analysis of overt semantic generation. Brain Topogr. 21:22–35. doi:10.1007/s10548-008-0043-8.

Essick GK, McGlone F, Dancer C, Fabricant D, Ragin Y, Phillips N, Jones T, Guest S. 2010. Quantitative assessment of pleasant touch. Neurosci Biobehav Rev. 34:192–203. doi:10.1016/j.neubiorev.2009.02.003.

Fabri M, Del Pesce M, Paggi A, Polonara G, Bartolini M, Salvolini U, Manzoni T. 2005. Contribution of posterior corpus callosum to the interhemispheric transfer of tactile information. Brain Res. 24:73–80.

Ferri F, Frassinetti F, Ardizzi M, Costantini M, Gallese V. 2012. A sensorimotor network for the bodily self. J Cogn Neurosci. 24:1584–95. doi:10.1162/jocn_a_00230.

Flor H, Diers M. 2009. Sensorimotor training and cortical reorganization. NeuroRehabilitation. 25:19–27.

Freiherr J, Lundström JN, Habel U, Reetz K. 2013. Multisensory integration mechanisms during aging. Front Hum Neurosci. 7:863. doi:10.3389/fnhum.2013.00863.

Fu C, Vythelingu G, Brammer M, Williams S, Amaro E, Andrew C, Yaguez L, van Haren NE, Matsumoto K, McGuire P. 2006. An fMRI study of verbal self-monitoring: neural correlates of auditory verbal feedback. Cereb Cortex. 16:969–77. doi:10.1093/cercor/bhj039.

Gabbard C. 2012. The role of mental simulation in embodied cognition. Early Child Dev Care. 1:37–41.

Gallace A, Spence C. 2008. The cognitive and neural correlates of "tactile consciousness": A multisensory perspective. Conscious Cogn. 17:370–407. doi:10.1016/j.concog.2007.01.005.

Gallagher S. 2000. Philosophical conceptions of the self: Implications for cognitive science. Trends Cogn Sci. 4:14–21. doi:10.1016/S1364-6613(99)01417-5.

Gardini S, De Beni R, Cornoldi C, Bromiley A, Venneri A. 2005. Different neuronal pathways support the generation of general and specific mental images. NeuroImage. 27:544–52. doi:10.1016/j.neuroimage.2005.04.032.

Gazzola V, Spezio ML, Etzel JA, Castelli F, Adolphs R, Keysers C. 2012. Primary somatosensory cortex discriminates affective significance in social touch. Proc Natl Acad Sci USA. 109:E1657–E1666. doi:10.1073/pnas.1113211109.

Geng J, Vossel S. 2013. Re-evaluating role TPJ attentional control: Contextual updating? Neurosci Biobehav Rev. 37:2608–20.

Gentile G, Björnsdotter M, Petkova VI, Abdulkarim Z, Ehrsson HH. 2015. Patterns of neural activity in the human ventral premotor cortex reflect a whole-body multisensory perception. NeuroImage. 109:328–40. doi:10.1016/j.neuroimage.2015.01.008.

Georgopoulos AP. 2000. Neural aspects of cognitive motor control. Curr Opin Neurobiol. 10:238–41. doi:10.1016/S0959-4388(00)00072-6.

Gianelli C, Scorolli C, Borghi AM. 2013. Acting in perspective: the role of body and language as social tools. Psychol Res. 77:40–52. doi:10.1007/s00426-011-0401-0.

Gillihan SJ, Farah MJ. 2005. Is self special? A critical review of evidence from experimental psychology and cognitive neuroscience. Psychol Bull. 131:76–97. doi:10.1037/0033-2909.131.1.76.

Glickstein M, Sultan F, Voogd J. 2011. Functional localization in the cerebellum. Cortex. 47:59–80. doi:10.1016/j.cortex.2009.09.001.

Goebel R, van Atteveldt N. 2009. Multisensory functional magnetic resonance imaging: A future perspective. Exp Brain Res. 198:153–64. doi:10.1007/s00221-009-1881-7.

Goldman AI. 2012. Theory of mind. In: Margolis E, Samuels R, Stich S, editors. Oxford handbook of philosophy and cognitive science. London: Oxford University Press. p. 402.

Goldman AI, De Vignemont F. 2009. Is social cognition embodied? Trends Cogn Sci. 13:154–59. doi:10.1016/j.tics.2009.01.007.

Guest S, Essick G, Dessirier JM, Blot K, Lopetcharat K, McGlone F. 2009. Sensory and affective judgments of skin during inter and intrapersonal touch. Acta Psychol. 130:115–26. doi:10.1016/j.actpsy.2008.10.007.

Gutchess AH, Kensinger EA, Schacter DL. 2010. Functional neuroimaging of self-referential encoding with age. Neuropsychologia. 48:211–19. doi:10.1016/j.neuropsychologia.2009.09.006.

Guterstam A, Bjo M, Gentile G, Ehrsson HH. 2015. Posterior cingulate cortex integrates the senses of self-location and body ownership. Curr Biol. 25:1416–25. doi:10.1016/j.cub.2015.03.059.

Hanakawa T, Honda M, Sawamoto N, Okada T, Yonekura Y, Fukuyama H, Shibasaki H. 2002. The role of rostral Brodmann area 6 in mental operation tasks: An integrative neuroimaging approach. Cereb Cortex. 12:1157–70. doi:10.1093/cercor/12.11.1157.

Hauk O, Davis MH, Kherif F, Pulvermüller F. 2008. Imagery or meaning? Evidence for a semantic origin of category-specific brain activity in metabolic imaging. Eur J Neurosci. 27:1856–66. doi:10.1111/j.1460-9568.2008.06143.x.

Hauk O, Tschentscher N. 2013. The body of evidence: what can neuroscience tell us about embodied semantics? Front Psycho. 4:50.

Jirak D, Menz MM, Buccino G, Borghi AM, Binkofski F. 2010. Grasping language: A short story on embodiment. Conscious Cogn. 19:711–20. doi:10.1016/j.concog.2010.06.020.

Johansson BB. 2012. Multisensory stimulation in stroke rehabilitation. Front Hum Neurosci. 6:60. doi:10.3389/fnhum.2012.00060.

Josse G, Joseph S, Bertasi E, Giraud A. 2012. The brain 's dorsal route for speech represents word meaning: Evidence from gesture. Plos One. 7:e46108. doi:10.1371/journal.pone.0046108.

Kemmerer D, Gonzalez-Castillo J. 2010. The two-level theory of verb meaning: An approach to integrating the semantics of action with the mirror neuron system. Brain Lang. 112:54–76. doi:10.1016/j.bandl.2008.09.010.

Keysers C, Kaas JH, Gazzola V. 2010. Somatosensation in social perception. Nat Rev Neurosci. 11:417–28. doi:10.1038/nrn2833.

Kolb B, Whishaw IQ. 1998. Brain plasticity and behavior. Annu Rev Psychol. 49:43–64. doi:10.1146/annurev.psych.49.1.43.

Kuehn E, Trampel R, Mueller K, Turner R, Schütz-Bosbach S. 2012. Judging roughness by sight - a 7-Tesla fMRI study on responsivity of the primary somatosensory cortex during observed touch of self and others. Hum Brain Mapp. 34:1882–95. doi:10.1002/hbm.22031.

Kvaal K, Ulstein I, Nordhus IH, Engedal K. 2005. The Spielberger State-Trait Anxiety Inventory (STAI): The state scale in detecting mental disorders in geriatric patients. Int J Geriatr Psychiatry. 20:629–34. doi:10.1002/(ISSN)1099-1166.

LeDoux J. 2003. The Self - Clues from de Brain. Ann NY Acad Sci. 1001:295–304. doi:10.1196/annals.1279.017.

Legrand D. 2007. Subjectivity and the body: Introducing basic forms of self-consciousness. Conscious Cogn. 16:577–82. doi:10.1016/j.concog.2007.06.011.

Lindgren L, Westling G, Brulin C, Lehtipalo S, Andersson M, Nyberg L. 2012. Pleasant human touch is represented in pregenual anterior cingulate cortex. NeuroImage. 59:3427–32. doi:10.1016/j.neuroimage.2011.11.013.

Lloyd D. 2002. Functional MRI and the study of human consciousness. J Cogn Neurosci. 14:818–31. doi:10.1162/089892902760191027.

Löken LS, Evert M, Wessberg J. 2011. Pleasantness of touch in human glabrous and hairy skin: Order effects on affective ratings. Brain Res. 1417:9–15. doi:10.1016/j.brainres.2011.08.011.

Lopez C, Halje P, Blanke O. 2008. Body ownership and embodiment: Vestibular and multisensory mechanisms. Clin Neurophysiology. 38:149–61. doi:10.1016/j.neucli.2007.12.006.

Mahon BZ, Caramazza A. 2008. A critical look at the embodied cognition hypothesis and a new proposal for grounding conceptual content. J Physiol. 102:59–70.

Mahy CE, Moses LJ, Pfeifer JH. 2014. How and where: Theory-of-mind in the brain. Dev Cogn Neurosci. 9:68–81. doi:10.1016/j.dcn.2014.01.002.

Manni E, Petrosini L. 2004. A century of cerebellar somatotopy: A debated representation. Nat Rev Neurosci. 5:241–49. doi:10.1038/nrn1347.

Matsuhashi M, Ikeda A, Ohara S, Matsumoto R, Yamamoto J, Takayama M, Satow T, Begum T, Usui K, Nagamine T, et al. 2004. Multisensory convergence at human temporoparietal junction - Epicortical recording of evoked responses. Clin Neurophysiology. 115:1145–60. doi:10.1016/j.clinph.2003.12.009.

McCabe C, Rolls ET, Bilderbeck A, McGlone F. 2008. Cognitive influences on the affective representation of touch and the sight of touch in the human brain. Soc Cogn Affect Neurosci. 3:97–108. doi:10.1093/scan/nsn005.

Northoff G, Bermpohl F. 2004. Cortical midline structures and the self. Trends Cogn Sci. 8:102–07. doi:10.1016/j.tics.2004.01.004.

Northoff G, Heinzel A, Greck M, Bermpohl F, Dobrowolny H, Panksepp J. 2006. Self-referential processing in our brain: A meta-analysis of imaging studies on the self. NeuroImage. 31:440–57. doi:10.1016/j.neuroimage.2005.12.002.

Olausson H, Wessberg J, Morrison I, McGlone F, Vallbo Å. 2010. The neurophysiology of unmyelinated tactile afferents. Neurosci Biobehav Rev. 34:185–91. doi:10.1016/j.neubiorev.2008.09.011.

Olivetti Belardinelli M, Palmiero M, Sestieri N, Di Matteo R, Londei A, D'Ausillo A, Ferretti A, Del Gratta C, Romani GL. 2009. An fMRI investigation on image generation in different sensory modalities: The influence of vividness. Acta Psychol. 132:190–200. doi:10.1016/j.actpsy.2009.06.009.

Orlov T, Makin TR, Zohary E. 2010. Topographic representation of the human body in the occipitotemporal cortex. Neuron. 68:586–600. doi:10.1016/j.neuron.2010.09.032.

Panksepp J. 2005. Affective consciousness: Core emotional feelings in animals and humans. Conscious Cogn. 14:30–80. doi:10.1016/j.concog.2004.10.004.

Panksepp J, Northoff G. 2009. The trans-species core SELF: the emergence of active cultural and neuro-ecological agents through self-related processing within subcortical-cortical midline networks. Conscious Cogn. 18:193–215. doi:10.1016/j.concog.2008.03.002.

Petkova VI, Björnsdotter M, Gentile G, Jonsson T, Li TQ, Ehrsson HH. 2011. From part to whole body ownership in the multisensory brain. Curr Biol. 21:1118–22. doi:10.1016/j.cub.2011.05.022.

Premack D, Woodruff G. 1978. Does chimpanzee have theory mind? Behav Brain Sci. 4:515–26. doi:10.1017/S0140525X00076512.

Pulvermüller F, Kherif F, Hauk O, Mohr B, Nimmo-Smith I. 2009. Distributed cell assemblies for general lexical and category-specific semantic processing as revealed by fMRI cluster analysis. Hum Brain Mapp. 30:3837–50.

Rizzolatti G, Fogassi L, Gallese V. 2002. Motor and cognitive functions of the ventral premotor cortex. Curr Opin Neurobiol. 12:149–54.

Rochat P, Striano T. 2000. Perceived self in infancy. Infant Behav Dev. 23:513–30.

Ruby P, Legrand D. 2007. Neuroimaging the self?. In: Rosseti Y, Haggard P, Kawato M, editors. Sensorimotor foundations of higher cognition. New York: Oxford University Press. pp. 293–318. doi.org/10.1037/a0014172

Rueschemeyer SA, Pfeiffer C, Bekkering H. 2010. Body schematics: On the role of the body schema in embodied lexical-semantic representations. Neuropsychologia. 48:774–81.

Schaefer M, Heinze H, Rotte M. 2012. Touch and personality: Extraversion predicts somatosensory brain response. NeuroImage. 62:432–38.

Schroeder CE, Foxe J. 2005. Multisensory contributions to low-level, "unisensory" processing. Curr Opin Neurobiol. 15:454–58.

Schurz M, Radua J, Aichhorn M, Richlan F, Perner J. 2014. Fractionating Theory of Mind: A meta-analysis of functional brain imaging studies. Neurosci Biobehav Rev. 42:9–34.

Selzer ME, Clarke S, Cohen LG, Duncan PW, Gage FH. 2006. Textbook of neural repair and rehabilitation. Vol. 2. New York: Cambridge University Press.

Serino A, Alsmith A, Costantini M, Mandrigin A, Tajadura-Jimenez A, Lopez C. 2013. Bodily ownership and self-location: components of bodily self-consciousness. Conscious Cogn. 22:1239–52.

Seth AK. 2013. Interoceptive inference, emotion, and the embodied self. Trends Cogn Sci. 17:565–73.

Shams L, Seitz AR. 2008. Benefits of multisensory learning. Trends Cogn Sci. 12:411–17.

Sheehan PW. 1967. A shortened form of Betts' questionnaire upon mental imagery. J Clin Psychol. 23:386–89.

Shimojo S, Shams L. 2001. Sensory modalities are not separate modalities: Plasticity and interactions. Curr Opin Neurobiol. 11:505–09.

Sliz D, Smith A, Wiebking C, Northoff G, Hayley S. 2012. Neural correlates of a single session massage treatment. Brain Imaging Behav. 6:77–87.

Sperduti M, Delaveau P, Fossati P, Nadel J. 2011. Different brain structures related to self and external agency attribution: A brief review and meta-analysis. Brain Struct Funct. 216:151–57.

Stoodley CJ, Valera EM, Schmahmann JD. 2012. Functional topography of the cerebellum for motor and cognitive tasks: An fMRI study. NeuroImage. 59:1560–70.

Suzuki K, Garfinkel SN, Critchley HD, Seth AK. 2013. Multisensory integration across exteroceptive and interoceptive domains modulates self-experience in the rubber-hand illusion. Neuropsychologia. 51:2909–17.

Tajadura-Jiménez A, Grehl S, Tsakiris M. 2012. The other in me: Interpersonal multisensory stimulation changes the mental representation of the self. PloS One. 7:e40682.

Tamè L, Braun C, Lingnau A, Schwarzbach J, Demarchi G, Li Hegner Y, Farne A, Pavani F. 2012. The contribution of primary and secondary somatosensory cortices to the representation of body parts and body sides: an fMRI adaptation study. J Cogn Neurosci. 24:2306–20.

Tariq SH, Tumosa N, Chibnall JT, Perry MH, Morley JE. 2006. Comparison of the Saint Louis university mental status examination and the minimental state examination for detecting dementia and mild neurocognitive disorder: A pilot study. Am J Geriatr Psychiatry. 14:900–10.

Tessari A, Tsakiris M, Borghi AM, Serin A. 2010. The sense of body: A multidisciplinary approach to body representation. Neuropsychologia. 48:643–44.

Tsakiris M. 2010. My body in the brain: A neurocognitive model of body-ownership. Neuropsychologia. 48:703–12.

Tsakiris M, Costantini M, Haggard. 2008. The role of the right temporo-parietal junction in maintaining a coherent sense of one's body. Neuropsychologia. 46:3014–18.

Tsakiris M, Hesse MD, Boy C, Haggard P, Fink GR. 2007a. Neural signatures of body ownership: A sensory network for bodily self-consciousness. Cereb Cortex. 17:2235–44.

Tsakiris M, Longo M, Haggard P. 2010. Having a body versus moving your body: Neural signatures of agency and body-ownership. Neuropsychologia. 48:2740–49.

Tsakiris M, Schütz-Bosbach S, Gallagher S. 2007b. On agency and body-ownership: Phenomenological and neurocognitive reflections. Conscious Cogn. 16:645–60.

Van Dam WO, Rueschemeyer SA, Bekkering H. 2010. How specifically are action verbs represented in the neural motor system: An fMRI study. NeuroImage. 53:1318–25.

Veldman F. 2001. Haptonomie - Science de l'Affectivité. 8th ed. Paris: Presses Universitaires de France.

Vieira AI, Ramos AV, Cavalheiro LM, Almeida P, Nogueira D, Reis E, Castro-Caldas A. 2016. Reliability and Validity of the European Portuguese Version of the Social Touch Questionnaire. J Nonverbal Behav. 40:363–377. doi.org/10.1007/s10919-016-0239-7.

Vogeley K, May M, Ritzl A, Falkai P, Zilles K, Fink GR. 2004. Neural correlates of first-person perspective as one constituent of human self-consciousness. J Cogn Neurosci. 16:817–27.

Ward L. 2013. The thalamus: Gateway to the mind. Cogn Sci. 4:609–22.

Wilhelm FH, Kochar AS, Roth WT, Gross JJ. 2001. Social anxiety and response to touch: Incongruence between self-evaluative and physiological reactions. Biol Psychol. 58:181–202.

Yaoi K, Osaka N, Osaka M. 2009. Is the self special in the dorsomedial prefrontal cortex? An fMRI study. Soc Neurosci. 4:455–63.