Increased Functional Connectivity between Superior Colliculus and Brain Regions Implicated in Bodily Self-Consciousness during the Rubber Hand Illusion

Isadora Olivé,^{1,2*} Claus Tempelmann,¹ Alain Berthoz,² and Hans-Joachim Heinze¹

¹Universitätsklinik für Neurologie, Otto-von-Guerrick Universität Magdeburg, Leipziger Chaussee 44 39120 Magdeburg SA, Deutschland

²Laboratoire de Physiologie de l'Action et de la Perception, UMR 7152, Collège de France CNRS, 11 Place Marcelin Berthelot 75005 Paris, France

Abstract: Bodily self-consciousness refers to bodily processes operating at personal, peripersonal, and extrapersonal spatial dimensions. Although the neural underpinnings of representations of personal and peripersonal space associated with bodily self-consciousness were thoroughly investigated, relatively few is known about the neural underpinnings of representations of extrapersonal space relevant for bodily self-consciousness. In the search to unravel brain structures generating a representation of the extrapersonal space relevant for bodily self-consciousness, we developed a functional magnetic resonance imaging (fMRI) study to investigate the implication of the superior colliculus (SC) in bodily illusions, and more specifically in the rubber hand illusion (RHi), which constitutes an established paradigm to study the neural underpinnings of bodily self-consciousness. We observed activation of the colliculus ipsilateral to the manipulated hand associated with eliciting of RHi. A generalized form of context-dependent psychophysiological interaction analysis unravelled increased illusion-dependent functional connectivity between the SC and some of the main brain areas previously involved in bodily self-consciousness: right temporoparietal junction (rTPJ), bilateral ventral premotor cortex (vPM), and bilateral postcentral gyrus. We hypothesize that the collicular map of the extrapersonal space interacts with maps of the peripersonal and personal space generated at rTPJ, vPM and the postcentral gyrus, producing a unified representation of space that is relevant for bodily self-consciousness. We suggest that processes of multisensory integration of bodily-related sensory inputs located in this unified representation of space constitute one main factor underpinning emergence of bodily self-consciousness. *Hum Brain Mapp* 36:717–730, 2015. © 2014 Wiley Periodicals, Inc.

Key words: bodily self-consciousness; body ownership; self-location; rubber hand illusion; superior colliculus; rTPJ; vPM; fMRI; gPPI

INTRODUCTION

Bodily self-consciousness refers to body ownership and self-location processes, and it represents the most basic manifestation of self-consciousness [Blanke and Metzinger, 2009]. Dysfunction in any of these processes has far-reaching disruptive consequences for the constitution of the conscious experience of being a subject [Blanke and Metzinger, 2009; Blanke et al., 2004; Simeon and Abugle, 2006; Vallar and Ronchi, 2008]. One main approach to the

*Correspondence to: Isadora Olivé, Universitätsklinik für Neurologie, Otto-von-Guerrick Universität Magdeburg, Leipziger Chaussee 44 39120 Magdeburg SA, Deutschland. E-mail: isadora.olive@med.ovgu.de
Conflict of interest: There is no conflict of interest to declare.

Received for publication 16 May 2014; Revised 1 September 2014; Accepted 6 October 2014.

DOI: 10.1002/hbm.22659

Published online 24 October 2014 in Wiley Online Library (wileyonlinelibrary.com).

Figure 1.

Experiments A, I sample LEFT; B, I sample RIGHT; and C, 2 manipulating a left, right and left rubber hand, respectively. Coronal, transversal and sagittal sections show that in all three experiments the contrast interaction group*congruency*synchronicity resulted in significant signal increase only at the superior colliculus ipsilateral to the manipulated side. Clusters are thresh-

olded at $P < 0.005$ (uncorrected) for display purposes and projected onto each group mean brain image. T-scores are presented in the color scales. Plot showing sizes of activation in the ipsilateral SC. The plot shows the contrasts estimates for each of the four experimental conditions. Error bars show standard errors of the means across participants (SE).

investigation of the neurocognitive principles and neural underpinnings of bodily self-consciousness in healthy subjects is the so-called illusion studies, such as the rubber hand illusion (RHi) [Botvinick and Cohen, 1998; Ehrsson et al., 2004], the induced out-of-body experience [Ehrsson, 2007; Lenggenhager et al., 2007], or the body-swap illusion [Petkova and Ehrsson, 2008]. Altogether, illusion studies identified processes of multisensory integration of bodily-related sensory inputs located at personal and peripersonal space and operating in egocentric, body-part reference frames, as one of the main factors contributing to the generation of bodily self-consciousness in healthy individuals [Ehrsson et al., 2004; Guterstam et al., 2013; Makin et al., 2008; Petkova et al., 2011]. Nevertheless, a growing body of evidence are demonstrating that disturbances of bodily self-consciousness as observed in neurological and psychiatric cohorts, such as in autoscopic spectrum disorders [Blanke et al., 2004], somatoparaphrenia [Bisiach et al., 1991; Fotopoulou et al., 2011; Rode et al., 1992], and depersonalization disorders [Sang et al., 2006], are associated with dysfunctional higher order spatial representation systems [Vallar and Ronchi, 2008], involving a cognitive representation of the extrapersonal space operating in allocentric, gaze-centered, and gravitational, earth-fixed

reference frames [Previc, 1998]. Lesion studies suggest that maps of extrapersonal space generated in most of the main structures integrating spatial representation systems, such as the hippocampus [O'Keefe et al., 1998; Zaehle et al., 2007], the posterior parietal cortex [Zhang and Ekstrom, 2013; Zaehle et al., 2007], and the temporoparietal junction (TPJ) [Chechlacz et al., 2010; Zaehle et al., 2007], are not relevant for emergence of bodily self-consciousness [Gandola et al., 2012; Jenkinson et al., 2013]. As such, it remains to be determined which brain structures integrating spatial representation systems would underpin coding of extrapersonal space relevant for bodily self-consciousness.

To investigate the neural underpinnings of extrapersonal space representation relevant for bodily self-consciousness, we developed a hypothesis driven functional magnetic resonance imaging (fMRI) study aiming to investigate the implication of the superior colliculus (SC) in bodily illusions, and more specifically in RHi. The SC is a key structure of multisensory integration, computing sensorimotor transformations of sensory spatial information from visual, somatosensory, and auditory modalities to motor commands [Stein and Meredith, 1993]. An adaptive mechanism of topographic map alignment underpins the

Figure 2.

Experiment 2, gPPI analysis of task-related functional connectivity of the left SC during RHi manipulating left hand. A, Composite coronal sections depicting left and right ventral premotor cortices activations; B, Sagittal section depicting the functional connectivity increases in the right TPJ and rFBA; C, Sagittal section depicting the functional connectivity increases in the right Insula; D, Composite coronal sections depicting the functional

connectivity increases in the left and right postcentral gyrus; E, Composite coronal sections depicting the functional connectivity increases in right and left cerebellum. Clusters are thresholded at $P < 0.005$ (uncorrected) for display purposes and projected onto the group mean brain image. T-scores are presented in the color scales.

generation of a unified map of the space between sensory modalities and motor maps [King, 2004]. In this process, a dynamic, ever-updating cognitive map of the extrapersonal space [Hall and Colby, 2011], operating in allocentric [Cooper et al., 1998], gaze-centered and vestibular gravitational, earth-fixed reference frames [Hall and Colby, 2011; Maeda et al., 1979; Previc, 1998], works as a template instructing spatial alignment of sensory spatial maps [Hyde and Knudsen, 2002; King, 2004; May, 2006]. In this way, collicular sensory spatial representations, in spite of exhibiting a basic modality-specific topographic representation, are not locked in space, but rather they are dynamically updated to the changes of the cognitive map of the extrapersonal space [King, 2004]. This is to say that in SC bodily-related multisensory inputs are represented as stimuli in the extrapersonal space. In the current study, we aim to investigate whether this collicular multisensory integration of bodily-related input anchored in the extrapersonal space is relevant for emergence of bodily self-consciousness.

This article presents the results of two fMRI studies developed to investigate our hypothesis of the implication

of the SC in bodily illusions. In the first study, participants were submitted to the RHi replicated for both left and right body hemispaces. We found evidence of the implication in RHi of the SC ipsilateral to the manipulated hand. In the second experiment, a functional connectivity study, we provide evidence of increased illusion-dependent functional connectivity between the bilateral SC and brain regions previously implicated in both body-part and full-body illusions, which were reported to integrate multisensory bodily-related input represented in peripersonal or personal space in body-part reference frames.

MATERIAL AND METHODS

Experiment I

Participants

In Experiment 1, we worked with two different samples, one manipulating the left hand (LEFT) and another the right hand (RIGHT). The LEFT sample was constituted of seventeen healthy subjects, 8 females and 9 males

TABLE I. Illusion related activity in the superior colliculus in experiments 1, sample LEFT and sample RIGHT, and experiment 2

	<i>x</i>	<i>y</i>	<i>z</i>	<i>T</i>
Experiment 1 : LEFT sample				
Superior colliculus left	-2	-30	-10	3.031
Superior colliculus right	n/a	n/a	n/a	n/a
Experiment 1 : RIGHT sample				
Superior colliculus left	n/a	n/a	n/a	n/a
Superior colliculus right	2	-34	-2	2.34
Experiment 2 : gPPI left rubber hand				
Superior colliculus left	-2	-30	-14	2.795
Superior colliculus right	n/a	n/a	n/a	n/a

ROI-based analysis shown $P < 0.05$, small-volume corrected for anatomy-based ROIs. All coordinates are given in MNI (Montreal Neurological Institute) space.

(mean age 25.33 years $\pm$ 2.45 standard deviation). The RIGHT sample was constituted of eighteen healthy subjects, 7 females and 11 males (mean age 26 years $\pm$ 3, 61 standard deviation). Both samples were partially overlapping with 1 woman and 3 men participating in both experiments. All participants voluntarily participated in the study. All were right-handers, with normal or corrected to normal vision and no history of motor or neurological problems. Participants signed an informed consent after being informed of the aims and procedures of the experiments, which adhered to the declaration of Helsinki and was approved by the local human subjects' committee.

Experimental design and procedures

In experiment 1, we adapted a previous brain imaging (fMRI) study of the classical RHi [Ehrsson et al., 2004]. For both LEFT and RIGHT samples the study was organized in two phases, one brain imaging (fMRI) experiment, followed by a behavioral experiment.

With the LEFT sample we used a left prosthetic rubber hand and the left hand of participants and with the RIGHT sample a right rubber hand and the right hand of participants.

In the brain imaging (fMRI) study, participants were not screened prior to experiment to check whether they could experience the RHi or not. As any prior knowledge or experience of the illusion could have confounded the neuroimaging data, we decided to test unscreened volunteers [Petkova et al., 2011; Tsakiris et al., 2007]. Therefore, all participants were naïve as to the illusion and purposes of the experiment. Subjects observed in direct view a left or right life size prosthetic rubber hand, neutral in relation to gender (Otto Bock GmbH, Duderstadt, Germany), supported by a set of foams placed on their lower belly, whilst their real left or right hand was hidden from view

being covered by a blanket. The distance between the rubber hand and the participant's hand was 15 cm. We customized our mattresses and set of fixation foams for the head-coil, so that subjects could tilt their heads approximately 20° to obtain a direct view of the prosthetic rubber hand without discomfort, avoiding any risk of movement of the head during the scanning phase.

As in the classical behavioral RHi study, we explored the two main factors that are assumed to influence the eliciting of the illusion, that is, the position of the prosthetic rubber hand in relation to the participant's body and the synchronicity of application of tactile stimulation on the prosthetic rubber hand and the participant's hidden real hand.

The rubber hand assumed two positions, one named Congruent, that is, it was positioned in an anatomical plausible way in relation to the participant's body, pointing toward the body midline. In the so-called Incongruent position, the rubber prosthesis was turned 180°, facing the subject.

The tactile stimulation on the prosthetic rubber hand and the hidden real hand was applied in two different ways: in a Synchronous and in an Asynchronous, alternated way. The stimulation was applied by the experimenter who touched the index finger of the rubber hand and the index finger of the real hand with two small paint brushes. She listened via headphones to a recorded sequence of instructions informing her of the changes of condition, the pauses when the rubber hand should change positions, as well as the type of stimulation to apply, synchronous or asynchronous and their frequency (1 Hz). The sequence of instructions was presented by a program Presentation (Presentation Package Player, version 14.5, Neurobehavioural Systems).

Our experimental design was consequently a 2×2 factorial one, with four experimental conditions labeled as

TABLE II. Illusion-dependent functional connectivity increases between the left superior colliculus and brain networks implicated in body-part and full-body illusions

	<i>x</i>	<i>y</i>	<i>z</i>	<i>T</i>
Premotor ventral left	-62	-1	32	11.7
Premotor ventral right	69	9	12	8.7
Postcentral gyrus left	-54	-41	54	11.1
Postcentral gyrus right	70	-11	23	6.1
Temporoparietal junction right	46	-38	28	4.5
Insula right	38	8	6	4.3
Fusiform body area right	48	-48	-8	4.2
Cerebellum left	-18	-90	-29	9.6
Cerebellum right	4	-86	-38	13.8

Results from ROI-based analyses are shown $P < 0.05$, small-volume FWE-corrected for literature-based ROIs, or ROIs derived from experiment 3 or the WFU Pickatlas. All coordinates are given in MNI (Montreal Neurological Institute) space.

TABLE III. Illusion-dependent functional connectivity increases between the right superior colliculus and brain networks implicated in body-part and full-body illusions

	<i>x</i>	<i>y</i>	<i>z</i>	<i>T</i>
Premotor ventral left	−8	2	54	6.4
Premotor ventral right	70	10	15	8.8
Postcentral gyrus left	−48	−26	62	6.5
Postcentral gyrus right	70	−41	8	9.6
Fusiform body area right	46	−46	10	5.8
Cerebellum left	−22	−90	−30	6.6
Cerebellum right	31	−28	−30	16.3

Results from ROI-based analyses are shown $P < 0.05$, small-volume FWE-corrected for ROIs derived from experiment 3 or the WFU Pickatlas. All coordinates are given in MNI (Montreal Neurological Institute) space.

follows: congruent-synchronous (CS), where the rubber hand was positioned in an anatomical plausible position in relation to the participant's body, and the touch of the paint brushes was delivered synchronously on the rubber hand and the participant's hidden hand; congruent-asynchronous (CA), where the rubber hand was positioned in an anatomical plausible position in relation to the participant's body, and the touch of the paint brushes was delivered asynchronously on the rubber hand and the participant's hand; incongruent-synchronous (IS), where, the rubber hand was positioned in an anatomical implausible position in relation to the participant's body, and the touch of the paint brushes was delivered synchronously at the rubber hand and the participant's hidden hand; and incongruent-asynchronous (IA), where the rubber hand was positioned in an anatomical implausible position in relation to the participant's body, and the touch of the paint brushes was delivered asynchronously at the rubber hand and the participant's hidden hand. Each condition or stimulation epoch lasted for 40 s.

The study was constituted of 3 runs each lasting 10 min. The four experimental conditions were repeated 3 times in each run in a pseudorandomized order, that is, 9 times altogether. Between the experimental epochs there was a period of 5 s, which the experimenter used to change the position of the prosthetic rubber hand whenever necessary.

The behavioral RHi experiment aimed at distinguishing two groups of participants which would be compared to each other: participants prone to the illusion (ILLU) and participants irresponsive to it (NILLU). Each of the four experimental conditions of the scanning phase, CS, CA, IS, IA, were repeated outside the scanner. During this repetition, each condition lasted for 2 min and the order of the conditions was randomized across subjects. After each experimental condition a standard questionnaire was answered. It was constituted of seven questions, the three first indicating eliciting of the illusion (Q1 "It seemed as if I was feeling the touch of the paintbrush in the location

where I saw the rubber hand touched"; Q2 "It seemed as though the touch I felt was caused by the paintbrush touching the rubber hand"; Q3 "I felt as if the rubber hand was my hand") and the remaining four serving as control. The actual text was in German.

Data acquisition

Both brain imaging (fMRI) experiments were conducted using a Siemens TRIO 3T (Siemens, Erlangen, Germany) scanner with a standard head-coil system, to acquire T2*-weighted echo-planar images (EPI) for blood oxygen level-dependent (BOLD) based imaging.

We opted for partial-head volume acquisition in an axial slice orientation in order to maintain a suitable ratio between voxel size, set at $2 \times 2 \times 4$ mm, and TR value, set at 1,500 ms, and sufficient number of slices, providing a high-resolution rendering of SC activity (128×128 matrix, TE = 30 ms, FOV = 256 mm). We collected 380 volumes by run, making a total of 1,140 volumes per subject for the entire experience that was constituted of 3 runs. Each functional image volume comprised 18 slices of 4 mm thickness. Additionally, high-resolution T1-weighted whole-head anatomical volumes were acquired using a MP-RAGE sequence (TR = 2,500 ms, TE = 4.77 ms, FOV = 256 mm, voxel size = $1 \times 1 \times 1$ mm, 256×256 matrix, 192 slices, slice thickness 1 mm).

Image analysis

Image preprocessing was performed using Statistical Parametric Mapping Software 8 (SPM8; Wellcome Department of Imaging Neuroscience, London, UK) implemented in Matlab R2011b (Mathworks, Inc., Sherborn, MA). The functional images and the anatomical T1 image were reoriented. The functional images were realigned. Subsequently, the anatomical T1 volume was coregistered to the mean of the functional EPI images, the coregistered anatomical image was segmented, and the gray matter image of each subject was entered as source image in the normalisation process of functional images, where the SPM8 apriori_grey template was entered as template image. Normalization included resampling of the images to 2 mm isotropic voxels. Normalised

TABLE IV. Experiment 3 localization of bilateral extrastriate body area and fusiform body area

	<i>x</i>	<i>y</i>	<i>z</i>
Extrastriate body area left	−40	−72	−6
Extrastriate body area right	38	−64	−12
Fusiform body area left	−38	−56	−12
Fusiform body area right	42	−48	−14

Localization was done with voxel selection threshold $P < 0.0001$ uncorrected. All coordinates are given in MNI (Montreal Neurological Institute) space.

Graph 1.

The result of the RHi questionnaire for the LEFT sample of experiment 1. Top, sample responsive to the illusion; Bottom, sample irresponsive to the illusion. Mean scores for each of the seven questions during each four experimental and control conditions. Error bars correspond to the standard deviation (SD). Questions 1, 2, and 3 are relevant for the illusory experience and the others serve as control. For displaying purposes questionnaire scale was represented with values from 1 to 7. Values 1 to 3 represent levels of disagreement, 5–7 levels of agreement, and 4, no opinion.

images were smoothed with an isotropic 6 mm full width at half maximum (FWHM) Gaussian kernel.

The statistical analysis was performed with a standard two-stage mixed effects model. First level analysis was developed in SPM8 as a linear regression model (general linear model) for the data of each participant. The four experimental conditions were modelled each with a boxcar function and convoluted with an adapted SPM8 hemodynamic response function (HRF) where the parameters $p(1)$ delay of response was altered to 4.5s, $p(2)$ delay of undershoot to 9s, and $p(5)$ ratio of response to undershoot to 2. These alterations were adopted to take into account the fact that the SC exhibits an earlier peak of activation, a faster delay of undershoot, and consequently a different ratio between response and undershoot [Wall et al., 2009]. The statistical analysis of the imaging data for the different experimental conditions was made with adoption of a high-pass temporal filter of 160s, and definition of six regressors capturing residual movement-related artefacts (three rigid-body translations and three rotations determined from realignment procedure). Temporal autocorre-

lation of errors was accommodated by an AR(1) model implemented in SPM8.

The second level analysis was developed in GLM FLEX (Donald McLaren & Aaron P. Schultz, Athinoula A. Martinos Center & Massachusetts General Hospital, Harvard Medical School, 2012), and Peak_nii, a data extraction tool providing statistics and location information for the peak voxel(s) in each activated cluster (Donald McLaren, Athinoula A. Martinos Center & Massachusetts General Hospital, Harvard Medical School, 2012). Both toolboxes were implemented in MatLab R2011b, and required some SPM8 functions.

All beta images of the four conditions of each participant obtained in the first level analysis were entered in a complex mixed two-way flexible factorial ANOVA, with one between-subjects factor group (two levels: ILLU and NILLU) and two within-subject factors congruency of position of the rubber hand in relation to the participant's body (two levels: congruent and incongruent), and synchronicity (two levels: synchronous and asynchronous) of application of touch on the rubber hand and the participant's hand.

Graph 2.

The result of the RHi questionnaire for the sample RIGHT of experiment 1. Top, sample responsive to the illusion; Bottom, sample irresponsive to the illusion. Mean scores for each of the seven questions during each four experimental and control conditions. Error bars correspond to the standard deviation (SD). Questions 1, 2, and 3 are relevant for the illusory experience and the others serve as control. For displaying purposes questionnaire scale was represented with values from 1 to 7. Values 1 to 3 represent levels of disagreement, 5–7 levels of agreement, and 4, no opinion.

As we had an *a priori* hypothesis concerning the implication of the SC in the illusion, we only evaluated voxels localized within this structure. Therefore, all results are reported with small volume correction, $P < 0.05$ family wise error (FWE) corrected within a mask of the bilateral SC. For each sample the mask was created manually with MRICRON (Chris Rorden's, copyright 2012) on the mean of all subjects normalized T1 anatomical images. The SC were localized in agreement with Martin's neuroanatomy atlas [Martin, 2003].

The behavioral data collected right after the scanning phase of the brain imaging (fMRI) experiments consisted mainly in 7-point Likert scale questionnaire reports repeated for each of the four experimental conditions CS, CA, IS, IA. Participants were required to rate the degree of agreement or disagreement to each statement. The values related to the questions assessing experiencing the illusion were used to calculate an illusion index, allowing selection of participants who experienced the illusion (ILLU) from participants that did not (NILLU) according to the formula: $[(Q1_CS - Q1_CA) + (Q2_CS - Q2_CA) + (Q3_CS - Q3_CA)] - [(Q1_IS - Q1_IA) + (Q2_IS - Q2_IA) + (Q3_IS - Q3_IA)] / 2$. A result greater than "0" would indicate that the participant experienced a greater illusion during experimental condition CS in comparison to the three controls, while a score equal or smaller than "0" would mean that the participant did not experience the illusion.

Experiment 2

Participants

In experiment 2 the sample was constituted of eighteen healthy subjects, 7 females and 11 males (mean age 26 years $\pm$ 3.61 standard deviation), and totally overlapped with the RIGHT sample of experiment 1. All participants voluntarily participated in the study. All participants were right-handers, with normal or corrected to normal vision and no history of motor or neurological problems. Participants signed an informed consent after being informed of the aims and procedures of the experiments, which adhered to the declaration of Helsinki and was approved by the local human subjects' committee.

Experimental design and procedures

In experiment 2, the experimental design and procedures were identical to experiment 1. In experiment 2 sample we used a left prosthetic rubber hand and the left hand of participants.

Data acquisition

In experiment 2 we proceeded to a whole-brain volume acquisition in an axial slice orientation. Voxel size was set at $2.5 \times 2.5 \times 3$ mm and TR at 3,000 ms (96×96 matrix,

TE = 30 ms, FOV = 240 mm). We collected 190 volumes by run, making a total of 570 volumes per subject for the entire experience that was constituted of 3 runs. Each functional image volume comprised 42 slices of 3 mm thickness. Additionally, high-resolution T1-weighted whole-head anatomical volumes were acquired using a MP-RAGE sequence (TR = 20 ms, TE = 5 ms, FOV = 280 mm, voxel size = $2.1 \times 1.1 \times 10.0$ mm, 256×256 matrix, 1 slice, slice thickness 10 mm).

Image analysis

In experiment 2 image preprocessing and statistical analysis up to the second level analysis were identical to experiment 1. Second level analysis was developed with a small volume correction, $P < 0.05$ FWE corrected, with the same mask of SC created for the sample RIGHT of experiment 1.

In experiment 2, we developed two additional generalized form of context-dependent psychophysiological interaction (gPPI) analyses using each colliculus as seed region. Therefore, anatomically derived regions of interest (ROIs) of the ipsilateral left and contralateral right colliculus were created. Both colliculus were localized in agreement with Martin's neuroanatomy atlas [Martin, 2003]. The gPPI analysis were developed with the Generalized PPI toolbox [McLaren et al., 2012] (<https://www.nitrc.org/projects/gppi/>), implemented in MatLab R2011b, and requiring some SPM8 functions. For each gPPI analysis developed, the physiological variable was created for each subject by deconvolving the mean time series of all voxels within the anatomically derived ROI of the ipsilateral left or contralateral right SC. The psychological regressors were created by separately convolving the 25 psychological/task vectors with the HRF. The interaction terms (PPIs) were then computed by multiplying the time series from the psychological regressors with the physiological variable. Individual con_PPI images were subsequently entered in a second random effects analysis in which illusion effects between groups (ILLU > NILLU; NILLU > ILLU) were investigated using a 2-sample-T-test analysis implemented in GLMFLEX (Donald McLaren & Aaron P. Schultz, Athinoula A. Martinos Center & Massachusetts General Hospital, Harvard Medical School, 2012), unravelling differential task-induced functional connectivity between the SC and other brain structures previously implicated in body-part- and full-body illusions. Statistics and location information for the peak voxel(s) in each activated cluster were calculated with Peak_nii (Donald McLaren, Athinoula A. Martinos Center & Massachusetts General Hospital, Harvard Medical School, 2012).

The behavioral data collected right after the scanning phase of the brain imaging (fMRI) experiment was the same 7-point Likert scale questionnaire reports used in experiment 1 RIGHT sample. Further information on data analysis procedures is to be searched in experiment 1 data analysis subsection.

Experiment 3

Participants

In experiment 318 healthy subjects, seven females and 11 males (mean age 26 years $\pm$ 3.61 standard deviation) voluntarily participated in the study. Experiment 3 sample totally overlapped with the RIGHT sample of experiment 1. All were right-handers, with normal or corrected to normal vision and no history of motor or neurological problems. Participants signed an informed consent after being informed of the aims and procedures of the experiments, which adhered to the declaration of Helsinki and was approved by the local human subjects' committee.

Experimental design and procedures

Experiment 3 was a localizer study reproducing a previously established paradigm designed to determine ROIs for the extrastriate body area (EBA) and the fusiform body area (FBA), which were implicated in body-part and full-body visual representation, respectively [Taylor et al., 2007].

The localizer study was constituted of two runs. In run, one participants lying in the fMRI scanner were presented images of naked headless female and male human bodies in different postures, which were alternated with images of chairs. In run, two participants were presented with images of body-parts such as hands, headless torsos, legs, and so forth, which were alternated with images of objects or objects parts exhibiting an equivalent morphology. Images were intercalated with white screens. Visual stimulation was provided by a DLA-G150CL video projector (JVC) projecting stimuli onto a rear projection screen mounted at the head end of the patient table. The screen is observed via the mirror system of the head coil.

Participants attention was maintained and monitored during both localizer runs using a one-back task (two randomly placed instances per block).

Each localizer run consisted of 21 blocks of 15s each. Blocks 1, 6, 11, 16, and 21 were fixation-only baseline epochs, consisting of a red box on a white background. The remaining blocks displayed 20 images of each image type. Images were presented in a pseudorandomized order. Each run last in total 5 min 25 s.

Data acquisition

In experiment 3, we also opted for a whole-brain volume acquisition in an axial slice orientation. Voxel size was set at $2.5 \times 2.5 \times 3$ mm and TR at 3,000 ms (96×96 matrix, TE = 30 ms, FOV = 240 mm). We collected 116 volumes by run, making a total of 232 volumes per subject for the entire experience that was constituted of 2 runs. Each functional image volume comprised 42 slices of 3 mm thickness. Additionally, high-resolution T1-weighted whole-head anatomical volumes were acquired using a MP-RAGE sequence (TR = 20 ms, TE = 5 ms, FOV = 280 mm, voxel

size = $2.1 \times 1.1 \times 10.0$ mm, 256×256 matrix, 1 slice, slice thickness 10 mm).

Image analysis

All beta images of the four conditions of each participant obtained in the first level analysis were entered in a two-way within-subjects factorial ANOVA, with factors body (two levels: full-body and body-parts), and objects (two levels: chairs and object-parts). The ROIs were defined by the contrast [full-body + body-parts] – [chairs + object-parts], and created with MRICRON (Chris Rorden's, copyright 2012) on the mean of all experiment 2 subjects normalized T1 anatomical images as spheres of 9mm centred on the peak voxels that met an uncorrected statistical threshold of $P < 0.0001$.

RESULTS

Experiment 1

In the brain imaging (fMRI) experiment of the LEFT sample, a hypothesis driven analysis performed with small volume correction for the bilateral SC unravelled a significant activation in the ipsilateral left SC for the interaction factor Group*Congruency*Synchronicity (FWEp = 0.04; $T = 3.031$; Montreal Neurological Institute (MNI) coordinates = $[-2 -30 -10]$) (Fig. 1A; Table 1).

Main factors congruency and synchronicity did not elicit any differential pattern of activation for either colliculi.

In the RIGHT sample, the same hypothesis driven analysis performed with small volume correction for the bilateral SC unravelled a significant activation in the ipsilateral right SC for the interaction factor Group*Congruency*Synchronicity (FWEp = 0.039; $T = 2.34$; MNI coordinates = $[2 -34 -2]$) (Fig. 1B, Table 1).

Main factors congruency and synchronicity did not elicit any differential pattern of activation for either colliculi.

Following brain imaging (fMRI) studies of both LEFT and RIGHT samples, a RHi behavioral study was run in order to screen subjects responsive to the illusion (ILLU) from subjects nonresponsive to the illusion (NILLU). The data collected after each study consisted of 7-point Likert scale questionnaire reports repeated for each of the four experimental conditions CS, CA, IS, IA. Participants were required to rate the degree of agreement or disagreement to each statement.

We started questionnaire data analysis by filtering of individual questionnaires searching for invalidating errors such as misresponding, acquiescence and central tendency bias. No subject was excluded. Subjects were screened for their responsiveness to the illusion through evaluation of the ratings of the three questions concerning the illusion according to the formula: $[(Q1_CS - Q1_CA) + (Q2_CS - Q2_CA) + (Q3_CS - Q3_CA)] - [(Q1_IS - Q1_IA) + (Q2_IS - Q2_IA) + (Q3_IS - Q3_IA)] / 2$. In the LEFT sample, 10 subjects obtained a result greater than "0," indicating that they

experienced a greater illusion during experimental condition CS, and in consequence they were labeled ILLU subjects. Other 7 subjects obtained a score equal or smaller than “0,” demonstrating that they did not experience the illusion, being labeled as NILLU subjects. In the RIGHT sample, 12 subjects obtained a result greater than “0,” being labeled as ILLU subjects, whilst the remained 6 subjects obtained a score equal or smaller than “0,” being labeled as NILLU subjects.

We performed further two questionnaires’ analysis aiming to certify that the illusion was actually elicited. First, in a one-way within subjects ANOVA, we compared the ratings of the three questions concerning the illusion with the ratings on the four control questions. In the LEFT sample (Graph 1), only the ratings of subjects ILLU for the three questions concerning the illusion in the CS were significantly greater than the ratings of the four control questions ($F_{6,54} = 2,36$; $P < 0.05$). In the RIGHT sample, we obtained an equivalent result ($F_{6,66} = 2,86$; $P < 0.05$).

In the second analysis, we compared the ratings of the three questions concerning the illusion across the four conditions of the two-way within subjects ANOVA design. In the LEFT sample, only subjects ILLU, and only during the CS condition, felt that they localized the feeling of touch of the paintbrush in the location where they saw the rubber hand being touched (interaction position X timing, $F_{1,9} = 6,48$; $P < 0.05$), that it seemed as though the touch they felt was caused by the paintbrush touching the rubber hand (interaction position X timing, $F_{1,9} = 6,23$; $P < 0.05$) and that they felt as if the rubber hand was their hands (interaction position X timing, $F_{1,9} = 5,37$; $P < 0.05$). In the RIGHT sample (Graph 2), we obtained equivalent results for question 1 (interaction position X timing, $F_{1,11} = 12,89$; $P < 0.01$), question 2 (interaction position X timing, $F_{1,11} = 16,04$; $P < 0.01$) and question 3 (interaction position X timing, $F_{1,11} = 21,25$; $P < 0.01$). Altogether these results demonstrate that we robustly elicited the RHi in the ILLU samples in both LEFT and RIGHT samples, which was typically characterized by the interaction between hand orientation and timing of application of the brushstrokes.

Experiment 2

In experiment 2, where we used the same mask of bilateral SC for small volume correction as the one used with the RIGHT sample of experiment 1, we observed a strong trend towards a significant activation in the ipsilateral left SC for the interaction factor Group*Congruency*Synchronicity ($\text{FWEp} = 0.055$; $T = 1.965$; MNI coordinates = $[-4 \ -34 \ -2]$) (Fig.1C, Table 1).

Main factors congruency and synchronicity did not elicit any differential pattern of activation for either colliculi.

The results of the gPPI analysis using an anatomically derived ROI of the activated ipsilateral left SC as seed region (Fig. 2, Table 2) for the same contrast interaction Group*Congruency*Synchronicity, unravelled at whole-brain level a sig-

nificant increase in task-induced functional connectivity between the ipsilateral left SC and the left ventral premotor cortex (l PMv) ($\text{FWEp} = 0.004$; $T = 11.6949$; MNI coordinates = $[-62 \ -1 \ 32]$), the left postcentral gyrus ($\text{FWEp} = 0.007$; $T = 11.0580$; MNI coordinates = $[-54 \ -41 \ 54]$), and the bilateral cerebellum ($\text{FWEp} = 0.0350$; $T = 9.6210$; MNI coordinates = $[-18 \ -90 \ -29]$ and $\text{FWEp} < 0.001$; $T = 13.8480$; MNI coordinates = $[4 \ -86 \ -38]$).

The whole-brain analysis also revealed some areas of interest whose activation level did not reach the threshold for significant activation $\text{FWEp} = 0.05$ corrected: the right ventral PM (r PMv), the right TPJ (r TPJ), the right (rFBA), the right anterior Insula, and the right postcentral gyrus. We applied a small volume correction, $P < 0.05$ FWE corrected for multiple comparisons within a mask combining all these five structures. The mask was created manually with MRICROn (Chris Rorden’s, copyright 2012) on the mean of the normalized T1 anatomical image of all sample subjects. We observed a significant enhancement in task-related functional connectivity between the left SC and the right PMv ($\text{FWEp} = 0.001$; $T = 8.696$; MNI coordinates = $[69 \ 9 \ 12]$), the right postcentral gyrus ($\text{FWEp} = 0.002$; $T = 6.148$; MNI coordinates = $[70 \ -11 \ 23]$), the right TPJ ($\text{FWEp} = 0.024$; $T = 4.476$; MNI coordinates = $[46 \ -38 \ 28]$), the right anterior Insula ($\text{FWEp} = 0.034$; $T = 4.254$; MNI coordinates = $[38 \ 8 \ 6]$), and the rFBA ($\text{FWEp} = 0.04$; $T = 4.174$; MNI coordinates = $[48 \ -48 \ -8]$).

The results of the gPPI analysis using an anatomically derived ROI of the contralateral right SC as seed region (Table 3) exhibited a highly overlapping pattern of task-induced functional connectivity to the one observed for the ipsilateral left SC. The whole-brain analysis unravelled significant increase of task-induced functional connectivity between the right SC and the right cerebellum ($\text{FWEp} = 0.001$; $T = 16.349$; MNI coordinates = $[31 \ -28 \ -30]$), and the right postcentral gyrus ($\text{FWEp} = 0.038$; $T = 9.553$; MNI coordinates = $[70 \ -4 \ 18]$).

Again the whole-brain analysis revealed some areas of interest whose activation level did not reach the threshold for significant activation $\text{FWEp} < 0.05$ corrected for multiple comparisons: the bilateral ventral PM (PMv), r TPJ, the rFBA, the right anterior Insula, the left postcentral gyrus, and the left cerebellum. We applied a small volume correction, $P < 0.05$ FWE corrected within a mask combining all these seven structures. The mask was created manually with MRICROn (Chris Rorden’s, copyright 2012) on the mean of the normalized T1 anatomical image of all sample subjects. We observed a significant enhancement in task-related functional connectivity between the right SC and the bilateral PMv ($\text{FWEp} = 0.001$; $T = 8.825$; MNI coordinates = $[70 \ 10 \ 15]$ & $\text{FWEp} = 0.01$; $T = 6.398$; MNI coordinates = $[-8 \ 2 \ 54]$), the left cerebellum ($\text{FWEp} = 0.008$; $T = 6.593$; MNI coordinates = $[-22 \ -90 \ -30]$), the left postcentral gyrus ($\text{FWEp} = 0.009$; $T = 6.513$; MNI coordinates = $[-48 \ -26 \ 62]$), and the rFBA ($\text{FWEp} = 0.027$; $T = 5.757$; MNI

coordinates = [46 -46 -10]). We also observed a trend toward increased task-induced functional connectivity between the right SC as seed region and the right TPJ (FWEp = 0.12; $T = 4.574$; MNI coordinates = [46 -38 28]), and the right anterior Insula (FWEp = 0.45; $T = 3.497$; MNI coordinates = [33 12 2]).

As the sample of experiment 2 totally overlaps with the RIGHT sample of experiment 1, the results of the analysis of questionnaire data from the behavioral study are to be searched in experiment 1 results subsection.

Experiment 3

The left and right EBA, as well as the right and the left FBA, were successfully identified for the voxel selection threshold ($P < 0.0001$). The MNI coordinates of these regions were: left EBA [-40 -72 -6]; right EBA [38 -64 -12]; rFBA [42 -48 -14]; left FBA [-38 -56 -12] (Table 4). Coordinate conversion to Talairach space done with mni2tal function of MatLab R2011b, demonstrated that these coordinates are in agreement with those obtained in the original study [Taylor et al., 2007].

DISCUSSION

Our study provides the first experimental evidence of the implication of the SC in bodily self-consciousness. Altogether, experiments 1 and 2 findings suggest that collicular representation of extrapersonal space is relevant for emergence of bodily self-consciousness, influencing both processes of body ownership and self-location, previously reported to operate in a representation of the peripersonal and personal space. These three spatial representations of extrapersonal, peripersonal and personal space would interact producing a unified representation of space that is relevant for bodily self-consciousness. Multisensory integration of bodily-related sensory input represented in this unified representation of the space would constitute one of the main factors enabling emergence of bodily self-consciousness.

The SC generates a Map of the Extrapersonal Space that is Relevant for Bodily Self-Consciousness

Studies in clinical cohorts, such as patients with somatoparaphrenia, have demonstrated that it is possible to elicit a temporary remission of abnormal bodily self-consciousness by procedures manipulating a higher order cognitive representation of the space such as caloric vestibular stimulation [Bisiach et al., 1991; Rode et al., 1992] and mirror viewing altering perspective taking mechanisms [Fotopoulou et al., 2011; Jenkinson et al., 2013]. Nevertheless, lesion analysis studies suggest that many of the most important brain structures engaged in generation of a representation of the extrapersonal space, such as the hippocampus, the posterior parietal lobe, or TPJ, are impaired in

these patients [Gandola et al., 2012; Jenkinson et al., 2013], and as such cannot underpin the temporary remission effect obtained with experimental manipulation. The results of the current study implicating the SC in RHi suggest that this structure generates a representation of the extrapersonal space relevant for emergence of bodily self-consciousness. This evidence, altogether with the fact that, to date, there is no report associating SC with lesional profiles underlying somatoparaphrenia or depersonalization, make it a plausible candidate to underpin the temporary remission effect obtained with experimental manipulation. Further studies investigating activation of SC in clinical cohorts associated with experimentally induced remission of abnormal bodily self-consciousness are needed to validate this hypothesis.

Our observed lateralization implicating only the colliculus ipsilateral to the manipulated hand robustly supports the hypotheses that the SC is engaged in spatial computations relevant for bodily self-consciousness. More specifically, our observed lateralization evokes models of cooperative action between bilateral colliculi, where imbalance of activity between colliculi associated with unilateral collicular (in)activation systematically induces a directional bias towards the hemispace contralateral to the activated colliculus, or ipsilateral to the inactivated, impaired colliculus [Flandrin and Jeannerod, 1981; Rushmore et al., 2006]. This effect was thoroughly investigated for a series of motor and cognitive tasks in animal studies, a recent case report providing evidence that a similar mechanism may be associated to unilateral collicular lesion in humans [Weddell, 2004].

In the field of research in spatial cognition, studies of spatial neglect associate this effect with a deranged representation of space due to cortical or collicular impairment, characterized by an ipsilesional shift of spatial reference frames, which is likely accompanied by a contraction of the contralesional space [Feinberg and Farah, 2000; Karnath et al., 2002; Weddell, 2004]. By analogy, the collicular lateralization observed in the current study suggests a shift in the collicular spatial representation contralateral to the activated colliculus, that is, in the same orientation of the spatial dissociation experimentally established between the real hand and the prosthetic rubber hand. Transfer of ownership from the real hand to the prosthetic rubber hand would be associated with this contralateral shift in collicular spatial representation.

Our observed enhancement of functional connectivity between SC and the rTPJ, the bilateral PMv, and bilateral postcentral gyrus suggest that the shift of collicular spatial representation influences the cortical representation of the body in the peripersonal action space, and the somatotopic representation of the body space. Whether it influences activity in collicular somatotopic maps in a fashion previously observed in the Barn owl for the collicular audiovisual integration [Hyde and Knudsen, 2002], is dependent in the model of collicular somatotopies adopted. This interpretation is incompatible with classical models, which

are based on contralateral body hemispace representation [Stein and Meredith, 1993]. Conversely, it is plausible with ecological animal models of collicular somatotopies, which, based on studies in freely moving animals and under the light of evidence demonstrating that collicular somatosensory receptive fields are very large and highly overlapping [Clemo and Stein, 1991], advocate the possibility of a redundant bilateral representation of the body, enabling a dynamic interplay between vision and the moving body [Groh and Sparks, 1996]. Our observed enhanced functional connectivity pattern between the SC and the bilateral cerebellum supports the pertinence of this second model. Through the tecto-cerebello-tectal circuit, the cerebellum coordinates activity between the two colliculi, exactly associated with integration of bilateral modality maps [May, 2006; May et al., 1990]. New methods of receptive field mapping in humans with fMRI that are under development will allow further investigation of this hypothesis [Dumoulin and Wandell, 2008; Lee et al., 2013].

Alternatively, our observed lateralization may also be attributed to attentional mechanisms, which were also hypothesized to underlie neglect, postulating that the representation of space is not affected, rather mechanisms of allocation of attention across space are impaired [Robertson and Marshall, 1994]. The basic consequences are, though, quite equivalent, with imbalance of activity between colliculi generating a gradient of directional bias oriented to the side contralateral to the activated colliculus [Kinsbourne, 2006, 1970]. Such hypothesis is in agreement with recent studies reporting the role of attentional mechanisms in modulation of limb ownership in somatoparaphrenia [Jenkinson et al., 2013]. Nevertheless, it was suggested that attentional mechanisms may only play a role in body ownership in the framework of very specific lesional profiles, and that they play no role in body ownership in healthy individuals [Jenkinson et al., 2013]. As such, they would not be implicated in the current study developed with healthy participants. Further studies are needed to assess this hypothesis.

Whatever the exact cognitive process associated with the observed activation of the SC in this study, spatial representation or attention orienting processes, our findings demonstrating a highly overlapping pattern of projections from bilateral colliculi during RHi support our interpretation that they are operating cooperatively in emergence of bodily self-consciousness.

Bodily Self-Consciousness is Underpinned by Processes of Multisensory Integration of Bodily Sensory Inputs Located in a Unified Representation of the Space

The findings of experiment 1 suggesting that collicular representation of extrapersonal space operating in allocentric, gaze-centered, and vestibular, gravitational, earth-

fixed reference frames is relevant to bodily self-consciousness extends previous findings postulating the role of representation of peripersonal and personal space operating in egocentric, body-part reference frames in bodily self-consciousness [Blanke and Metzinger, 2009; Ehrsson et al., 2004; Guterstam et al., 2013; Makin et al., 2008; Petkova et al., 2011; Pfeiffer et al., 2014].

Experiment 2 demonstrates that during RHi the SC is functionally connected with brain structures previously demonstrated to generate a representation of the personal and peripersonal spaces relevant for bodily self-consciousness, such as PMv [Ehrsson et al., 2004; Gentile et al., 2013; Petkova et al., 2011], and rTPJ [Blanke et al., 2004; Pfeiffer et al., 2014], the role of rTPJ in generation of a representation of extrapersonal space relevant for bodily self-consciousness being under debate [Gandola et al., 2012]. Moreover, we also observed enhancement of functional connectivity between the SC and the bilateral postcentral gyrus, which generate a somatotopic representation of the body space [Martin, 2003]. Although neuropsychological studies have robustly demonstrated that internal representations of space are dissociated from individual peripheral sensory codes [Bottini et al., 2001; Vallar and Ronchi, 2008], the role of postcentral gyrus in bodily self-consciousness is supported by illusion studies [Schaefer et al., 2009, 2006], and as such is relevant for the current study.

Altogether, experiment 2 findings robustly support the interpretation that the bilateral SC, the bilateral vPM, rTPJ and the bilateral postcentral gyrus constitute a functional network relevant for emergence of bodily self-consciousness. Moreover, these findings suggest that in this network a unified representation of space integrating the maps of extrapersonal, peripersonal, and personal space represented at each node of the network is generated through a process of spatial coordinate transformation decomposed in analytic steps ranging from allocentric, gaze-centered, and vestibular, gravitational, earth-fixed reference frames up to body-part and somatotopic reference frames [Desmurget et al., 1998; Graziano, 2001; Olivé and Berthoz, 2012].

By analogy with previous studies, we propose that processes of multisensory integration of bodily-related inputs located in a unified representation of the space generated from dynamically interacting maps of extrapersonal, peripersonal, and personal spaces, constitute one of the main factors underpinning bodily self-consciousness.

Collicular Activity is Relevant for the Ensemble of Bodily Processes Constituting Bodily Self-Consciousness

In the current study, we sought to demonstrate the implication of SC in bodily self-consciousness. For so doing, we used the RHi paradigm that is supposed to inform processes of body ownership [Botvinick and

Cohen, 1998; Ehrsson et al., 2004], and for some authors, exclusively processes of body-part ownership as opposed to full-body ownership [Lenggenhager et al., 2007]. As such, RHi would not allow investigation of the full range of bodily processes constituting bodily self-consciousness, restricting the current results and conclusions to processes of body ownership, and not relating to processes of self-location (but see Olivé and Berthoz, 2012). This would partially explain why maps of extrapersonal space generated in rTPJ would be irrelevant to emergence of bodily self-consciousness, restricting such assertion to the context of body ownership, see body-part ownership that are assessed by somatoparaphrenia. In the context of self-location processes, most likely rTPJ extrapersonal maps would play a central role [Blanke et al., 2004]. Nevertheless, a case report demonstrated that somatoparaphrenia and autoscopic spectrum disorders, and as such body-part ownership and self-location are closely linked in rTPJ [Heydrich et al., 2011]. This finding suggests that collicular projections to rTPJ are essential to provide a representation of the extrapersonal space influencing processes of self-location.

The pattern of functional connectivity between SC and vPM further support our interpretation of the pertinence of collicular activity associated with RHi to the ensemble of bodily processes constituting bodily self-consciousness. The vPM was equally implicated in RHi, body-ownership of a real limb and in neurological disorders affecting body-part representation and ownership [Ehrsson et al., 2004; Gentile et al., 2013; Hilti et al., 2013; Kumral et al., 2012; van Dijk et al., 2013; Zeller et al., 2011]. Moreover, its left aspect was implicated in full-body representation and ownership [Petkova et al., 2011].

In a similar manner, increased functional connectivity between bilateral SC and the rFBA, suggest that collicular computations associated with emergence of bodily self-consciousness modulate visual representation of the full-body [Taylor et al., 2007].

Most unexpected, though very interesting, is the enhancement of functional connectivity between the SC and the anterior insula observed in the current study. The anterior insula does not seem to be directly implicated with bodily self-consciousness, a role played rather by the posterior insula [Baier and Karnath, 2008; Tsakiris, 2010]. Conversely, functional connectivity between SC and anterior insula during RHi may be associated with a correlated process of disownership of the manipulated real hand which accompanies allocation of ownership in the rubber hand. It was demonstrated that this process induces a decrease in skin temperature of the disowned real limb [Moseley et al., 2008], and the anterior insula is one main brain structure responsible for the body's thermoregulation [Klega et al., 2009].

In a broader perspective, this connectivity with the anterior insula may imply that the SC shares this last role in

modulation of bodily self-consciousness through action of interoceptive cues [Tajadura-Jimenez and Tsakiris, 2014]. The influence of interoceptive afferences in collicular neurons activity was demonstrated in early studies in the cat, with inputs of somatic origin exerting mainly an excitatory influence [Pityk, 1981].

Whether influencing only processes of body ownership or the ensemble of processes constituting bodily self-consciousness, experiment 2 findings demonstrate the pervasive impact of collicular activity during RHi in the main structures associated with bodily self-consciousness.

CONCLUSION

In this study, we demonstrated for the first time the implication of the SC in the RHi, and consequently in bodily self-consciousness. We hypothesize that the SC generates a cognitive map of the extrapersonal space that is relevant to bodily self-consciousness. Our observed functional connectivity pattern suggests that this collicular map of the extrapersonal space interacts with maps of the peripersonal and personal space generated at TPJ, vPM, and the postcentral gyrus, producing a unified representation of space that is relevant for bodily self-consciousness. We suggest that processes of multisensory integration of bodily-related sensory inputs located in this unified representation of space constitute one main factor enabling emergence of bodily self-consciousness.

ACKNOWLEDGMENTS

The authors would like to thank Donald McLaren for help on data analysis; Eric I. Knudsen, R. J. Rushmore III, Russell A. Poldrack, Thomas Nichols, Mircea Ariel Schoenfeld and Alexei Grantyn for helpful discussion; and Mircea Ariel Schoenfeld and Alexei Grantyn for comments on an earlier version of this manuscript.

REFERENCES

- Baier B, Karnath HO (2008): Tight link between our sense of limb ownership and self-awareness of actions. *Stroke* 39:486–488.
- Bisiach E, Rusconi ML, Vallar G (1991): Remission of somatoparaphrenic delusion through vestibular stimulation. *Neuropsychologia* 29:1029–1031.
- Blanke O, Landis T, Spinelli L, Seeck M (2004): Out-of-body experience and autoscopia of neurological origin. *Brain* 127(Pt 2): 243–258.
- Blanke O, Metzinger T (2009): Full-body illusions and minimal phenomenal selfhood. *Trends Cogn Sci* 13:7–13.
- Bottini G, Karnath HO, Vallar G, Sterzi R, Frith CD, Frackowiak RS, Paulesu E (2001): Cerebral representations for egocentric space: Functional-anatomical evidence from caloric vestibular stimulation and neck vibration. *Brain* 124(Pt 6):1182–1196.
- Botvinick M, Cohen J (1998): Rubber hands 'feel' touch that eyes see. *Nature* 391:756.

- Chechlacz M, Rotshtein P, Bickerton WL, Hansen PC, Deb S, Humphreys GW (2010): Separating neural correlates of allocentric and egocentric neglect: Distinct cortical sites and common white matter disconnections. *Cogn Psychol* 27:277–303.
- Clemo HR, Stein BE (1991): Receptive field properties of somatosensory neurons in the cat superior colliculus. *J Comp Neurol* 314:534–544.
- Cooper BG, Miya DY, Mizumori SG (1998): Superior colliculus and active navigation: Role of visual and non-visual cues in controlling cellular representations of space. *Hippocampus* 8:340–372.
- Desmurget M, Pelissier D, Rossetti Y, Prablanc C (1998): From eye to hand: Planning goal-directed movements. *Neurosci Biobehav Rev* 22:761–788.
- Dumoulin SO, Wandell BA (2008): Population receptive field estimates in human visual cortex. *Neuroimage* 39:647–660.
- Ehrsson HH (2007): The experimental induction of out-of-body experiences. *Science* 317:1048.
- Ehrsson HH, Spence C, Passingham RE (2004): That's my hand! Activity in premotor cortex reflects feeling of ownership of a limb. *Science* 305:875–877.
- Feinberg TE, Farah MJ (2000): Patient-based Approaches to Cognitive Neuroscience. A Bradford Book. ISBN 978-0262562133. 272pp.
- Flandrin JM, Jeannerod M (1981): Effects of unilateral superior colliculus ablation on oculomotor and vestibulo-ocular responses in the cat. *Exp Brain Res* 42:73–80.
- Fotopoulou A, Jenkinson PM, Tsakiris M, Haggard P, Rudd A, Kopelman MD (2011): Mirror-view reverses somatoparaphrenia: Dissociation between first- and third-person perspectives on body ownership. *Neuropsychologia* 49:3946–3955.
- Gandola M, Invernizzi P, Sedda A, Ferre ER, Sterzi R, Sberna M, Paulesu E, Bottini G (2012): An anatomical account of somatoparaphrenia. *Cortex* 48:1165–1178.
- Gentile G, Guterstam A, Brozzoli C, Ehrsson HH (2013): Disintegration of multisensory signals from the real hand reduces default limb self-attribution: An fMRI study. *J Neurosci* 33:13350–13366.
- Graziano MS (2001): Is reaching eye-centered, body-centered, hand-centered, or a combination? *Rev Neurosci* 12:175–185.
- Groh JM, Sparks DL (1996): Saccades to somatosensory targets III: Eye-dependent somatosensory activity in superior colliculus. *J Neurophysiol* 75:439–453.
- Guterstam A, Gentile G, Ehrsson HH (2013): The Invisible Hand Illusion: Multisensory Integration Leads to the Embodiment of a Discrete Volume of Empty Space. *J Cogn Neurosci* 25:1078–1099.
- Hall NJ, Colby CL (2011): Remapping for visual stability. *Philos Trans R Soc Lond B Biol Sci* 366:528–539.
- Heydrich L, Lopez C, Seeck M, Blanke O (2011): Partial and full own-body illusions of epileptic origin in a child with right temporoparietal epilepsy. *Epilepsy Behav* 20:583–586.
- Hilti LM, Hanggi J, Vitacco DA, Kraemer B, Palla A, Luechinger R, Jancke L, Brugger P (2013): The desire for healthy limb amputation: Structural brain correlates and clinical features of xenomelia. *Brain* 136(Pt1):318–329.
- Hyde PS, Knudsen EI (2002): The optic tectum controls visually guided adaptive plasticity in the owl's auditory space map. *Nature* 415:73–76.
- Jenkinson PM, Haggard P, Ferreira NC, Fotopoulou A (2013): Body ownership and attention in the mirror: Insights from somatoparaphrenia and the rubber hand illusion. *Neuropsychologia* 51:1453–1462.
- Karnath HO, Milner AD, Vallar G (2002): The Cognitive and Neural Bases of Spatial Neglect. Oxford University Press. ISBN 978-0198508335. 416pp.
- King AJ (2004): The Superior Colliculus. *Curr Biol* 14:335–338.
- Kinsbourne M (1970): A model for the mechanism of unilateral neglect of space. *Trans Am Neurol Assoc* 95:143–146.
- Kinsbourne M (2006): From unilateral neglect to the brain basis of consciousness. *Cereb Cortex* 42:869–874.
- Klega A, Fehér M, Buchholz HG, Birklein F, Schreckenberger M (2009): Thermoregulatory sympathetic activation: The inhibitory control of the cortex on autonomic brainstem centers. *J Nucl Med* 50:1278.
- Kumral E, Evyapan D, Sirin T, Alpaydin S (2012): Hyposchematia without spatial neglect in 2 patients with lesions involving the insula. *Cogn Behav Neurol* 25:149–153.
- Lee S, Papanikolaou A, Logothetis NK, Smirnakis SM, Keliris GA (2013): A new method for estimating population receptive field topography in visual cortex. *Neuroimage* 81:144–157.
- Lenggenhager B, Tadi T, Metzinger T, Blanke O (2007): Video ergo sum: manipulating bodily self-consciousness. *Science* 317:1096–1099.
- Maeda M, Shibasaki T, Yoshida K (1979): Labyrinthine and visual inputs to the superior colliculus neurons. *Prog Brain Res* 50:735–743.
- Makin TR, Holmes NP, Ehrsson HH (2008): On the other hand: Dummy hands and peripersonal space. *Behav Brain Res* 191:1–10.
- Martin J (2003): Neuroanatomy: Text and Atlas. 3rd edition, McGraw Hill, Medical Publishing Division.
- May PJ (2006): The mammalian superior colliculus: laminar structure and connections. *Prog Brain Res* 151:321–378.
- May PJ, Hartwich-Young R, Nelson J, Sparks DL, Porter JD (1990): Cerebellotectal pathways in the macaque: Implications for collicular generation of saccades. *Neuroscience* 36:305–324.
- McLaren DG, Ries ML, Xu G, Johnson SC (2012): A generalized form of context-dependent psychophysiological interactions (gPPI): A comparison to standard approaches. *Neuroimage* 61:1277–1286.
- Moseley GL, Olthof N, Venema A, Don S, Wijers M, Gallace A, Spence C (2008): Psychologically induced cooling of a specific body part caused by the illusory ownership of an artificial counterpart. *Proc Natl Acad Sci USA* 105:13169–13173.
- O'Keefe J, Burgess N, Donnett JG, Jeffery KJ, Maguire EA (1998): Place cells, navigational accuracy, and the human hippocampus. *Philos Trans R Soc Lond B Biol Sci* 353:1333–1340.
- Olivé I, Berthoz A (2012): Combined induction of rubber-hand illusion and out-of-body experiences. *Front Psychol* 3. pp 1–8.
- Petkova VI, Bjornsdotter M, Gentile G, Jonsson T, Li TQ, Ehrsson HH (2011): From part- to whole-body ownership in the multisensory brain. *Curr Biol* 21:1118–1122.
- Petkova VI, Ehrsson HH (2008): If I were you: Perceptual illusion of body swapping. *PLoS One* 3:e3832.
- Pfeiffer C, Serino A, Blanke O (2014): The vestibular system: A spatial reference for bodily self-consciousness. *Front Int Neurosci* 8:31.
- Pityk NI (1981): Participation of interoceptive afferent impulses in polymodal responses of superior collicular neurons in the cat. *Neurosci Behav Physiol* 11:293–298.
- Previc FH (1998): The neuropsychology of 3D space. *Psychol Bull* 124:123–164.
- Robertson IH, Marshall JC (1994): Unilateral neglect: Clinical and experimental studies. Psychology Press. ISBN 978-0863772085. 352pp.

- Rode G, Charles N, Perenin MT, Vighetto A, Trillet M, Aimard G (1992): Partial remission of hemiplegia and somatoparaphrenia through vestibular stimulation in a case of unilateral neglect. *Cortex* 28:203–208.
- Rushmore RJ, Valero-Cabre A, Lomber SG, Hilgetag CC, Payne BR (2006): Functional circuitry underlying visual neglect. *Brain* 129(Pt7):1803–1821.
- Sang FY, Jauregui-Renaud K, Green DA, Bronstein AM, Gresty MA (2006): Depersonalisation/derealisation symptoms in vestibular disease. *J Neurol Neurosurg Psychiatry* 77:760–766.
- Schaefer M, Flor H, Heinze HJ, Rotte M (2006): Dynamic modulation of the primary somatosensory cortex during seeing and feeling a touched hand. *Neuroimage* 29:587–592.
- Schaefer M, Heinze HJ, Rotte M (2009): My third arm: Shifts in topography of the somatosensory homunculus predict feeling of an artificial supernumerary arm. *Hum Brain Mapp* 30:1413–1420.
- Simeon D, Abugel J (2006): *Feeling Unreal: Depersonalization Disorder and the Loss of the Self*. Oxford University Press. ISBN 978-0195385212. 256pp.
- Stein BE, Meredith MA (1993): *The Merging of the Senses*. The MIT Press. ISBN978-0162193313. 224pp.
- Tajadura-Jimenez A, Tsakiris M (2014): Balancing the "inner" and the "outer" self: Interoceptive sensitivity modulates self-other boundaries. *J Exp Psychol Gen* 143:736–744.
- Taylor JC, Wiggett AJ, Downing PE (2007): Functional MRI analysis of body and body part representations in the extrastriate and fusiform body areas. *J Neurophysiol* 98:1626–1633.
- Tsakiris M (2010): My body in the brain: A neurocognitive model of body-ownership. *Neuropsychologia* 48:703–712.
- Tsakiris M, Hesse MD, Boy C, Haggard P, Fink GR (2007): Neural signatures of body ownership: A sensory network for bodily self-consciousness. *Cereb Cortex* 17:2235–2244.
- Vallar G, Ronchi R (2008): Somatoparaphrenia: A body delusion. A review of the neuropsychological literature. *Exp Brain Res* 192:533–551.
- van Dijk MT, van Wingen GA, van Lammeren A, Blom RM, de Kwaasteniet BP (2013): Neural basis of limb ownership in individuals with body integrity identity disorder. *PLoS One* 8: e72212.
- Wall MB, Walker R, Smith AT (2009): Functional imaging of the human superior colliculus: An optimised approach. *Neuroimage* 47:1620–1627.
- Weddell RA (2004): Subcortical modulation of spatial attention including evidence that the Sprague effect extends to man. *Brain Cogn* 55:497–506.
- Zaehle T, Jordan K, Wüstenberg T, Baudewig J, Dechent P, Mast FW (2007): The neural basis of the egocentric and allocentric spatial frame of reference. *Brain Res* 1137:92–103.
- Zeller D, Gross C, Bartsch A, Johansen-Berg H, Classen J (2011): Ventral premotor cortex may be required for dynamic changes in the feeling of limb ownership: A lesion study. *J Neurosci* 31:4852–4857.
- Zhang H, Ekstrom A (2013): Human neural systems underlying rigid and flexible forms of allocentric spatial representation. *Hum Brain Mapp* 34:1070–1087.