

Cortico–thalamic disconnection in a patient with supernumerary phantom limb

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Abstract Supernumerary phantom limb (SPL) designates the experience of an illusory additional limb occurring after brain damage. Functional neuroimaging during SPL movements documented increased response in the ipsilesional supplementary motor area (SMA), premotor cortex (PMC), thalamus and caudate. This suggested that motor circuits are important for bodily related cognition, but anatomical evidence is sparse. Here, we tested this hypothesis by studying an extremely rare patient with chronic SPL, still present 3 years after a vascular stroke affecting cortical and subcortical right-hemisphere structures. Anatomical

analysis included an advanced in vivo reconstruction of white matter tracts using diffusion-based spherical deconvolution. This reconstruction demonstrated a massive and relatively selective disconnection between anatomically preserved SMA/PMC and the thalamus. Our results provide strong anatomical support for the hypothesis that cortico–thalamic loops involving motor-related circuits are crucial to integrate sensorimotor processing with bodily self-awareness.

Keywords Supernumerary phantom limb · Thalamus · Supplementary motor area · Premotor cortex

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Introduction

Phantom limb is a neurological syndrome frequently observed in amputees, defined by phantom sensations and pain coming from the amputated limb. A similar perceptual distortion can occur in unilateral brain damage, with patients experiencing the vivid illusion of an additional limb that duplicates the real plegic limb. This phenomenon has been referred to as supernumerary phantom limb (SPL) (Brugger 2006) or phantom third limb (Fredericks 1963; Melzack 1990). Importantly, SPL patients are fully aware of the illusory nature of their perception, which is self-criticized (Halligan et al. 1993; Hari et al. 1998). Therefore, SPL is distinct and double dissociates from other disorders of motor awareness, such as anosognosia for hemiplegia, or from disorders of body awareness, such as somatoparaphrenia (Sellal et al. 1996; Bakheit 2000; Bakheit and Roudhill 2005; Staub et al. 2006; Feinberg et al. 2010). While anosognosia for hemiplegia or somatoparaphrenia are well described in acute stroke patients, only a handful of cases of SPL have been reported in the literature (Table 1).

Table 1 Existing reports of SPL

Report	Age/sex	Lesion side	Etiology	Lesion site	Associated sensory-motor deficits	SPL location	SPL component	SPL frequency of occurrence
Halligan et al. (1993)	65/M	R	H	Basal ganglia	Hypoesthesia and hemiplegia	Middle of the arm	Visual	Occasional
Halligan and Marshall (1995)	80/M	R	I	MCA territory	Hypoesthesia and hemiplegia	Left hand	Visual	–
Sellal et al. (1996)	77/M	R	I	MCA territory	Hypoesthesia and hemiplegia	Arms	Visual, kinesthetic	Occasional
Mazzoni et al. (1997)	66/M	R	I	Lenticular nucleus, medially to the internal segment of the internal capsule and superiorly to the head and body of the caudate nucleus and corona radiata	Hypoesthesia and hemiplegia	Left arm	Motor	Occasional
Vuilleumier et al. (1997)	64/F	R	Tumor resection	Bilateral parietal lobe	Bilateral hypoesthesia and paresis	Legs (2 on the right, 2 on the left)	Somesthetic, proprioceptive	Continuous
Hari et al. (1998)	37/F	R, CC	H	Mesial frontal lobe, anterior and body of the CC	–	Left arm and leg	Motor	Occasional
Canavero et al. (1999)	61/F	R	H	Thalamus, internal capsule and deep subparietal corona radiata	Anesthesia	Left arm	Motor	Occasional
Bakheit (2000)	66/M	L	H	Corona radiata	Hemiplegia	Right hand	Motor	–
McGonigle et al. (2002)	42/F	R, CC	H	Frontomesial including pre-SMA and cingulate motor areas	Hypoesthesia and hemiparesis	Left arm, left leg	Motor	Occasional
Grossi et al. (2002)	60/M	R	H	Temporal lobe	Hypoesthesia and hemiplegia	Left arm	Motor	Occasional
Miyazawa et al. (2004)	42/M	L	H	Thalamus	Anesthesia and hemiparesis	Right arm	Visual, kinesthetic	Occasional
Bakheit and Roundhill (2005)	71/M	R	H	Lentiform nucleus and thalamus with extension into the lateral and fourth ventricles	Hypoesthesia and hemiplegia	Left leg	Visual	Occasional

Table 1 (continued)

Report	Age/sex	Lesion side	Etiology	Lesion site	Associated sensory-motor deficits	SPL location	SPL component	SPL frequency of occurrence
Staub et al. (2006)	70/F	L	I	Internal capsule, thalamus, pallidum, putamen, posterior corona radiata, medial temporal lobe, caudate nucleus	Hypoesthesia and hemiplegia	Right arm and leg	Motor	Occasional
Tanaka et al. (2008)	Case 1: 47/F Case 2: 55/M	Bilateral	H	Pons	Anesthesia and hemiplegia	Arm and leg	Case 1: motor, somesthetic, visual Case 2: Motor, visual	Case 1: continuous (motor, visual) and occasional (somes- thetic) Case 2: continuous then occasional Continuous
Srivastava et al. (2008)	59/F	R	H	Globus pallidus, putamen, adjacent internal capsule and subcortical white matter with intraventricular extension	Hemiparesis and hemiplegia	Arm and hand	Visual, somesthetic	Continuous
Khateb et al. (2009)	64/F	R	H	Subcortical capsulolenticular	Hypoesthesia, anesthesia, and hemiplegia	Left arm	Motor, visual	Occasional
Millonig et al. (2011)	70/M	R	Epilepsy	Mild frontotemporal atrophy, right temporo-parietal junction	-	Left arm and leg	Motor	Occasional
Cipriani et al. (2011)	75/M	R	I	Temporo parietal junction	Hypoesthesia and hemiparesis	Left arm	Visual, motor	Occasional

M male, F female, R right, L left, H hemorrhage, I ischemic, CC corpus callosum, MCA middle cerebral artery

Of these, only a single report described a case of persistent SPL in the chronic post-stroke phase (Staub et al. 2006).

SPL patients may experience unpleasant burning or freezing sensations (Tanaka et al. 2008), or illusory sensations of objects or body parts (Bakheit 2000; Bakheit and Roundhill 2005; Khateb et al. 2009). Nonetheless, motor manifestations are usually prominent, with patients reporting experiences of SPL illusory movements (Staub et al. 2006; Tanaka et al. 2008; Khateb et al. 2009; Cipriani et al. 2011). Some patients reported uncontrollable (Cipriani et al. 2011) or purposeless (Grossi et al. 2002) movements, whereas others described voluntary, controllable SPL movements, mirroring the movements of the ipsilateral, real limb (Bakheit 2000). SPL manifestations are mostly related to the duplication of a plegic limb, which typically recovers in parallel with motor impairment (Halligan et al. 1993; Hari et al. 1998).

Although occasionally associated to left hemisphere damage (Miyazawa et al. 2004) or to bilateral damage (Vuilleumier et al. 1997), SPL mainly occurs after lesions in the right hemisphere, perhaps reflecting its crucial role in controlling and updating multiple sensory inputs integration (tactile, vestibular, visual, proprioceptive) and in maintaining and monitoring internal representation of the body state (Bartolomeo 2014). However, little is known about the lesion locations within the right hemisphere. SPL has been associated with damage to frontal regions (Hari et al. 1998; McGonigle et al. 2002), to parietal regions (Vuilleumier et al. 1997) or to the basal ganglia and thalamus (Halligan and Marshall 1995; Mazzoni et al. 1997; Canavero et al. 1999; Miyazawa et al. 2004; Bakheit and Roundhill 2005; Staub et al. 2006; Srivastava et al. 2008) (see Table 1). Damage to long-range white matter fascicles has received less attention, although an important role of dysfunctional thalamo-cortical circuits has been hypothesized in the pathophysiology of SPL (McGonigle et al. 2002; Staub et al. 2006). Functional MRI studies of SPL illusory movements documented activity in the right supplementary motor area (SMA) (McGonigle et al. 2002), premotor cortex (PMC) (Khateb et al. 2009), or in the thalamus and caudate

nucleus (Staub et al. 2006). These results suggest that in these patients a preserved sense of agency provided by intact premotor processes is not properly integrated with bodily self consciousness mechanisms. However, this hypothesis requires more direct anatomical confirmation. Here, we describe a rare case of chronic SPL. We aimed at testing the hypothesis of a direct implication of thalamo-cortical circuits involving motor-related cortical regions in the pathophysiology of SPL. To this end, we had the opportunity to use spherical deconvolution, an advanced method of white matter tractography, to track the thalamic projections in this patient, as well as the connections between the thalamus and the anatomically preserved SMA/PMC.

Patient description

VS, a right-handed woman with no previous neurological or psychiatric history, was 58-year-old at the time of our first observation. She was admitted to the hospital upon the sudden occurrence of a left-sided hemiplegia and hypoaesthesia (deep and superficial), both predominant in the upper limb. She was fully aware of her deficits and never showed any signs of anosognosia or anosodiaphoria. There were no signs of mental confusion, or of impaired judgment or reasoning. MMSE (Folstein et al. 1975) was 29/30. There were mild signs of left visual neglect without visual field defects, and mild dysexecutive deficits (Table 2). VS provided written informed consent for publication of her case, and the Salpêtrière Hospital ethical committee (Paris, France) approved the study.

MRI showed a fronto-temporal haemorrhagic stroke in the right hemisphere, with substantial involvement of the subcortical white matter (Fig. 1). Since the disease onset, VS experienced the intermittent feeling of having “a third hand”, which she described as being in close proximity to her hemiplegic left upper limb (Fig. 2).

She reported that she could execute movements or actions with her left “other hand”. For example, she had the feeling that she could open a cupboard with it. In

Table 2 Neuropsychological assessment of VS 1 and 18 months after onset

Time after onset	Bisection of 200-mm lines (mm of rightward deviation)	Letter cancellation (left/right hits, max = 30/30)	Reading task (left/right hits, max = 61/55)	Landscape drawing score (/6)	Hayling test (category A errors/category B errors, max = 15/15)	N-back-2 (/10)	Plus/minus (/30)
1 month	10*	26*/29	60*/55	6	0/15*	1*	30
18 months	5	30/30	61/55	5.5*	0/5	4*	30

Normative data: Letter cancellation (Mesulam 1985); Line bisection and reading task (Azouvi et al. 2006); Landscape drawing (Gainotti et al. 1986); Hayling test (Burgess and Shallice 1997); N-back test from TAP, Test of Attentional Performance (Zimmermann and Fimm 1994); Plus/minus task (Miyake et al. 2000)

Asterisks denote pathological performance

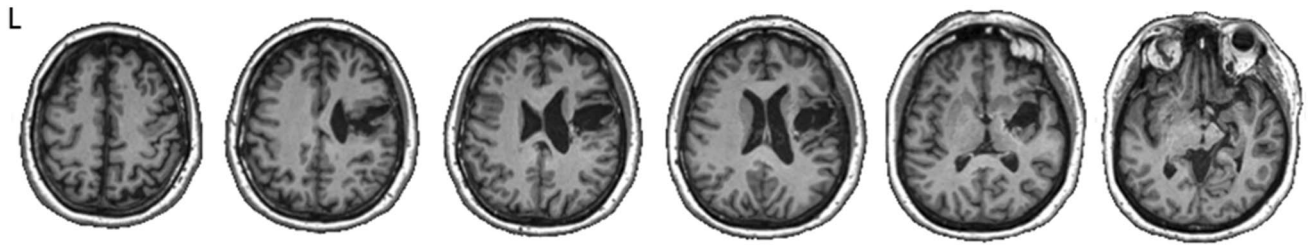


Fig. 1 Axial T1 images showing the sequelae of the lesion in the right hemisphere



Fig. 2 A drawing made by the patient, representing her own body with the location of the SPL (arrow)

addition to this movement illusion, she reported phantom sensations of touching tissues, of warmth and heaviness. As she said in conversation with the examiner:

Examiner: How many hands do you have?

VS: I feel I have three hands. I know that's not possible because I have my right healthy hand and my left paralyzed hand, which makes two. But sometimes I have the vivid sensation to have a third hand that helps me in the daily life.

Examiner: Can you see it?

VS: No. But I feel its presence as if it existed. I seem to touch tissues (with it); it's very hot like when I touch a hot plate, and I also have a feeling of heaviness.

SPL feelings occurred several times a day, for a few seconds or minutes. Importantly, even if she could not directly control her phantom movements, VS did not perceive them as being controlled by an external force (such as in cases of alien/anarchic hand, Marchetti and Della Sala 1998); instead, SPL movements seemed to be triggered by an intention of action. She was fully aware of the illusory nature of her feeling.

Examiner: How does your third hand work? Does it work well?

VS: Yes. It can massage my head when I feel pain. It's really strange.

Examiner (*presenting a pen to the patient*): Can you close your eyes and catch this pen with your right hand?

VS (*does it*): Yes, done.

Examiner: Now open your eyes. Can you write your name?

VS (*writes her name on a paper sheet*): Yes

Examiner: Now, can you do the same with your third hand?

VS (*does nothing*): Yes, now I've the pen in my hand

Examiner: Can you write your name?

VS: No, because it's not my right hand. I know it's not possible because my third hand doesn't work, although I have the feeling it does.

At follow-up examination 18 months post-stroke, the motor deficit remained unchanged. There was some improvement in somatosensory deficits. Signs of left visual neglect and dysexecutive deficits had also improved (see Table 2). However, feelings of SPL were still present, if less vivid and less frequent. Specifically, VS reported the persistence of sensations of movement, warmth and heaviness.

Lesion analysis

Imaging data

The patient underwent an MRI scan during the chronic post-stroke phase (20 months post onset), when the brain lesion was likely to be stable and the edema reabsorbed. A control group of five healthy controls, with no history of

neurological or psychiatric disease and matched for age, gender and education were also recruited.

MRI scans were obtained on a Siemens 3-Tesla VERIO TIM MRI scanner. The acquisition sequence included a three-dimensional (3D) structural T_1 -weighted MRI (TR = 2300 ms, TE = 2.98 ms; acquisition matrix: $240 \times 256 \times 176$; voxel resolution: $1 \times 1 \times 1 \text{ mm}^3$), as well as a diffusion sequence using echo-planar imaging (b value = 1500 s/mm^2 , TR = 690 ms, TE = 85 ms, acquisition matrix: $110 \times 110 \times 140$, voxel resolution = $2 \times 2 \times 2 \text{ mm}^3$). Using a 32-channel array coil and a maximum gradient of 28 mT/m, diffusion weighting isotropically distributed along 60 directions and 6 non diffusion-weighted volumes were acquired.

Grey matter analysis

We followed a previously described procedure (Lunven et al. 2015) to reconstruct the lesion. We first manually drawn the lesion extent onto the original 3D T1 MRI, using the MRICro software (Rorden and Brett 2000) (<http://www.mricro.com>). Then, the 3D brain scans and lesion volumes were normalized to the standard Montreal Neurological Institute (MNI) brain template in Statistical Parametric Mapping-5 (<http://www.fil.ion.ucl.ac.uk/spm>) running under Matlab 7.5 (<http://www.mathworks.com>). To reduce lesion-induced registration errors, spatial normalization was performed using a mask that excluded the damaged areas of the brains, thereby preventing these areas from biasing the transformation (Brett et al. 2001). The anatomical distribution of the lesion was assessed using the Automated Anatomical Labeling map (template AAL; Tzourio-Mazoyer et al. 2002) implemented in MRICron (<http://www.mccauslandcenter.sc.edu/mricro/mricron>).

White matter analysis

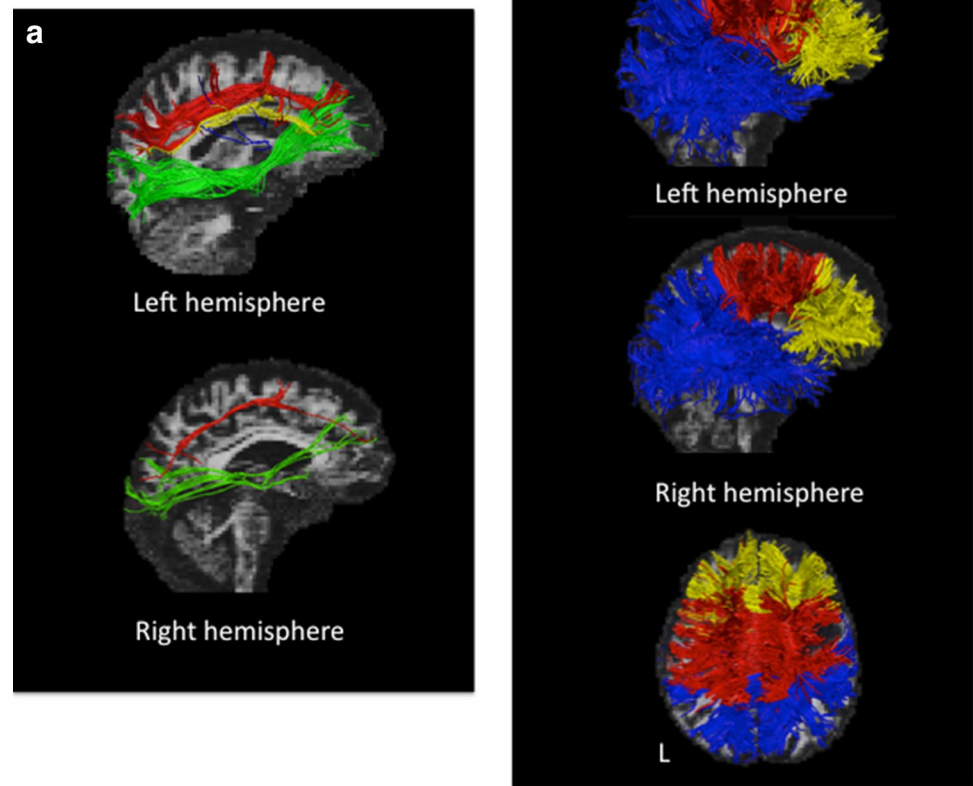
Following a previously described procedure (Thiebaut de Schotten et al. 2014), we performed an advanced in vivo reconstruction of white matter tracts using diffusion-based spherical deconvolution. The reversed phase-encoding image was used to estimate the susceptibility-induced off-resonance field using a method similar to that described in Andersson et al. (2003) as implemented in FSL (<http://www.fsl.fmrib.ox.ac.uk/fs>; Smith et al. 2004). Eddy currents and head movements were then simultaneously corrected using eddy tool in FSL. A spherical deconvolution approach based on the damped version of the Richardson Lucy algorithm (Dell'Acqua et al. 2010) was employed to estimate fiber orientation distribution (FOD) in each white matter voxel. A first absolute threshold was used to exclude small spurious

local maxima due to noise or isotropic voxels and a second relative threshold of 5% of the maximum amplitude of the FOD was applied to remove the remaining local maxima with values greater than the absolute threshold. To assess the potential implication of thalamo-cortical circuits in SPL, we tracked the thalamic projections, as well as the connections between the thalamus and the anatomically preserved SMA/PMC. In addition, long-range caudo-rostral fasciculi were tracked in each hemisphere. In particular, the trajectories of the following tracts were reconstructed: the three subcomponents of the parieto-frontal superior longitudinal fasciculus (SLF I–III), the inferior fronto-occipital fasciculus (IFOF), in each hemisphere, as well as the genu, body and splenium of the corpus callosum. Following a previously described procedure (Rojkova et al. 2016), a multiple region of interests (ROIs) approach was used to isolate the three components of the superior longitudinal fasciculus (i.e. SLF I, SLF II and SLF III). Four ROIs were defined around the superior, middle and inferior frontal gyri and posteriorly in the parietal region. To exclude the fibers of the arcuate fasciculus projecting to the temporal lobe, we defined a “NOT” ROI in the temporal white matter. Two ROIs were used to reconstruct the IFOF. A coronal ROI was delineated around the white matter of the external/extreme capsule, and another coronal ‘AND’ ROI in the occipital lobe. Finally, we used a one-ROI approach to extract fibres traversing the genu, the body and the splenium of the corpus callosum.

All these fasciculi were chosen on the basis of their potential damage given the lesion localization, and because of their implication in visual neglect (Bartolomeo et al. 2007; Doricchi et al. 2008; Urbanski et al. 2011; Ciaraffa et al. 2012; Lunven et al. 2014, 2015). Tract reconstructions were performed in VS and compared to healthy controls.

Regions of interest (ROI) of the thalamus and its main nuclei (anterior, centro-median, pulvinar) were issued from a three-dimensional histological atlas of the human basal ganglia (Yelnik et al. 2007; Bardinet et al. 2009). Subsequently, these ROIs were superimposed on the normalized anatomical T1 of each subject, and then placed on the diffusion space. Using spherical deconvolution (Dell'Acqua et al. 2013), we first visualized left and right thalamic projections and of its main nuclei using a one-ROI approach. Then, a two-ROI approach was used to reconstruct the white matter connections for each hemisphere between the thalamus and the SMA, and between the thalamic and the PMC. Following a previously described procedure (Lehericy et al. 2004), the SMA was anatomically defined as a region extending from the brain vertex to the cingulate sulcus in the superior–inferior direction, and from the precentral sulcus caudally to a line intersecting the anterior commissure. Mean hindrance modulated orientational anisotropy (HMOA), was individually extracted for each fasciculus.

Fig. 3 **a** Tractography dissections: reconstruction of the SLF I (*red* connections), SLF II (*yellow* connections), SLF III (*blue* connections), IFOF (*green* connections) in the *left* and in the *right* hemisphere. **b** Reconstruction of the genu (*yellow*), the body (*red*), and the splenium (*blue*) of the corpus callosum. *L* left



HMOA is a new index employed as a surrogate for tract microstructural organization, because it produces a better estimate of white matter bundle microstructure when crossing with other fiber populations and is considered more sensitive to axonal myelination, fiber diameter and axonal density than voxel-specific measures such as the Fractional Anisotropy (Dell'Acqua et al. 2013). Statistical analysis of diffusion imaging output values was conducted using significant two-tailed *t* test comparing an individual case with small control samples (Crawford and Garthwaite 2002; Migliaccio et al. 2011; see also Bourgeois et al. 2012). A False Discovery Rate (FDR) of .015 was used to correct for multiple comparisons (Benjamini and Hochberg 1995).

Results

Grey matter

VS presented a right hemispheric stroke involving cortical and subcortical regions, including the putamen, the pallidum, the insula, the amygdala, the superior temporal gyrus,

the pre- and post-central gyri, the Heschl gyri, the Rolandic operculum, and the inferior frontal operculum (Fig. 1). With a volume of 36 mm³, the lesion was far from being massive, but it was situated at a strategic crossroad of several pathways connecting cortical and subcortical sites.

White matter

Tractography analysis of long-range of white matter tracts indicated a complete disconnection of SLF II and III in the patient's right hemisphere (HMOA, 0). Signs of callosal disconnection were also observed in the genu (HMOA, 0.110, $p = .003$) and in the splenium (HMOA, 0.149, $p = .012$).

The homologous tracts in the left hemisphere, as well as all the other explored tracts, did not differ from controls' (left SLF II, HMOA, 0.059; left SLF III, 0.057; right SLF I, HMOA, 0.057; left SLF I, HMOA, 0.059; right IFOF, HMOA, 0.093; left IFOF, HMOA, 0.095; callosal body, HMOA, 0.150; all $ps > 0.088$) (Fig. 3).

Table 3 shows the HMOA values for intrathalamic and thalamo-cortical connections. Analysis of intrathalamic connections in VS compared to healthy controls

Table 3 Mean hindrance modulated orientational anisotropy (HMOA) for thalamic tracts in VS and healthy controls

	VS	Controls
Thalamic nuclei		
Thalamus	R 0.078 (0.047)*	0.091 (0.003)
	L 0.082 (0.052)	0.088 (0.011)
Anterior thalamic nuclei	R 0.075 (0.043)	0.054 (0.036)
	L 0.081 (0.050)	0.070 (0.009)
Centro-median thalamic nuclei	R 0.075 (0.041)*	0.094 (0.004)
	L 0.091 (0.059)	0.086 (0.014)
Pulvinar	R 0.080 (0.045)**	0.086 (0.007)
	L 0.077 (0.046)	0.083 (0.013)
Thalamo–cortical connections		
Thalamus-SMA	R 0*	0.096 (0.010)
	L 0.090 (0.054)	0.096 (0.016)
Thalamus-PMC	R 0***	0.0956 (0.007)
	L 0.097 (0.056)	0.092 (0.006)

SD is reported in parentheses

R right, L left, SMA supplementary motor area, PMC premotor cortex

* $p < .05$; ** $p < .01$; *** $p < .001$ (One-tailed t tests, with a FDR of .15 for multiple comparisons corrections)

demonstrated an overall disconnection of the right thalamus, of the pulvinar and of the centro-median thalamic nuclei.¹ Importantly, there was a massive disconnection between the right thalamus and the SMA, and between the right thalamus and the PMC (Table 3; Fig. 4).

Discussion

We described a patient who experienced vivid SPL feelings after a right hemispheric stroke, with a highly unusual persistence over 1 year after onset. In our patient, SPL feelings had motor components (illusion of unintended but purposeful movements) and somesthetic components (illusions of touching tissue, of warmth and heaviness). The anatomical study demonstrated a predominantly subcortical lesion, with massive corticothalamic disconnection between the right thalamus and anatomically preserved SMA and PMC.

Self-awareness is a complex construct, often considered to encompass three distinct but related aspects: body awareness, sense of agency and motor awareness (Tsakiris 2010). The sense of ownership or self-identification is described as the recognition of the body as one's own. This aspect

¹ To assess the potential influence of cerebellar disconnection on our results, we also reconstructed tracts between the right thalamus and the SMA, and between the right thalamus and the PMC, while excluding the cerebellar tracts. The pattern of results did not change (Right thalamus/SMA; HMOA in VS, 0; in controls, 0.094; $p < 0.05$. Right thalamus/PMC; HMOA in VS, 0; in controls, 0.094, $p < 0.001$).

may be impaired by perceptual illusions, such as the rubber hand illusion (Botvinick and Cohen 1998; Tsakiris 2010), or by right hemisphere damage, such as in asomatognosia/somatoparaphrenia (Sellal et al. 1996; Bakheit 2000; Bakheit and Roundhill 2005; Staub et al. 2006; Feinberg et al. 2010; Bartolomeo 2014; Bartolomeo et al. 2017a). Other right brain-damaged patients do recognize their left hand as belonging to them, but are also prone to claim that another person's left hand is their own (Garbarini et al. 2013). At variance with these conditions, our patient had fully preserved awareness of the existence and ownership of her left limbs, and full insight into the illusory character of her SPL. The second aspect, sense of agency, may be impaired in cases of anarchic (alien) hand, whereby the patient is unable to experience complex, goal-directed movements as originating from his/her will (Marchetti and Della Sala 1998). Direct electrical stimulation of the SMA during awake brain surgery can provoke an irrepressible urge to move (Desmurget et al. 2009), a result which might be related to our patient's feeling of unintended but purposeful movements of her SPL. However, our patient never experienced the compulsive character of anarchic hand movements.

The third aspect, motor awareness, is considered to be impaired in anosognosia for hemiplegia (Berti et al. 2005), and is often discussed in relation to the forward model for action generation (Wolpert and Miall 1996). According to the internal models of motor system (Frith et al. 2000; Blakemore et al. 2002), motor control and awareness originate from the comparison between the execution of an action and the representation of the predicted consequences of the executed action (efference copy). It relies on the integrity of predictors, which estimate the sensory consequences of the motor command prior to the execution of a movement, and of comparators, which provide the motor commands for movement and check for the congruency between the awareness of the intended movement and the actual state of the motor system. According to this model, a perception of a movement is often based on the predicted outcome rather than on its actual consequences, which might lead to a sensation of a movement even though the action is lost or compromised. Under normal circumstances, an update of the predictors should then occur, to prevent illusory movements. SPL in our patient was often associated to a feeling of goal-directed movement, and occasionally triggered by the examiner's instruction to make a movement with her supernumerary limb (take a pen with your third hand). In our patient, spared PMC or SMA activity in the right hemisphere might generate some experience of movement. However, because of the cortico–thalamic disconnection, this activity would not be integrated with multisensory signals (visual, kinesthetic, somatosensory, proprioceptive), which normally contribute

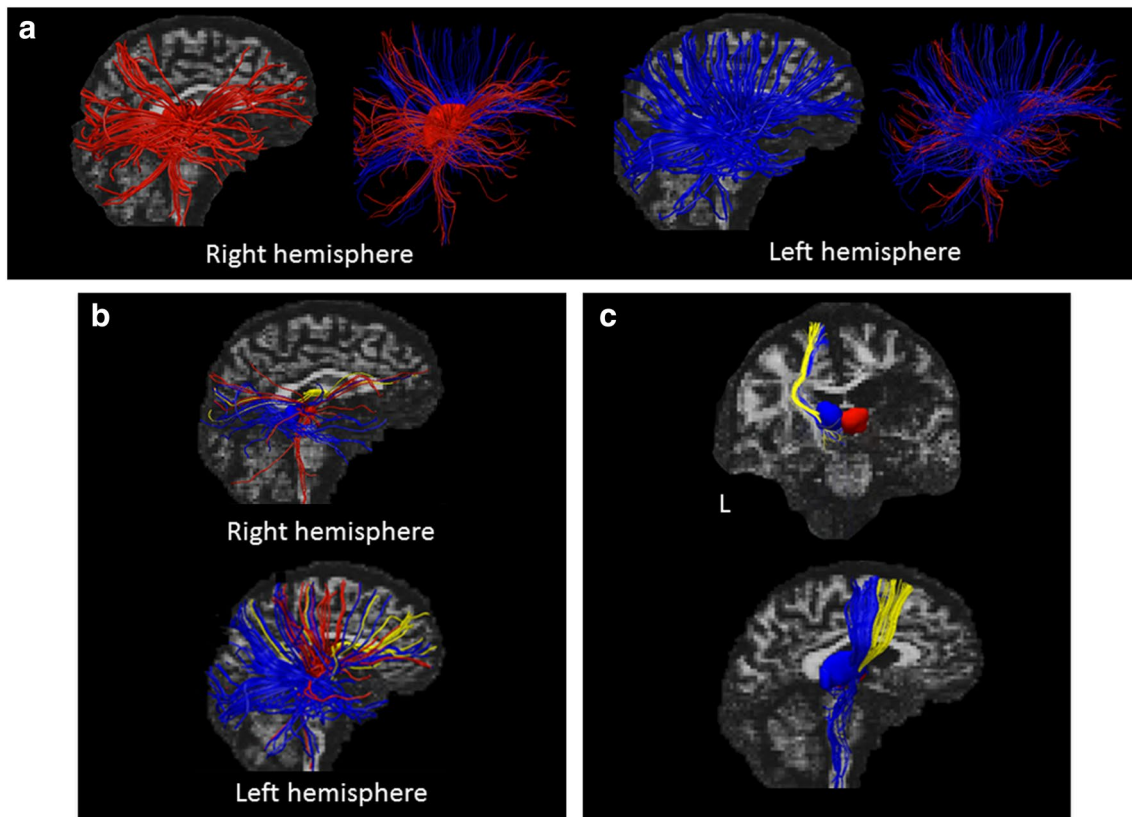


Fig. 4 **a** Thalamo–cortical connections in the *right* hemisphere (*red* connections) and in the *left* hemisphere (*blue* connections). **b** Tractography dissections: reconstruction of the anterior thalamic (*yellow*), centro-median (*red*) and pulvinar nuclei (*blue*) in the *right* and in the

left hemisphere. **c** Tractography dissections: *white* matter connections between the *left/right* thalamus, the SMA (*blue* connections) and the PMC (*yellow* connections). Note the complete lack of visualization of the *right* hemispheric connections. *L* left

to a unitary percept of the body (Blanke 2012). The attribution of sensorimotor activity to a SPL might result from spared processes in our patient, such as successful comparison between intended and executed movements (Berti and Pia 2006), or intact reality monitoring processes (Jenkinson et al. 2009; Saj et al. 2014). Consistent with this hypothesis, our patient always remained cognizant of the illusory nature of her SPL. In this view, SPL might be conceived as a compromise construct to ground on a phantom body part sensorimotor experiences which could not be attributed to the real left limb. This proposal is reminiscent of the possibility of perceptual completion resulting from residual processing occurring in a damaged brain network (Feinberg and Roane 2003), or from the activity of the left hemisphere when it does no longer receive integrated information from its right counterpart (confabulatory completion; Geschwind 1965; Bartolomeo et al. 2017a). In our patient, the anterior callosal disconnection could have indeed jeopardized the inter-hemispheric integration of SMA/PMC activity.

Neuroimaging evidence in healthy subjects has stressed the role of PMC in the multisensory integration of bodily

signals giving rise to bodily conscious experience (Ehrsson et al. 2004; Macaluso and Driver 2005). Our demonstration of a massive white matter disconnection between the thalamus and SMA/PMC are consistent with this hypothesis, as well as with fMRI results revealing SMA activation (McGonigle et al. 2002) or impaired functioning of the thalamo–cortical system (Staub et al. 2006) in SPL patients.

Anatomically, premotor regions are densely connected to the thalamus, especially the pulvinar and the centro-median nucleus (Fang et al. 2006; Benarroch 2008; Cappe et al. 2009). Thalamic nuclei constitute key nodes integrating multisensory processing by means of thalamo–cortical feed forward connections (Fang et al. 2006; Benarroch 2008; Cappe et al. 2009). Indeed, although the pulvinar is mainly associated with visual processes, electrophysiological evidence demonstrated a key role of this structure in multisensory and sensorimotor integration (Cappe et al. 2009; Tyll et al. 2011). In our patient, the cortico–thalamic disconnection of the pulvinar nucleus and of the centro-median nucleus might disrupt the coupling of SMA/PMC activity with multisensory integration (Fang et al. 2006; Benarroch 2008; Cappe et al. 2009).

Thus, our findings indicate that disruption of a thalamo–cortical network in the right hemisphere, crucial to integrate motor programming with multisensory information, can give rise to SPL.

To the best of our knowledge, there is only another case report of chronic SPL, persisting 4 years after stroke onset (Staub et al. 2006). In that study, fMRI suggested the presence of an abnormal closed-loop functioning of the thalamocortical system. The rarity of SPL cases only permits single case reports, with their accompanying drawbacks (Bartolomeo et al. 2017b). In particular, quantitative anatomo-clinical correlations (e.g., between indexed of thalamo–cortical disconnection and measures of SPL) are precluded. On the other hand, our approach usefully complements the existing fMRI data, which are neutral with respect to directional causality. Taken together, fMRI results (McGonigle et al. 2002; Staub et al. 2006; Khateb et al. 2009) and our tractography findings suggest that the interruption of thalamic afferents might induce the chronic persistence of SPL by preventing any corrections of the mismatch between expected and effective movement.

The insula, which was also damaged in VS, participates to the integration of somatosensory and somesthetic information (Berlucchi and Aglioti 2010) through its connections with other brain regions, including SMA and PMC (Flynn 1999). Together with cortical damage to the post-central gyrus, this may account for the illusory sensations of touch, warmth or heaviness reported by VS. Note, moreover, that the sensation or urge of movement (Penfield and Faulk 1955) or even true movements could be elicited by electrical stimulation of the insula in humans (Showers and Lauer 1961), suggesting a role for this region in sensorimotor integration.

Importantly, long-range white matter tracts were largely preserved in VS, except for the thalamo–cortical connections, for the ventral and intermediate branches of the right SLF, and for callosal connections in the genu and splenium. Fronto-parietal disconnections have been related to the presence of signs of left visual neglect (Bartolomeo et al. 2007; Doricchi et al. 2008; Urbanski et al. 2011; Ciaraffa et al. 2012). An additional splenial disconnection may result in the chronic persistence of neglect (Lunven et al. 2015).

To conclude, we demonstrated a severe disconnection between thalamic nuclei and motor processing-related regions in the right hemisphere of a patient with chronic supernumerary phantom limb, a rarely occurring neurological condition. Our results provide anatomical support to the hypothesis that cortico–thalamic loops involving motor-related regions are crucial for important aspects of bodily self-consciousness.

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References

- Andersson JL, Skare S, Ashburner J (2003) How to correct susceptibility distortions in spin-echo echo-planar images: application to diffusion tensor imaging. *Neuroimage* 20:870–888. doi:[10.1016/S1053-8119\(03\)00336-7](https://doi.org/10.1016/S1053-8119(03)00336-7)
- Azouvi P, Bartolomeo P, Beis JM, Perennou D, Pradat-Diehl P, Rousseaux M (2006) A battery of tests for the quantitative assessment of unilateral neglect. *Restor Neurol Neurosci* 24:273–285
- Bakheit AM (2000) Illusory movements of the paralysed upper limb in stroke. *J Neurol Neurosurg Psychiatry* 69:837
- Bakheit AM, Roundhill S (2005) Supernumerary phantom limb after stroke. *Postgrad Med J* 81:e2. doi:[10.1136/pgmj.2004.027086](https://doi.org/10.1136/pgmj.2004.027086)
- Bardinet E, Bhattacharjee M, Dormont D et al (2009) A three-dimensional histological atlas of the human basal ganglia. II. Atlas deformation strategy and evaluation in deep brain stimulation for Parkinson disease. *J Neurosurg* 110:208–219. doi:[10.3171/2008.3.17469](https://doi.org/10.3171/2008.3.17469)
- Bartolomeo P (2014) Attention disorders after right brain damage: living in halved worlds. Springer, London
- Bartolomeo P, Thiebaut de Schotten M, Doricchi F (2007) Left unilateral neglect as a disconnection syndrome. *Cereb Cortex* 17:2479–2490
- Bartolomeo P, de Vito S, Malkinson TS (2017a) Space-related confabulations after right hemisphere damage. *Cortex* 87:166–173. doi:[10.1016/j.cortex.2016.07.007](https://doi.org/10.1016/j.cortex.2016.07.007)
- Bartolomeo P, Malkinson TS, de Vito S (2017b) Botallo's error, or the quandaries of the universality assumption. *Cortex* 86:176–185. doi:[10.1016/j.cortex.2016.09.026](https://doi.org/10.1016/j.cortex.2016.09.026)
- Benarroch EE (2008) The midline and intralaminar thalamic nuclei: anatomic and functional specificity and implications in neurologic disease. *Neurology* 71:944–949. doi:[10.1212/01.wnl.0000326066.57313.13](https://doi.org/10.1212/01.wnl.0000326066.57313.13)
- Benjamini Y, Hochberg Y (1995) Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc B* 57:488–491
- Berlucchi G, Aglioti SM (2010) The body in the brain revisited. *Exp Brain Res* 200:25–35. doi:[10.1007/s00221-009-1970-7](https://doi.org/10.1007/s00221-009-1970-7)
- Berti A, Pia L (2006) Understanding motor awareness through normal and pathological behavior. *Curr Directions Psychol Sci* 15:245–250
- Berti A, Bottini G, Gandola M et al (2005) Shared cortical anatomy for motor awareness and motor control. *Science* 309:488–491. doi:[10.1126/science.1110625](https://doi.org/10.1126/science.1110625)
- Blakemore SJ, Wolpert DM, Frith CD (2002) Abnormalities in the awareness of action. *Trends Cogn Sci* 6:237–242
- Blanke O (2012) Multisensory brain mechanisms of bodily self-consciousness. *Nat Rev Neurosci* 13:556–571. doi:[10.1038/nrn3292](https://doi.org/10.1038/nrn3292)
- Botvinick M, Cohen J (1998) Rubber hands 'feel' touch that eyes see. *Nature* 391:756. doi:[10.1038/35784](https://doi.org/10.1038/35784)
- Bourgeois A, Chica AB, Migliaccio R, Thiebaut de Schotten M, Bartolomeo P (2012) Cortical control of inhibition of return: evidence from patients with inferior parietal damage and visual neglect. *Neuropsychologia* 50:800–809
- Brett M, Leff AP, Rorden C, Ashburner J (2001) Spatial normalization of brain images with focal lesions using cost function masking. *Neuroimage* 14:486–500
- Brugger P (2006) From phantom limb to phantom body. In: Knoblich G, Thornton IM, Grosjean M, Shiffrar M (eds) Human

- body perception from the inside out. Oxford University Press, Oxford, pp 171–209
- Burgess P, Shallice T (1997) The Hayling and Brixton tests. Thurston, Suffolk
- Canavero S, Bonicalzi V, Castellano G, Perozzo P, Massa-Micon B (1999) Painful supernumerary phantom arm following motor cortex stimulation for central poststroke pain: case report. *J Neurosurg* 91:121–123. doi:[10.3171/jns.1999.91.1.0121](https://doi.org/10.3171/jns.1999.91.1.0121)
- Cappe C, Morel A, Barone P, Rouiller EM (2009) The thalamo-cortical projection systems in primate: an anatomical support for multisensory and sensorimotor interplay. *Cereb Cortex* 19:2025–2037. doi:[10.1093/cercor/bhn228](https://doi.org/10.1093/cercor/bhn228)
- Ciaraffa F, Castelli G, Parati EA, Bartolomeo P, Bizzi A (2012) Visual neglect as a disconnection syndrome? A confirmatory case report. *Neurocase*. doi:[10.1080/13554794.2012.667130](https://doi.org/10.1080/13554794.2012.667130)
- Cipriani G, Picchi L, Vedovello M, Nuti A, Fiorino MD (2011) The phantom and the supernumerary phantom limb: historical review and new case. *Neurosci Bull* 27:359–365
- Crawford JR, Garthwaite PH (2002) Investigation of the single case in neuropsychology: confidence limits on the abnormality of test scores and test score differences. *Neuropsychologia* 40:1196–1208
- Dell'Acqua F, Scifo P, Rizzo G, Catani M, Simmons A, Scotti G, Fazio F (2010) A modified damped Richardson–Lucy algorithm to reduce isotropic background effects in spherical deconvolution. *Neuroimage* 49:1446–1458
- Dell'Acqua F, Simmons A, Williams SC, Catani M (2013) Can spherical deconvolution provide more information than fiber orientations? Hindrance modulated orientational anisotropy, a true-tract specific index to characterize white matter diffusion. *Hum Brain Mapp* 34:2464–2483. doi:[10.1002/hbm.22080](https://doi.org/10.1002/hbm.22080)
- Desmurget M, Reilly KT, Richard N, Szathmari A, Mottolese C, Sirigu A (2009) Movement intention after parietal cortex stimulation in humans. *Science* 324:811–813. doi:[10.1126/science.1169896](https://doi.org/10.1126/science.1169896)
- Doricchi F, Thiebaut de Schotten M, Tomaiuolo F, Bartolomeo P (2008) White matter (dis)connections and gray matter (dys) functions in visual neglect: gaining insights into the brain networks of spatial awareness. *Cortex* 44:983–995
- 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. doi:[10.1126/science.1097011](https://doi.org/10.1126/science.1097011)
- Fang PC, Stepniewska I, Kaas JH (2006) The thalamic connections of motor, premotor, and prefrontal areas of cortex in a prosimian primate (*Otolemur garnettii*). *Neuroscience* 143:987–1020. doi:[10.1016/j.neuroscience.2006.08.053](https://doi.org/10.1016/j.neuroscience.2006.08.053)
- Feinberg TE, Roane DM (2003) Anosognosia. In: Feinberg TE, Farah MJ (eds) *Behavioral neurology and neuropsychology*. McGraw-Hill Professional, New York
- Feinberg TE, Venneri A, Simone AM, Fan Y, Northoff G (2010) The neuroanatomy of asomatognosia and somatoparaphrenia. *J Neurol Neurosurg Psychiatry* 81:276–281. doi:[10.1136/jnnp.2009.188946](https://doi.org/10.1136/jnnp.2009.188946)
- Flynn FG (1999) Anatomy of the insula functional and clinical correlates. *Aphasiology* 13:55–78
- Folstein MF, Folstein SE, McHugh PR (1975) “Mini mental state”: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 12:189–198
- Fredericks J (1963) Occurrence and nature of phantom limb phenomena following amputation of body parts and following lesions of the central peripheral nervous system. *Psychiatr Neurol Neurochir* 66:73–97
- Frith CD, Blakemore S, Wolpert DM (2000) Explaining the symptoms of schizophrenia: abnormalities in the awareness of action. *Brain Res Brain Res Rev* 31:357–363. doi:[10.1016/S0165-0173\(99\)00052-1](https://doi.org/10.1016/S0165-0173(99)00052-1)
- Gainotti G, D'Erme P, Monteleone D, Silveri MC (1986) Mechanisms of unilateral spatial neglect in relation to laterality of cerebral lesions. *Brain* 109:599–612
- Garbarini F, Pia L, Piedimonte A, Rabuffetti M, Gindri P, Berti A (2013) Embodiment of an alien hand interferes with intact-hand movements. *Curr Biol* 23:R57–R58. doi:[10.1016/j.cub.2012.12.003](https://doi.org/10.1016/j.cub.2012.12.003)
- Geschwind N (1965) Disconnexion syndromes in animals and man: part II. *Brain* 88:585–644
- Grossi D, Di Cesare G, Tamburro RP (2002) On the syndrome of the “spare limb”: one case. *Percept Mot Skills* 94:476–478. doi:[10.2466/pms.2002.94.2.476](https://doi.org/10.2466/pms.2002.94.2.476)
- Halligan PW, Marshall JC (1995) Supernumerary phantom limb after right hemispheric stroke. *J Neurol Neurosurg Psychiatry* 59:341–342
- Halligan PW, Marshall JC, Wade DT (1993) Three arms: a case study of supernumerary phantom limb after right hemisphere stroke. *J Neurol Neurosurg Psychiatry* 56:159–166
- Hari R, Hanninen R, Makinen T, Jousmaki V, Forss N, Seppa M, Salonen O (1998) Three hands: fragmentation of human bodily awareness. *Neurosci Lett* 240:131–134
- Jenkinson PM, Edelstyn NM, Drakeford JL, Ellis SJ (2009) Reality monitoring in anosognosia for hemiplegia. *Conscious Cogn* 18:458–470. doi:[10.1016/j.concog.2008.12.005](https://doi.org/10.1016/j.concog.2008.12.005)
- Khateb A, Simon SR, Dieguez S et al (2009) Seeing the phantom: a functional magnetic resonance imaging study of a supernumerary phantom limb. *Ann Neurol* 65:698–705. doi:[10.1002/ana.21647](https://doi.org/10.1002/ana.21647)
- Lehericy S, Ducros M, Krainik A, Francois C, Van de Moortele PF, Ugurbil K, Kim DS (2004) 3-D diffusion tensor axonal tracking shows distinct SMA and pre-SMA projections to the human striatum. *Cereb Cortex* 14:1302–1309. doi:[10.1093/cercor/bhh091](https://doi.org/10.1093/cercor/bhh091)
- Lunven M, Thiebaut De Schotten M, Glize B et al (2014) Effector-dependent neglect and splenial disconnection: a spherical deconvolution tractography study. *Exp Brain Res* 232:3727–3736. doi:[10.1007/s00221-014-4051-5](https://doi.org/10.1007/s00221-014-4051-5)
- Lunven M, Thiebaut De Schotten M, Bourlon C, Duret C, Migliaccio R, Rode G, Bartolomeo P (2015) White matter lesional predictors of chronic visual neglect: a longitudinal study. *Brain* 138:746–760. doi:[10.1093/brain/awu389](https://doi.org/10.1093/brain/awu389)
- Macaluso E, Driver J (2005) Multisensory spatial interactions: a window onto functional integration in the human brain. *Trends Neurosci* 28:264–271. doi:[10.1016/j.tins.2005.03.008](https://doi.org/10.1016/j.tins.2005.03.008)
- Marchetti C, Della Sala S (1998) Disentangling the alien and anarchic hand. *Cognitive Neuropsychiatry* 3:191–207
- Mazzoni M, Lucchin C, Meucci G, Vista M, Moretti P, Sartucci F (1997) Supernumerary phantom limb after ischaemic stroke. *Neurocase* 3:223–230
- McGonigle DJ, Hanninen R, Salenius S, Hari R, Frackowiak RS, Frith CD (2002) Whose arm is it anyway? An fMRI case study of supernumerary phantom limb. *Brain* 125:1265–1274
- Melzack R (1990) Phantom limbs and the concept of a neuromatrix. *Trends Neurosci* 13:88–92. doi:[10.1016/0166-2236\(90\)90179-E](https://doi.org/10.1016/0166-2236(90)90179-E)
- Mesulam MM (1985) *Principles of behavioral neurology*. F.A. Davis, Philadelphia
- Migliaccio R, Agosta F, Toba MN et al (2011) Brain networks in posterior cortical atrophy: a single case tractography study and literature review. *Cortex*. doi:[10.1016/j.cortex.2011.10.002](https://doi.org/10.1016/j.cortex.2011.10.002)
- Millonig A, Bodner T, Donnemiller E, Wolf E, Unterberger I (2011) Supernumerary phantom limb as a rare symptom of epileptic seizures—case report and literature review. *Epilepsia* 52:e97–e100. doi:[10.1111/j.1528-1167.2011.03156.x](https://doi.org/10.1111/j.1528-1167.2011.03156.x)
- Miyake A, Friedman NP, Emerson MJ, Witzki AH, Howerter A, Wager TD (2000) The unity and diversity of executive functions and their contributions to complex “Frontal Lobe” tasks: a

- latent variable analysis. *Cogn Psychol* 41:49–100. doi:[10.1006/cogp.1999.0734](https://doi.org/10.1006/cogp.1999.0734)
- Miyazawa N, Hayashi M, Komiya K, Akiyama I (2004) Supernumerary phantom limbs associated with left hemispheric stroke: case report and review of the literature. *Neurosurgery* 54:228–231 (**discussion 231**)
- Penfield W, Faulk ME Jr (1955) The insula; further observations on its function. *Brain* 78:445–470
- Rojkova K, Volle E, Urbanski M, Humbert F, Dell'Acqua F, Thiebaut de Schotten M (2016) Atlasing the frontal lobe connections and their variability due to age and education: a spherical deconvolution tractography study. *Brain Struct Funct* 221:1751–1766. doi:[10.1007/s00429-015-1001-3](https://doi.org/10.1007/s00429-015-1001-3)
- Rorden C, Brett M (2000) Stereotaxic display of brain lesions. *Behav Neurol* 12:191–200
- Saj A, Vocat R, Vuilleumier P (2014) Action-monitoring impairment in anosognosia for hemiplegia. *Cortex* 61:93–106. doi:[10.1016/j.cortex.2014.10.017](https://doi.org/10.1016/j.cortex.2014.10.017)
- Sellal F, Renaseau-Leclerc C, Labrecque R (1996) The man with 6 arms. An analysis of supernumerary phantom limbs after right hemisphere stroke. *Rev Neurol (Paris)* 152:190–195
- Showers MJ, Lauer EW (1961) Somatovisceral motor patterns in the insula. *J Comp Neurol* 117:107–115
- Smith SM, Jenkinson M, Woolrich MW et al (2004) Advances in functional and structural MR image analysis and implementation as FSL. *Neuroimage* 23(Suppl 1):S208–S219. doi:[10.1016/j.neuroimage.2004.07.051](https://doi.org/10.1016/j.neuroimage.2004.07.051)
- Srivastava A, Taly AB, Gupta A et al (2008) Stroke with supernumerary phantom limb: case study, review of literature and pathogenesis. *Acta Neuropsychiatr* 20:256–264. doi:[10.1111/j.1601-5215.2008.00294.x](https://doi.org/10.1111/j.1601-5215.2008.00294.x)
- Staub F, Bogousslavsky J, Maeder P et al (2006) Intentional motor phantom limb syndrome. *Neurology* 67:2140–2146. doi:[10.1212/01.wnl.0000249135.78905.75](https://doi.org/10.1212/01.wnl.0000249135.78905.75)
- Tanaka H, Arai M, Kadowaki T, Takekawa H, Kokubun N, Hirata K (2008) Phantom arm and leg after pontine hemorrhage. *Neurology* 70:82–83. doi:[10.1212/01.wnl.0000265394.80360.b5](https://doi.org/10.1212/01.wnl.0000265394.80360.b5)
- Thiebaut de Schotten M, Tomaiuolo F, Aiello M et al (2014) Damage to white matter pathways in subacute and chronic spatial neglect: a group study and 2 single-case studies with complete virtual “in vivo” tractography dissection. *Cereb Cortex* 24:691–706. doi:[10.1093/cercor/bhs351](https://doi.org/10.1093/cercor/bhs351)
- Tsakiris M (2010) My body in the brain: a neurocognitive model of body-ownership. *Neuropsychologia* 48:703–712. doi:[10.1016/j.neuropsychologia.2009.09.034](https://doi.org/10.1016/j.neuropsychologia.2009.09.034)
- Tyll S, Budinger E, Noesselt T (2011) Thalamic influences on multisensory integration. *Commun Integr Biol* 4:378–381. doi:[10.4161/cib.4.4.15222](https://doi.org/10.4161/cib.4.4.15222)
- Tzourio-Mazoyer N, Landeau B, Papathanassiou D et al (2002) Automated anatomical labeling of activations in SPM using a macroscopic anatomical parcellation of the MNI MRI single-subject brain. *Neuroimage* 15:273–289
- Urbanski M, Thiebaut de Schotten M, Rodrigo S et al (2011) DTI-MR tractography of white matter damage in stroke patients with neglect. *Exp Brain Res* 208:491–505
- Vuilleumier P, Reverdin A, Landis T (1997) Four legs: illusory reduplication of the lower limbs after bilateral parietal lobe damage. *Arch Neurol* 54:1543–1547
- Wolpert DM, Miall RC (1996) Forward models for physiological motor control. *Neural Netw* 9:1265–1279
- Yelnik J, Bardinet E, Dormont D et al (2007) A three-dimensional, histological and deformable atlas of the human basal ganglia. I. Atlas construction based on immunohistochemical and MRI data. *Neuroimage* 34:618–638. doi:[10.1016/j.neuroimage.2006.09.026](https://doi.org/10.1016/j.neuroimage.2006.09.026)
- Zimmermann P, Fimm B (1994) Tests d'Evaluation de l'Attention (TEA). *Psychologische Testsysteme*, Herzogenrath