A functional limitation to the lower limbs affects the neural bases of motor imagery of gait

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ABSTRACT

Studies on athletes or neurological patients with motor disorders have shown a close link between motor experience and motor imagery skills. Here we evaluated whether a functional limitation due to a musculoskeletal disorder has an impact on the ability to mentally rehearse the motor patterns of walking, an overlearned and highly automatic behaviour. We assessed the behavioural performance (measured through mental chronometry tasks) and the neural signatures of motor imagery of gait in patients with chronic knee arthrosis and in age-matched, healthy controls. During fMRI, participants observed (i) stationary or (ii) moving videos of a path in a park shown in the first-person perspective: they were asked to imagine themselves (i) standing on or (ii) walking along the path, as if the camera were "their own eyes" (gait imagery (GI) task). In half of the trials, participants performed a dynamic gait imagery (DGI) task by combining foot movements with GI. Behavioural tests revealed a lower degree of isochrony between imagined and performed walking in the patients, indicating impairment in the ability to mentally rehearse gait motor patterns. Moreover, fMRI showed widespread hypoactivation during GI in motor planning (premotor and parietal) brain regions, the brainstem, and the cerebellum. Crucially, the performance of DGI had a modulatory effect on the patients and enhanced activation of the posterior parietal, brainstem, and cerebellar regions that the healthy controls recruited during the GI task. These findings show that functional limitations of peripheral origin may impact on gait motor representations, providing a rationale for cognitive rehabilitation protocols in patients with gait disorders of orthopaedic nature. The DGI task may be a suitable tool in this respect.

1. Introduction

Motor experience influences motor imagery ability: musicians and athletes alike show higher performance in motor imagery tasks for actions within their domain of expertise (Olsson et al., 2008; Lotze et al., 2003). Conversely, alterations of motor imagery accompany neurological disorders affecting the motor system (see Di Rienzo et al., 2014 for a review). What remains unclear is whether a peripheral limitation, e.g., due to a musculoskeletal disorder, might influence the ability to rehearse motor acts through motor imagery. Here we explored the instance of walking, which in adults becomes an overlearned and highly automatic behaviour dependent on both subcortical and cortical control.

Motor imagery is defined as a mental state in which real movements and the corresponding neural activity are internally evoked without overt muscular contraction (Jeannerod and Frak, 1999). A functional equivalence between motor representations involved in motor imagery and movement planning has been postulated on the basis of two bodies of evidence: first, the time required to mentally evoke an action during motor imagery correlates with the time required to actually perform the same action ("isochrony", Decety and Michel, 1989, as tested with so-called mental chronometry tasks); second, neurofunctional studies have shown that the same neural resources are systematically recruited during both motor imagery and the execution of a given action (see Hétu et al., 2013 for a review), as confirmed by studies on corticospinal excitability measured by transcranial magnetic stimulation (Li et al.,

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Mental Chronometry

Timed Up and Go (TUG)

Hand Walking (HW)

fMRI tasks

Virtual Walking

Gait Imagery (GI)

Dynamic Gait Imagery (DGI)

Fig. 1. The mental chronometry tasks performed outside the MRI scanner (upper panel) and the "virtual walking" task performed during fMRI (lower panel). The mental chronometry tasks included the timed up and go (TUG) task and a control task performed with the right dominant hand (hand-walking task). During fMRI, participants imagined themselves standing on or walking along a path in a park shown from the first-person perspective: the explicit motor imagery task was combined with overt foot movement in 50% of the trials (dynamic gait imagery, DGI), while in the other half of the trials the participants did not move their feet (gait imagery, GI).

2004; Fourkas et al., 2006) that also show a relationship between the strength of corticospinal activation during imagery and individuals' motor imagery abilities (Williams et al., 2012). Overall, these data suggest that motor imagery allows one to practice movements without the need to physically perform them. For this reason, motor imagery has proven valuable in a variety of circumstances, such as training in athletes or musicians, training of surgical skills, and post-stroke rehabilitation (see Schuster et al., 2011; Jackson et al., 2001). Motor imagery may be particularly useful in treating conditions where practical limitations such as biomechanical rigidity and reduced physical strength constrain physical training and increase the risk of injury or pain and fatigue.

Motor performance and motor imagery abilities are strictly interrelated. Motor imagery has been successfully applied in sport science to boost performance (see Ridderinkhof and Brass, 2015; Jones and Stuth, 1997): motor experts like athletes and musicians show a higher temporal correspondence between actual and imagined movements and more focused neural activations in motor areas when they mentally evoke actions in their domain of expertise (Olsson et al., 2008; Lotze et al., 2003). In this regard, task-specificity plays a crucial role, as motor imagery is based on task-specific motor representations that are only created through previous motor experience. Indeed, no one would be able to imagine actions that he/she is unable to perform, at least not using motor imagery. In such instances, people would most likely apply a visual strategy when asked to perform an imagery task (Olsson and Nyberg, 2010).

Motor dysfunctions impact on motor imagery abilities. It has been suggested (see Di Rienzo et al., 2014) that functional equivalence is completely lost in certain circumstances, e.g., after parietal lesion (Sirigu et al., 1995, 1996; Tomasino et al., 2003). However, in most pathological conditions motor imagery may not be deteriorated per se, rather it may be adjusted to the current state of the motor system (e.g.,

in spinal cord injury, Decety and Boisson, 1990; Fiori et al., 2014; Scandola et al., 2017; or in Parkinson's Disease, Dominey et al., 1995; Helmich et al., 2007; see di Rienzo et al., 2014 for a review). In these latter conditions, patients show impairments in their motor imagery abilities that are selective for the body districts and actions in which they show impaired performance. Motor imagery is thus considered an effective method for studying the quality of motor representations in disease conditions (Crammond, 1997). For instance, it can be applied to investigate whether a functional limitation of purely peripheral origin might impact on the quality of motor representations and is paralleled by a plastic reorganization of motor representations at the neural level.

Orthopaedic patients, with no history of major neurological disorder, represent a case of special interest for studying maladaptive brain plasticity following chronic disuse of a body district and defining the eventual benefit of mental training programmes in subjects with functional limitations. We recently tested patients with trapeziometacarpal osteoarthritis and found signs of maladaptive plasticity, as shown by brain activation during finger opposition tasks (Gandola et al., 2017). One could argue that the hand, and the precision grip in particular, has a special status for human survival (Napier and Napier, 1985; Napier, 1993), making it an apt tool for detecting brain abnormalities associated with chronic disuse. This raises the question whether similar signs of maladaptive brain plasticity could be found for actions performed with other body districts and specifically with the lower limbs.

This is the hypothesis that we tested in the present study: we investigated whether a peripheral limitation to the lower limbs due to an orthopaedic disorder (i.e., chronic knee arthrosis) might alter motor representations of lower limb movements as assessed by gait motor imagery tasks. Two characteristics of our sample merit attention: first, knee arthrosis causes a strictly localized functional limitation that is not accompanied by major central injury or by major dysfunction in

afferent/efferent pathways. Yet, the localized pain in the affected limb results in perturbed gait dynamics. Second, orthopaedic patients tend to be older, which is why disturbances in gait motor control are particularly relevant in this population: falls during locomotion are a major source of injury and limited mobility that diminishes the quality of life in old age (Alexander, 1996).

We compared the behavioural performance and neural signatures of motor imagery of gait in 22 orthopaedic patients with those of 22 age-matched, healthy controls. We wanted to determine whether peripheral limitation modulates motor representations of gait and their neural correlates. Mental chronometry tasks were applied to behaviourally measure group differences in motor execution and motor imagery performance at baseline (i.e., independent of other experimental manipulations). The chronometry tasks were performed with eyes closed. Differently, during functional magnetic resonance imaging (fMRI), we used a novel "virtual walking" task our group developed (Sacheli et al., 2017; see also Iseki et al., 2008), which is based on naturalistic in-motion stimuli of viewing a path in a park from the first-person perspective. Participants were asked to imagine themselves walking along the path as if the camera were their own eyes (see **Supplementary Material** and Fig. 1). As a baseline condition, they viewed stationary videos in which no action took place and were asked to imagine themselves simply standing on in the park. Finally, in 50% of the trials, including 50% of the "standing" baselines, they were asked to move their feet and perform ankle dorsiflexion (Dobkin et al., 2004) while watching the video clips and performing the motor imagery task: this *dynamic motor imagery* condition (Guillot et al., 2013, named dynamic gait imagery task, DGI) was introduced to determine whether the association between motor imagery and compatible overt movements might favour the recruitment of motor representations especially in the patient group.

2. Materials and methods

2.1. Participants and neuropsychological assessment

The study population was 22 patients (16 women, age 68.14 ± 8.41 years, formal education 8.31 ± 3.48 years), who were candidates for a total knee arthroplasty (TKA), and 22 age-matched controls (9 women, age 66.73 ± 6.92 years, formal education 13.36 ± 4.21 years), who had no orthopaedic disorders or movement impairments. The patients were tested the day before surgery. None of the participants had a history of neurological or psychiatric disorders; all underwent a short battery of neuropsychological tests to exclude age-related cognitive deficits. The battery included the Mini-Mental State Examination (MMSE, Folstein et al., 1975, all scores > 24) and the Raven Colored Progressive Matrices (Basso et al., 1987, all scores above cut-off) as measures of global cognitive functioning, and a screening test for long- and short-term verbal memory (Novelli et al., 1986). Overall, the participants showed a cognitive profile within the normal range (see Supplementary Table S1). Finally, we asked all participants to complete the Vividness of Movement Imagery Questionnaire (VMIQ, Isaac et al., 1986) to measure self-reported general motor imagery abilities and exclude that they could differ between the two samples. On average participants reported good motor imagery abilities (scores lower than 72, Isaac et al., 1986), and scores showed no significant difference between the groups: the patients scored on average 53.32 ± 13.72 in motor imagery and 55.45 ± 20.44 in visual imagery, while healthy controls scored 47.14 ± 16.62 in motor imagery and 46.05 ± 16.48 in visual imagery (group comparisons, all ps_{uncorr} > 0.1).

All participants were right-handed as determined by the Edinburgh Handedness Inventory (Oldfield, 1971) and reported normal or corrected-to-normal vision. Both groups underwent the same behavioural and fMRI procedure.

The experimental protocol was approved by the Local Ethics

Committee (Comitato Etico dell'Ospedale San Raffaele di Milano) and carried out in accordance with the ethical standards of the 1964 Declaration of Helsinki and later amendments. All participants provided written, informed consent to take part in the study.

2.2. Behavioural tests

2.2.1. Timed up and go (TUG) and "hand-walking" tasks

In order to measure the severity of gait disturbances in the patient group, all participants performed the Timed Up and Go (TUG, Podsiadlo and Richardson, 1991) test in the version developed by Beauchet and collaborators (Beauchet et al., 2010) that obtains a measure of motor imagery abilities. Participants were seated and instructed to walk 3 m, turn around, walk back to the chair and sit down saying, "stop". Times were recorded with a stopwatch to the nearest 0.01 s: the stopwatch was started on the command "ready–set–go" and stopped when the participant sat down and said, "stop". In the imagined condition, the participants sat in the chair and were instructed to imagine performing the TUG (iTUG) with their eyes closed in a first person kinaesthetic perspective, and to say, "stop" when they were finished. The TUG and the iTUG were each performed twice; the times of the two trials were averaged. In order to assess mental chronometry abilities (MCA) we calculated the absolute time difference between the iTUG and the TUG using the following formula: MCA = absolute time difference (iTUG - TUG). MCA was separately calculated for each of the two trials, and the results were averaged to obtain one outcome measure. We assumed that the lower the MCA score, the smaller the difference between times recorded during the TUG and the iTUG, which would be an index of high motor imagery abilities.

For a control task we used a novel hand-motor task named "Hand-Walking" in which the participants used the index and middle fingers of their dominant right hand to simulate "walking" along an S-shaped path drawn on a sheet of paper (28 × 40 cm). The stopwatch was started on the command "ready–set–go" and stopped when the participant had covered the whole path and said, "stop". In the imagined condition, the participants kept their palm on the table and were instructed to imagine performing the hand-walking action with their eyes closed and to say, "stop", when they were finished. The executed and the imagined Hand-Walking tasks were performed twice; the times of the two trials were averaged. MCA was calculated the same way as for the TUG.

In all tasks, motor imagery was performed immediately after movement execution in order to facilitate recalling of sensorimotor and kinaesthetic information. Task order (TUG / Hand-Walking) was counterbalanced between participants.

2.2.2. Analysis of the time up and go (TUG) and hand-walking task

The aims of the behavioural tasks were (i) to assess between-group differences in the speed of movement execution, and (ii) to measure between-group differences in mental chronometry abilities (MCA), which would suggest differences in the quality of motor representations of actions regarding either gait or the control hand task. We compared the mean execution time and MCA between the groups for both the TUG and the Hand-Walking task. As the data were not normally distributed according to Shapiro-Wilks and Kolmogorov-Smirnov tests, we performed a series of between-group comparisons using non-parametric tests (Mann-Whitney *U* test) corrected for multiple comparisons.

2.2.3. Evaluation of pain

In order to quantify the degree of impairment perceived by the patients, they were asked to rate outside the scanner how much pain they felt in each knee (both the joint to be operated on and the healthy one) using a visual analogue scale (VAS) ranging from 0 ("no pain at all") to 10 ("the worst pain I could imagine"). The control group did not complete the VAS because the recruitment criteria explicitly excluded pain at rest and while walking; none reported pain in the month prior to

evaluation.

2.3. fMRI experiment

2.3.1. Stimuli and task

During the fMRI session, the participants watched for 15 s (s) naturalistic videos of a path through a park in two conditions: (i) in-motion, "virtual walking" condition (Walk), or (ii) stationary, standing condition (Stand) that served as baseline. Throughout the experiment, the participants were asked to imagine themselves standing on (Stand) or walking along the path (Walk) as if the camera were "their own eyes". In the Walk condition, the scene proceeded at a speed compatible with slow human walking ($\approx$ 1.1 m/s). The videos were filmed in a park with a steady-cam and depicted two paths shown as either ascending or descending (see Supplementary Material). At the beginning of each video, a written prompt displayed for 3 s either the instruction "no foot movement" (pure gait imagery condition, GI) or the instruction "move your feet" (dynamic gait imagery condition, DGI). In the DGI condition (50% of the trials), the participants executed alternating ankle dorsiflexion (see Dobkin et al., 2004) in-step with the rhythm of their imagined gait pattern. They were instructed to maintain this rhythm throughout the experiment whenever cued to perform foot movements (i.e., both in the Stand and the Walk condition): when the Stand condition was combined with foot movements, the participants were told that a daily life analogue of the task would be like marching in place. The experimenter monitored the foot movements during the entire session to ensure that the participants correctly followed the instructions. Scans in which a participant failed to respond to the prompt, i.e., did not move the feet when cued to "move your feet", or vice-versa, were discarded from the analysis (only two videos in one control participant). Finally, for eight times per run (one per type of video) the participants were asked whether the path that they had just seen ascended or descended. The purpose of these questions was simply to keep the participants' attention focused on the videos; the related fMRI brain volumes were not analyzed.

The experimental run lasted 11.5 min and 230 scans were acquired. The first ten scans, corresponding to visualization of task instructions, were discarded from the analysis. During the run, 32 15-s videos were shown, corresponding to 8 videos per experimental condition [i.e., Stand(GI), Walk(GI), Stand(DGI), Walk(DGI)]: they were presented in counterbalanced order, and corresponded to a total of 40 scans acquired per experimental condition.

Before starting the fMRI session, the participants practiced the task outside the fMRI scanner for about 10 min, so that they could familiarize themselves with the videos and learn to correctly execute ankle dorsiflexion when prompted. During fMRI, foam padding was applied around the head to minimize head movements and a semi-circular cushion supporting the legs was provided so that the participants could move their ankles freely without bending their knees.

Stimuli presentation was controlled by Cogent 2000 MATLAB Toolbox (MathWorks). Visual stimuli were delivered using VisuaStim fiber-optic goggles (800 × 600 pixel resolution). Responses were recorded through a response box placed under the right hand (Resonance Technology Inc., Northridge, CA, USA).

2.3.2. MRI data acquisition and analysis

2.3.2.1. Data acquisition. MRI scans were acquired using a Siemens Magnetom *Avanto* 1.5 T scanner equipped with gradient-echo echo-planar imaging (flip angle 90°, TE 60 ms, TR 3000 ms, FOV 280 × 210 mm, matrix 96 × 64, slice thickness 4 mm) (Siemens AG, Erlangen, Germany). The first two volumes recorded from each functional run were removed to allow for steady-state tissue magnetization; additional 10 volumes (corresponding to task instructions) were discarded from the analyses. MPRAGE high-resolution T_1-weighted structural images were also acquired (flip angle 35°, TE 5 ms, TR 21 ms, FOV 256 × 192 mm, matrix

256 × 256, TI 768, for a total of 160 axial slices with 1 × 1 × 1 mm voxels).

2.3.2.2. Preprocessing. After image reconstruction, raw data visualization and conversion from the DICOM to the NIfTI format were performed with MRIcron (www.mricro.com) software. All subsequent data analyses were performed in MATLAB R2014b (MathWorks) using Statistical Parametric Mapping software (SPM12, Wellcome Department of Imaging Neuroscience, London, UK). First, the fMRI scans were realigned and unwarped to account for any movement during the experiment; the unwarped images were co-registered with the T1-weighted structural image of each participant, which was then segmented and stereotactically normalized into the SPM12 template (tmp.nii) to allow for group analyses of the data (Ashburner and Friston, 2005). Deformation fields used for T1 segmentation were then applied to the unwarped and co-registered functional scans. At this stage, the data matrix was interpolated to produce voxels 2 × 2 × 2 mm in dimension. The stereotactically normalized scans were smoothed using a Gaussian filter of 10 × 10 × 10 mm to improve the signal-to-noise ratio.

Artifact Detection Tools (ART, Whitfield-Gabrieli, http://www.nitrc.org/projects/artifact_detect) was used to identify outlier scans in global signal and movement for each participant. Timepoints were marked as outliers when variations in the global signal exceeded 9 standard deviations from the mean, and when the compounded measure of movement parameters exceeded 1 mm scan-to-scan movement (on average, excluded volumes were 7.82 ± 7.73 in the Patient group and 5.45 ± 5.53 in the Control group, equal to $\approx$3% and $\approx$2% of total scans). Participants with > 20% of outlier time-points in a run were excluded from the analyses; no participant was excluded according to this criterion.

2.3.2.3. Voxel-Based Morphometry. As a control analysis to investigate group-differences in grey matter concentration that may account for group differences in functional activations, we applied voxel-based morphometry analysis. MRI data were processed using an optimized VBM protocol, as described by Good (Good et al., 2001). This procedure involves extraction of the brain from the native skull space to determine ideal stereotactic normalization parameters. Further, the native MRI scans were stereotactically normalized and segmented into grey matter (GM), white matter (WhM) and CSF compartments. Finally, Jacobian modulation was applied to the data to preserve the absolute regional amount of grey matter from the distortion introduced by stereotactic normalization (Ashburner and Friston, 2000). All data were then smoothed using a Gaussian filter of 10 × 10 × 10 mm.

The anatomical differences between the two groups (i.e., the areas of significant GM reduction in patients as compared to healthy controls) were estimated by *t*-test analysis on a voxel-by-voxel basis, once the intersubject variability of global brain volume was removed by correcting regional values with proportional scaling. Regional effects are reported at $p_{uncorr} < 0.001$ using the family-wise error correction (FWE) at the cluster level as implemented in SPM12

2.3.2.4. Statistical analyses of the fMRI data. A two-step statistical analysis, based on the general linear model (GLM), was performed. The blood oxygen level-dependent (BOLD) signal associated with each experimental condition was analyzed by convolution with a canonical hemodynamic response function (Worsley and Friston, 1995). Global differences in the fMRI signal were removed by proportional scaling from all voxels. High-pass filtering (128 s) was used to remove artifactual contributions to the fMRI signal, such as noise from cardiac and respiratory cycles. Realigning parameters calculated in the preprocessing step were added to the GLM as regressors of no interest. This first step implied a fixed-effect analysis, in which condition-specific effects were calculated. At this first level of statistical analysis (single-subject analysis), the experiment conforms

to a 2 × 2 design having Posture (imagery of Walking vs. Standing) and Imagery-Type (Gait Imagery, GI, vs. Dynamic Gait Imagery, DGI) as within-subject factors. We characterized the specific effects associated with imagery of walking (Walk) and imagery of standing (Stand) when the participants moved their feet as Walk(DGI) and Stand(DGI) or did not as Walk(GI) and Stand(GI).

These four effects were then compared to generate contrast images that were entered into a second-level ANOVA that conformed to random effect analyses (Holmes and Friston, 1998; Penny and Holmes, 2004). We investigated the neural correlates of motor imagery of gait during virtual walking in the two groups by comparing the brain responses during the in-motion videos (Walk videos) with those collected while the participants imagined themselves standing in place (Stand videos that served as baseline) separately for trials where explicit ankle dorsiflexion was present (DGI) or absent (GI), and calculated the following contrasts per each participant:

- **Gait Imagery** contrast (**GI**), i.e., Walk(GI) > Stand(GI)
- **Dynamic Gait Imagery** contrast (**DGI**), i.e., Walk(DGI) > Stand (DGI)

These two contrast images from each participant were entered into a second-level 2 × 2 full-factorial ANOVA with one between-subject factor (Group, Patients vs. Controls) and one within-subject factor (Imagery Type, GI vs. DGI).

The design matrix was organized as follows: Patients(GI), Patients(DGI), Controls (GI), Controls (DGI).

We calculated the following linear contrasts to generate SPM[t] maps:

(a) The main effect of all Tasks: contrast 1 1 1 1; this contrast describes the neural resources overall involved in gait imagery during Virtual Walking as compared to the imagery of standing;
(b) Group differences in GI: contrasts 1 0−1 0 and − 1 0 1 0; these contrasts describe group-differences in brain activations during the GI task;
(c) Group differences in DGI: contrasts 0 1 0−1 and 0−1 0 1; these contrasts describe group-differences in brain activations during the DGI task;
(d) Conjunction analyses: contrast 1 0 0 0 ∩ 0 0 1 0, corresponding to Patients(GI) ∩ Controls(GI), and contrast 0 1 0 0 ∩ 0 0 0 1, corresponding to Patients(DGI) ∩ Controls(DGI); these contrasts describe the activations common to Patients and Controls, separately for GI and DGI.
(e) Interaction effects between Group (Patients vs. Controls) and Imagery-Type (GI vs. DGI): contrasts −1 1 1−1 and 1−1 -1 1; these contrasts describe the activations that are stronger during DGI than GI in Patients and during GI than DGI in Controls (or vice-versa).

All analyses were conducted at the whole-brain level, thresholded at $p < .001_{uncorr}$ at the voxel level, and corrected for multiple comparisons (family-wise error, FWE correction) at the cluster level (Flandin and Friston, 2017).[1] The regional effects that also survived a voxel-wise FWE correction are indicated in the tables. For the sake of clarity, the simple effects of each condition [i.e., Patients(GI), Patients(DGI), Controls(GI), and Controls(DGI)] are also reported as Supplementary Tables (see Supplementary Tables S2 and S3).

Finally, we performed a control analysis in order to test for the presence of group differences in the neural correlates of ankle

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[1] We followed Flandin and Friston's (2017) recommendations based on evidence that data smoothed with a 10-mm wide Gaussian kernel are well suited for cluster-level correction, provided that the voxel-wise threshold is $p < .001$. Under such circumstances, false positives are within acceptable family-wise error rates.

dorsiflexion independent of imagery of gait. To do so, at the first level of statistical analysis (single-subject level) we calculated an additional contrast: Stand(DGI) > Stand(GI). These contrast images were entered into a second-level (group-level) analysis having Group as between subject variable (two-sample *t*-test).

3. Results

3.1. Behavioural tests

3.1.1. Time up and go (TUG) and hand-walking tasks

Group median values recorded for the TUG and the Hand-Walking tasks are reported in Table 1. The patients were significantly slower than the controls in executing the TUG (U = 38, $p_{corr} < .001$) but not the Hand-Walking task (U = 158, $p_{corr} > 0.1$). Moreover, MCA scores were significantly higher for the patients than for the controls on the TUG (U = 120, $p_{corr} = 0.016$) but not on the Hand-Walking task (U = 188, $p_{corr} > 0.1$), indicating the presence of between-group differences in the quality of motor representations related to gait. This suggests that performance during the imagery task was poorer for patients than for controls selectively for gait behaviours.

3.1.2. Evaluation of pain

Rating of perceived pain ranged between 10 and 0 (median 1.4) in the joint to be operated on, and between 3.7 and 0 (median 0) in the other knee, indicating moderate pain selectively in the affected leg. As expected, perceived pain in the leg to be operated on was significantly higher (Z = 3.12, $p = .002$) than in the other leg, as assessed by nonparametric Wilcoxon signed-rank test.

3.2. MRI and fMRI experiment

3.2.1. Voxel-based morphometry

The analysis showed no significant grey matter reduction in patients as compared to healthy controls.

3.2.2. fMRI data analysis (virtual walking task)

3.2.2.1. Main effect of Task. Activations for the Virtual Walking task (overall main effect of the task, 1 1 1 1 contrast) are reported in the Supplementary Tables (see Supplementary Table S4). Overall, the task recruited the superior frontal gyrus and a widespread posterior network as expected, given the visual complexity of virtual walking stimuli: it included the superior and inferior parietal lobules and the precuneus, the superior and middle occipital gyri, and the superior and middle temporal gyri.

3.2.2.2. Between-group differences in GI and DGI. There were no group differences in DGI but there was a widespread network of hypoactivations in the patients as compared to the healthy controls in GI (see Table 2 and Fig.2). This latter network included both motor and visual areas and comprised: the superior frontal gyrus, the SMA and the insula, the precentral and postcentral gyri, the superior and inferior parietal lobules, the angular gyrus, the precuneus, the superior and middle occipital gyri, the superior and middle temporal gyri, the basal ganglia (caudate and putamen), the cerebellum, and the brainstem. In other words, the whole network involved in gait imagery (Jahn et al., 2008; Jahn et al., 2004; Iseki et al., 2008) seemed to be hypoactivated in the patients on the GI (but not on the DGI) task. The opposite contrasts (Patients > Controls, on either the GI or the DGI task) gave no significant results.

In order to test whether the between-group differences in fMRI results in the GI condition could be related to group differences in motor imagery performance, we extracted single-subject values of the contrast of interest (Controls > Patients in GI) from the three most significant voxels, i.e., those local maxima that survived the FWE correction at the voxel level and that could be considered maximally trustworthy. These

Table 1

Group behavioural performance at the Timed up and go (TUG) and hand-walking (HW) tasks. Group execution times and mental chronometry abilities (MCA) are reported.

		TUG Execution (s)	MCA TUG (s)	HW Execution (s)	MCA HW (s)
Patients	Median	13.01	3.04	11.40	2.20
	Range	7.89–23.50	0.12–8.36	4.98–26.82	0.28–13.06
Controls	Median	7.63	1.83	7.94	1.42
	Range	5.24–11.35	0.28–4.40	4.05–17.21	0.39–3.08
Group comparison		$p_{corr} < 0.001$	$p_{corr} = 0.016$	$p_{corr} > .1$	$p_{corr} > .1$

included a voxel in the left SMA (x = −6, y = 8, z = 50; Z-score = 4.6), in the right superior parietal lobule (x = 22, y = −50, z = 56; Z-score = 4.6), and in the brainstem (x = −10, y = −30, z = −26; Z-score = 4.7). We correlated these values with the MCA index collected during the TUG outside the scanner, and corrected the results for multiple comparisons. We wanted to specifically test whether activation in one of these areas was negatively correlated with MCA (a negative direction was expected because the higher the MCA, the lower the performance). The non-parametric correlation with MCA was not significant for SMA (ρ = −0.195, p_{corr} > 0.1) or brainstem activations (ρ = −0.154, p_{corr} > 0.1). Differently, right superior parietal activations showed a significant correlation with MCA in the expected negative direction (ρ = −0.337, p_{corr} = 0.039, see Fig. 2b): this indicates that the participants who showed stronger activations in the right superior parietal lobule also showed better performance on the gait "mental chronometry" motor imagery task.

3.2.2.3. Conjunction analyses in GI and DGI. Consistent with the results reported above, conjunction analyses showed different results for GI and DGI (see Fig. 3). Conjunction analysis of GI [contrast 1 0 0 0 ∩ 0 0 1 0, corresponding to Patients(GI) ∩ Controls(GI)] revealed significant activations common to patients and healthy controls only in the occipital lobe, the middle temporal gyrus, and the cerebellum (Table 3a). In contrast, conjunction analysis of DGI [contrast 0 1 0 0 ∩ 0 0 0 1, Patients(DGI) ∩ Controls(DGI)] revealed additional significant activations common to patients and healthy controls bilaterally in the left superior parietal lobule (Table 3b).

3.2.2.4. Imagery-Type (GI vs. DGI) x Group (Patients vs. Controls) interaction effect. The interaction effect revealed significantly more active areas in the patients during DGI than during GI. These areas were the same as those recruited by the healthy controls to perform the GI task (see Table 4 and Fig. 3) and included the right precentral and postcentral gyrus, the left superior and inferior parietal lobules, the thalamus, and the cerebellar vermis. Moreover, a highly significant cluster, which yet did not survive FWE correction ($p_{FWE-corr}$ = 0.086), extended from the brainstem to the cerebellar lobules and included voxels compatible with the location of the mesencephalic locomotor region (x = −8, y = −28, z = −24 and x = 2, y = −26, z = −28, Jahn et al., 2008).

3.2.2.5. Group differences in the neural correlates of ankle dorsiflexion. The control analysis showed that, overall, the Stand (DGI) > Stand(GI) contrast was associated with activations compatible with foot movements execution as the analysis showed activations in the paracentral lobule on the median wall, in the SMA, the thalamus, the basal ganglia and the cerebellum (see Supplementary Table S5). Importantly, group comparisons showed no significant group difference in these activations.

4. Discussion

This study was designed to answer a simple question: do orthopaedic patients with severe knee arthrosis have behavioural and physiological signs of alterations in gait motor representations? A positive

answer to this question could have clinical implications for cognitive rehabilitation. This is important for us because the hypothesis tested in our long-term research plan is that cognitive rehabilitation should include mental motor training to reduce gait instability and the ensuing risk of falls in orthopaedic patients. Such trainings based on motor imagery have already been shown to be successful in neurological patients (Tong et al., 2017; Li et al., 2017).

Our results show that functional limitation due to chronic knee arthrosis had a strong impact on gait motor representations, at both the behavioural and the neurofunctional level. Performance on mental chronometry tasks was lower for the patients, specifically for gait movements, and the effect did not generalize to other complex rhythmic actions like our "hand-walking" control task. Moreover, hypoactivation in many brain regions involved in gait motor control was noted for the GI task performed during fMRI. Interestingly, hypoactivation was reduced when the patients were instructed to combine motor imagery with lower limb movements, which constitute a fMRI-compatible proxy of walking behaviours (i.e., during DGI): this suggests that dynamic motor imagery might have facilitated the recruitment of task-specific motor representations and trigger the rehearsal of a motor task in these patients. These results are discussed in light of possible applications to gait rehabilitation.

4.1. A functional limitation of peripheral origin is associated with lower isochrony between motor imagery and motor execution

Patient performance on the mental chronometry tasks was low, specifically for the movements executed with the lower limbs. Since the ability of movement mental rehearsal strongly correlates with the quality of motor representations available to subjects (Di Rienzo et al., 2014), the implications of these findings are twofold.

First, impairment of strictly peripheral origin, i.e., pain and functional limitation in walking due to chronic knee arthrosis, has an impact on central motor representations of gait. Our patients were tested near the end of a long period of impaired walking that not only made them slower during a short walk, as expected, but also undermined their ability to accurately imagine the task. This observation is in line with evidence for lower isochrony in hand movements in patients with trapeziometacarpal osteoarthritis (Gandola et al., 2017). The present study shows for the first time that a musculoskeletal disorder of the lower limbs might impact on central motor representations of gait, although gait is considered a highly automatic behaviour. Degradation of gait motor representations might have a strong impact on quality of life, given that everyday life activities rely on accurate estimates of the time needed to move in the environment in order to quickly adapt to dynamic stimuli. Second, our results showed a decay in motor imagery abilities that only affected movements of the impaired body district. Indeed, our patients executed and imagined complex hand movements as accurately as the healthy control group did: this suggests that they held spared motor representations relative to upper limb movements and, most likely, to other body parts that were not affected by their disorder. This rules out the possibility that their lower isochrony in gait motor imagery was due to a general impairment in motor imagery abilities or to cognitive impairment (which was also ruled out by neuropsychological screening; see Supplementary Table S1).

Table 2
Between-group differences in gait imagery (GI).

a. Healthy Controls > Patients in GI (contrast − 1 0 1 0)

Brain area (BA)	Left hemisphere				Right hemisphere			
	X	Y	Z	Z-score	X	Y	Z	Z-score
Insula					38	2	6	4.1
					34	2	8	4.1
					40	4	10	3.8
Rolandic operculum (6)					56	8	16	4.1
Sup. frontal gyrus (6)					22	−10	44	3.7
					22	−12	48	3.6
					22	−8	54	3.5
Mid. cingulum (32)					10	16	44	3.8
SMA (6)	−6	8	50	4.6*	4	0	58	3.7
	−16	−2	44	3.9				
	−18	−6	48	3.7				
	−6	−10	60	3.7				
Precentral gyrus (6)	−20	−18	60	4.6	26	−12	44	4.0
	−28	6	38	3.8	30	−12	40	3.9
					36	−10	36	3.3
Paracentral lobule (4)					18	−40	54	3.5
					16	−32	54	3.2
Postcentral gyrus (3)	−22	−36	50	3.7	28	−22	40	3.7
	−22	−38	54	3.7	32	−28	40	3.4
	−24	−32	60	3.2	34	−30	36	3.4
Sup. parietal lobule (7)	−28	−60	48	3.7	22	−50	56	4.6*
	−34	−60	60	3.4				
Supramarginal gyrus (40)					34	−40	36	4.0
Inf. parietal lobule (40)	−28	−44	48	4.0				
	−32	−44	46	4.0				
Angular gyrus (39/40)	−40	−58	36	3.3				
	−38	−54	36	3.3				
	−38	−62	36	3.2				
Precuneus (7)	−14	−60	52	3.3				
Precuneus (5)					12	−52	56	4.0
					8	−48	58	3.9
					14	−44	52	3.6
Cuneus (18/19)	−10	−82	28	3.6	18	−80	40	3.9
	−10	−80	40	3.4	18	−68	20	3.6
Sup. occipital gyrus (18/19)	−16	−88	10	3.7	24	−70	32	4.0
	−20	−72	36	3.2	24	−68	24	3.6
					20	−66	46	3.4
Mid. occipital gyrus (18/19)	−22	−72	20	4.2				
	−28	−88	6	3.9				
	−32	−86	10	3.9				
	−34	−78	2	3.9				
	−32	−80	6	3.7				
	−20	−90	6	3.5				
	−20	−84	10	3.4				
	−34	−76	18	3.4				
	−42	−78	2	3.2				
	−46	−78	0	3.2				
Calcarine fissure (17/18)					12	−66	12	3.7
					14	−66	16	3.8
Lingual gyrus (18/27/37)	−14	−58	−6	4.1				
	−12	−42	0	3.9				
	−24	−50	−8	3.2				
Sup. temporal gyrus (22)					62	−32	12	3.8
Mid. temporal gyrus (37)					42	−54	0	4.0
Mid. temporal gyrus (22)					62	−38	6	3.5
					58	−42	4	3.3

Table 2 (*continued*)

a. Healthy Controls > Patients in GI (contrast − 1 0 1 0)

Brain area (BA)	Left hemisphere				Right hemisphere			
	X	Y	Z	Z-score	X	Y	Z	Z-score
Mid. temporal gyrus (21)					54	−46	0	3.3
					64	−46	4	3.1
Thalamus	−16	−24	4	4.0	18	−26	0	4.3
	−20	−24	0	4.0	18	−10	10	4.1
	−24	−28	0	3.7	12	−24	−2	4.1
					18	−12	6	3.9
Caudate	−16	−2	14	3.7				
Putamen					22	−4	18	3.9
					20	−4	12	3.9
					20	10	2	3.8
					24	0	16	3.7
					24	−12	12	3.7
					20	10	8	2.5
Cerebellum - vermis	−2	−62	−10	3.3	2	−42	−6	3.7
					6	−60	−10	3.2
Cerebellum – IV/V lobule	−4	−58	−14	3.2				
Brainstem	−10	−30	−26	4.7*				
	−8	−28	−36	3.3				

x, y, and z are the stereotactic coordinates of the activations in the Montreal Neurological Institute (MNI) space.

Statistical threshold $p < .001_{uncorr}$. All reported voxels are included in clusters surviving the family-wise error (FWE) correction at the cluster level. (*) Z-scores statistically significant also after voxel-level FWE correction.
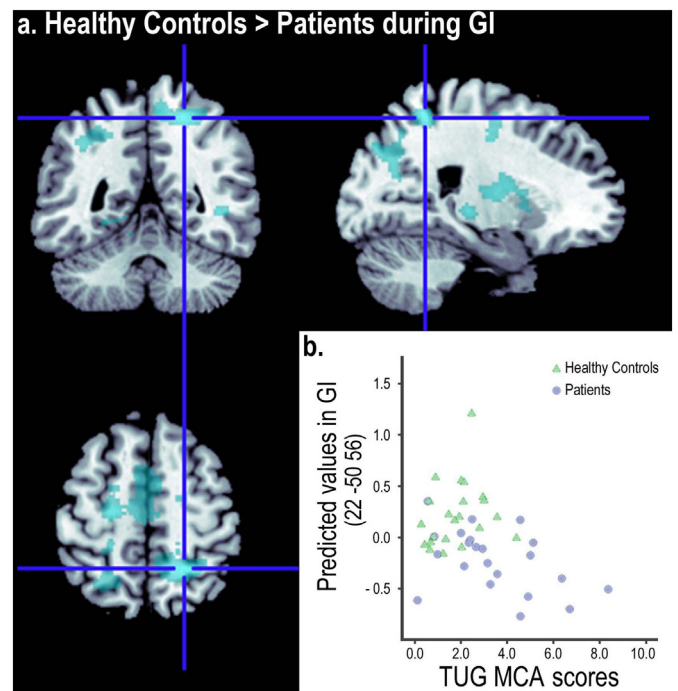
Fig. 2. (a) Brain regions showing hypoactivation in the patients as compared to the healthy controls during gait imagery (GI) when motor imagery was not combined with foot movements. Data are based on contrast-images that, at the first level of statistical analysis (single-subject level), show significant differences between imagery of walking and imagery of standing in place (Walk > Stand contrast). The coordinates of the activation maps shown in the figure match those listed in Table 2. The data are reported with the same statistical threshold as that reported in the tables and discussed in the text ($p_{uncorr} < .001$ at the voxel level and $p_{FWE-corr} < 0.05$ at the cluster level). (b) The significant correlation between activations in the superior parietal lobule during GI (individual predicted values in the MNI coordinate 22, −50, 56, "y" values in the GLM) and mental chronometry ability (MCA) scores during the timed up and go (TUG) test.
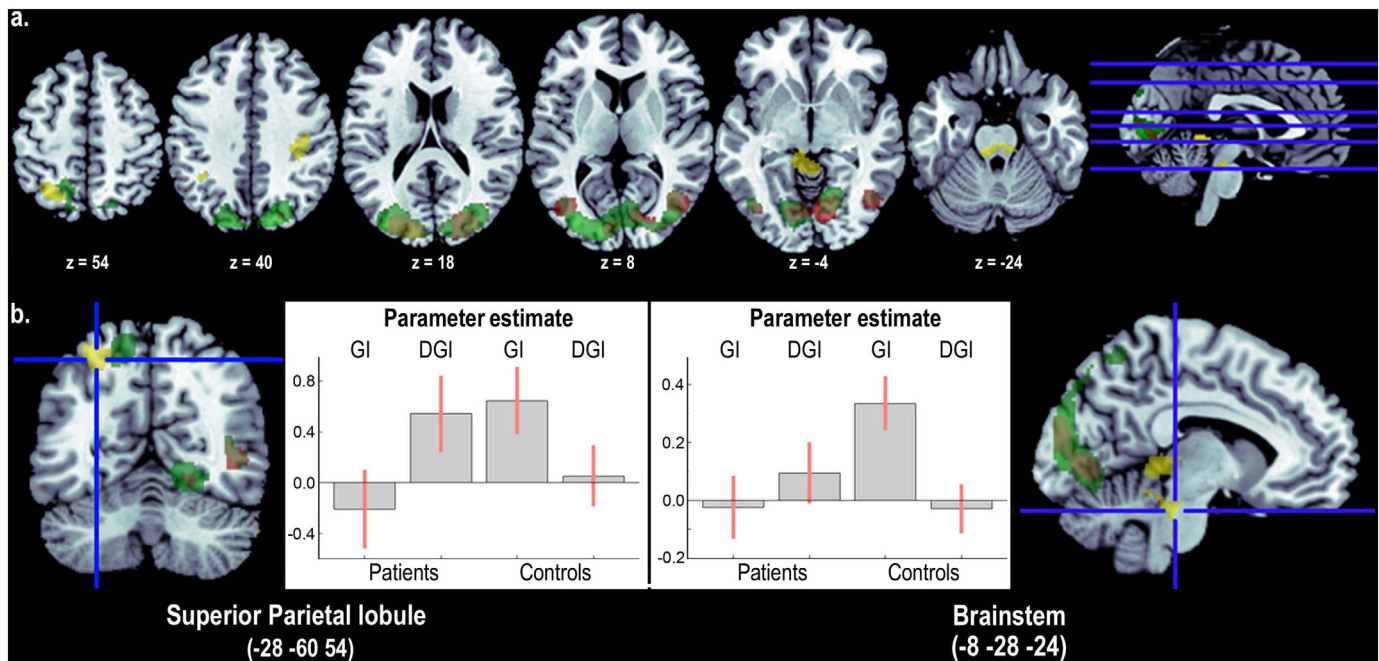
Fig. 3. The results from the conjunction analyses and the interaction effect. (a) Brain regions equally recruited by the patients and the healthy controls are shown in red for gait imagery (GI) and in green for dynamic gait imagery (DGI); the results of the interaction effect ([Patients(DGI) > Patients(GI)] > [Controls (DGI) > Controls(GI)]) are shown in yellow; during DGI, the patients recruited a wider network as compared with during GI, which included the superior parietal lobule. (b) The plot of the parameter estimate ("beta" values in the GLM), for both the local maxima in the superior parietal lobule (left) and in the brainstem (right), show that DGI in the patients was associated with a higher recruitment of those brain regions that the healthy controls recruited during the GI task. Error bars indicate the 90% confidence interval.

The coordinates of the activation maps match those listed in Table 3 and Table 4. Data are reported at the same threshold as that discussed in the main text and reported in the tables ($p_{uncorr} < .001$ at the voxel level and $p_{FWE-corr} < 0.05$ at the cluster level).

Taken together, our findings support the hypothesis that a musculoskeletal disorder can modify gait central motor representations because of its impact on the specific motor experience of walking; these findings paralleled the neurofunctional pattern in the patients during fMRI, as described below.

4.2. Impoverished motor representations of gait in orthopaedic patients

Between-group differences in the GI task (i.e., when gait imagery was not combined with explicit lower limb movements) showed extended hypoactivation in the patients. The patients were noted to have lower recruitment of both visuo-motor and motor areas directly involved in gait control, including the SMA, the precentral and postcentral gyri, the superior and inferior parietal lobules, and the basal ganglia. Such hypoactivation cannot be accounted for by a reduction in grey matter density in the patient group, as shown by voxel-based morphometry. Although gait is a highly automatic behaviour largely dependent on subcortical control, it is strongly modulated by cortical activity in humans, particularly when complex environmental stimuli are processed during locomotion. Central pattern generators (Grillner and Zangger, 1979) located in the spinal cord are controlled by supraspinal centres such as the mesencephalic locomotor region and its descending projections to the pontomedullary reticular formation, the subthalamic locomotor region, and the cerebellar locomotor region, as shown by brainstem and cerebellar activations in gait-related tasks performed in fMRI (Jahn et al., 2008; La Fougère et al., 2010). Supraspinal centres are controlled by the primary motor area (M1) and SMA through the basal ganglia (Takakusaki, 2013), while dorsal premotor and posterior parietal areas modulate the descending pathway (from M1/SMA to supraspinal centers) by adapting gait patterns according to environmental cues, as demonstrated by lesion studies (see Liston et al., 2003 and Nutt, 2013 for reviews). Our results show that the presence of a chronic functional limitation of gait due to knee

arthrosis rendered the patients incapable of recruiting the relevant motor control areas during the "virtual walking" imaginative task. The neurofunctional evidence paralleled the behavioural results, as the lower quality of gait-related motor representations (indexed by a lower isochrony between gait imagery and gait execution) was associated with hypoactivation in gait control cortical areas in the patients. Similarly, there was a significant correlation between mental chronometry abilities on the TUG test and activations in the superior parietal lobule.

These results confirm the role of motor experience in shaping sensorimotor representations (Pascual-Leone et al., 2005, see also Sacheli et al., 2015) The gait impairment in our patients seems to directly translate, at a behavioural level, in a selective impairment of gait motor imagery. This observation is consistent with evidence for a remapping of sensorimotor representations after limb amputation (Giraux et al., 2001; Grüsser et al., 2004; Raffin et al., 2012) or immobilization (Lissek et al., 2009, Weibull et al., 2011; see also Burianová et al., 2016), in which movement constraints led to phenomena of negative plasticity at the cortical level. However, the published literature regards mainly the shrinkage of sensorimotor representations and a higher activation threshold in M1/S1 but it rarely considers the *quality* of such representations (see Meugnot et al., 2016, Meugnot et al., 2014 for some exceptions), which can be assessed, for instance, by mental chronometry tasks, as we did in the present study. Moreover, while afferent and efferent signals are strongly reduced or completely absent in amputation and immobilization, orthopaedic patients are still able to freely move their legs, despite localized pain that impairs good locomotion. We suggest that it is limb misuse, and a reduced "practice" in walking, that generates impairment in correctly estimating the time needed to perform the motor act. This made it more difficult for the patients to recall the related kinaesthetic sensation on the "virtual walking" task during fMRI, so that they applied a mainly visual strategy to perform the task.

Table 3

Conjunction analyses, Patients ∩ Healthy Controls in gait imagery (GI) and dynamic gait imagery (DGI).

a. Conjunction analysis, Patients ∩ Healthy Controls in GI

Brain area (BA)	Left hemisphere				Right hemisphere			
	X	Y	Z	Z-score	X	Y	Z	Z-score
Sup. occipital gyrus (18/19)	−16	−90	18	6.2*	22	−82	22	4.7*
					20	−80	18	4.7*
					22	−78	42	3.5
Mid. occipital gyrus (37)	−40	−72	8	5.1*				
Inf. occipital gyrus (19)	−36	−76	−8	3.2				
	−32	−72	−8	3.1				
Cuneus (18/19)					10	−88	30	3.3
					20	−94	12	3.2
Lingual gyrus (18)	−10	−78	0	5.0*	14	−70	−6	5.9*
Mid. temporal gyrus (37)					46	−68	0	5.5*
Cerebellum – VI lobule	−16	−72	−12	4.0				

b. Conjunction analysis, Patients ∩ Healthy Controls in DGI

Brain area (BA)	Left hemisphere				Right hemisphere			
	X	Y	Z	Z-score	X	Y	Z	Z-score
Sup. parietal lobule (7)	−18	−80	48	5.3*				
Precuneus (5)	−14	−58	62	4.6*				
Sup. occipital gyrus (19)	−16	−86	40	5.5*	20	−80	40	6.2*
					28	−80	24	5.9*
Sup. occipital gyrus (18)	−14	−92	18	7.3*				
	−22	−90	22	6.7*				
Mid. occipital gyrus (18/19)	−22	−76	20	5.3*	30	−84	22	5.9*
	−32	−82	14	6.1*	42	−74	8	4.6*
	−40	−74	2	4.6*				
Calcarine fissure (17)	−10	−88	6	6.3*				
Lingual gyrus (18)	−14	−74	−8	4.7*	16	−68	−4	6.0*
Mid. temporal gyrus (37)					44	−66	2	4.9*

x, y, and z are the stereotactic coordinates of the activations in the Montreal Neurological Institute (MNI) space.

Statistical threshold $p < .001_{uncorr}$. All reported voxels are included in clusters surviving the family-wise error (FWE) correction at the cluster level. (*) Z-scores statistically significant also after voxel-level FWE correction.

Table 4

Task x Group interaction effect.

a. Interaction DGI > GI, Patients > Controls (contrast − 1 1 1–1)

Brain area (BA)	Left hemisphere				Right hemisphere			
	X	Y	Z	Z-score	X	Y	Z	Z-score
Precentral gyrus (6)					28	−14	38	3.2
Postcentral gyrus (3)					34	−28	38	4.1
					40	−18	34	4.1
					40	−24	46	3.3
Sup. parietal lobule (7)	−28	−60	54	4.1				
Inf. parietal lobule (40)	−28	−46	46	3.3	36	−44	38	3.2
	−34	−50	40	3.3				
	−38	−50	40	3.3				
	−32	−48	50	3.2				
	−36	−48	44	3.1				
Angular gyrus (40)	−30	−50	34	3.3				
Thalamus	−10	−38	0	4.4				
	−16	−24	4	3.3				
	−24	−28	0	3.6				
Cerebellum - vermis					2	−42	−4	4.0
Cerebellum – III lobule	−10	−36	−20	3.3%				
Cerebellum – IV/V lobule	−12	−40	−14	3.5%				
Brainstem	−8	−28	−24	4.3%	2	−26	−24	3.8%
	−8	−28	−36	3.5%	10	−28	−24	3.7%
	−12	−32	−38	3.2%	6	−32	−24	3.2%

b. Virtual Walking – Interaction DGI > GI, Controls > Patients (contrast 1–1 -1 1)

Brain area (BA)	Left hemisphere				Right hemisphere			
	X	Y	Z	Z-score	X	Y	Z	Z-score
N.S.								

x, y, and z are the stereotactic coordinates of the activations in the Montreal Neurological Institute (MNI) space.

Statistical threshold $p < .001_{uncorr}$. All reported voxels are included in clusters surviving the family-wise error (FWE) correction at the cluster level. (%) the brainstem cluster showed a trend toward significance when FWE correction at the cluster level was applied (k = 182, $p_{FWE-corr} = 0.086$).

Thus, the functional limitation might have translated into a visual approach to the imagery task. This is in line with the suggestion that no one would be able to imagine actions that he/she is no longer able to perform, at least not by means of motor imagery, but instead would fall back on visual imagery when asked to perform the task (Olsson and Nyberg, 2010). For instance, Olsson and Nyberg (2011) found that a paraplegic athlete recruits motor brain areas only when imagining actions that he is still able to perform, and that he turns to visual imagery for actions that he can no longer overtly execute. Similar results were obtained using an implicit motor imagery task in a group study of patients with spinal cord injury (Fiori et al., 2014). As shown here for the first time, a purely peripheral motor limitation might also have the same selective impact on central motor representations by impairing motor imagery and favouring a visual approach to the task.

4.3. The facilitatory role of dynamic gait imagery for orthopaedic patients

The scenario unveiled by the simple GI task was that the

orthopaedic patients were unable to recruit relevant motor networks, cortical and subcortical, when imagining themselves walking in a naturalistic environment. This pattern changed in a group-specific manner during the DGI task, when the imaginative task was coupled with performing overt foot movement (i.e., ankle dorsiflexion, an index of gait-related abilities, Dobkin et al., 2004): this combination represented our fMRI-compatible proxy for explicit walking.

In brief, we found that the combination of explicit foot movement with gait imagination "helped" patients recruit gait-related posterior parietal visuomotor areas and a mesencephalic locomotor area, the same regions that were active in the healthy controls during the GI task. No additional activations were observed in the healthy controls during the same DGI task. These apparently divergent patterns for the DGI task are yet easy to reconcile, as we will discuss below.

The healthy controls had good imagery abilities for gait, which ensured recruitment of relevant gait-related networks during the GI task. Because of their relatively old age, it is not difficult to assume that this ability was challenged to its limits, resulting in maximal activation

of the relevant areas during the GI task. Due to a sort of ceiling effect, additional recruitment of motor areas did not occur when active foot movements were combined with GI during the DGI task. In other words, the healthy, elderly controls might have already engaged their cognitive motor resources to perform the GI task so that no extra activation was possible by combining GI with an explicit foot dorsiflexion task.

In contrast, the patients were well below the ceiling during the GI task as they were only able to perform it in a visually oriented fashion; this is strongly suggested by the distribution of the brain areas during the task (see also the simple effect of GI in the patients, as reported in the Supplementary Table S2): occipital but not motor/premotor regions were recruited during GI by the patients. However, the coupling of explicit foot movements on the DGI task introduced a modality-specific trigger that promoted the engagement of motor-related processes during imagery. More specifically, the DGI led to greater recruitment of posterior parietal areas in the patients (in both the superior and inferior parietal lobules). This suggests that the "motor trigger" was capable of shifting the patients' approach to the imagery task. Recruitment of the posterior parietal areas is widely reported for motor imagery (see Hétu et al., 2013 for a review). With regard to gait, it is associated with the adaptation of gait patterns to environmental cues and obstacle negotiation (Marigold et al., 2011), and with the ability to adapt an automatic movement to everyday life needs and their contingencies.

Interestingly, a brainstem cluster including voxels compatible with the location of the human mesencephalic locomotor region (Jahn et al., 2008) followed the same pattern, suggesting that DGI also aided the patients in the recruitment of "internal pacemakers" during the virtual walking task. These brainstem activations did not depend on the mere execution of stepping movements, as these were subtracted out by the Stand(DGI) condition that was used as a baseline (where overt movements were present as well). Our point is that the higher brainstem activation was made possible by the mental imagery shift, whereby the foot movements were integrated within the mental simulation of a veridical locomotion rather than being perceived as an aimless ankle dorsiflexion.

In sum, we suggest that the additional neural resources recruited during DGI may reflect the fact that performing a movement compatible with gait behaviours during motor imagery served in our patients as a kind of cognitive scaffolding that helped them better recall gait kinaesthetic sensations while performing the task. Provided that the application of a kinaesthetic (rather than visual) strategy during imagery might be crucial to achieving improvement in motor performance through mental training (see Guillot et al., 2009), these results may have clinical implications for the rehabilitation of movement in musculoskeletal disorders.

4.4. Conclusions and potential implications for rehabilitation

Our results demonstrate that limb misuse due to a musculoskeletal disorder that causes functional limitations has an impact on motor representations at a central level. We provide evidence from both a behavioural and a neurofunctional perspective and show that gait impairments translate into impaired gait imagery and reduced activation of the gait motor control network during motor imagery, as measured with fMRI. These findings may have implications for clinical practice, as they strongly suggest that rehabilitation of a musculoskeletal disorder might also benefit from "mental training" to restore efficient gait motor control. Current rehabilitation protocols in physical therapy, e.g., after orthopaedic surgery, focus on re-mobilizing the affected part, taking it for granted that there is a spared central ability to control walking patterns. Our findings suggest that this might not necessarily be the case. With regard to gait, this is particularly relevant as orthopaedic patients tend to be elderly: gait disturbances increase the risk of falls, which is one of the primary causes of cognitive and physical decline in the elderly due to prolonged immobilization and reduced autonomy (Alexander, 1996). Application of complementary

rehabilitation strategies (e.g., based on motor imagery) to help restore efficient motor control may improve clinical outcomes. Evidence that DGI is associated with the recruitment of additional motor-imagery-related neural resources suggests that it could be applied as a strategy to boost motor imagery and that it might be especially effective in old age. This will be a future area of focus of our group.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.nicl.2018.07.003.

Conflict of interest statement

The authors declare no conflict of interest that could have direct or potential influence on the work.

All procedures in the study were performed in accordance with the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all participants included in the study.

Data availability

Data will be made available by authors upon request.

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