NeuroImage 202 (2019) 116061

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/neuroimage

Cortical, subcortical and spinal neural correlates of slackline training-induced balance performance improvements

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ARTICLE INFO

Keywords:
H-reflex
Motor learning
MRI
Functional connectivity
Rehabilitation

ABSTRACT

Humans develop posture and balance control during childhood. Interestingly, adults can also learn to master new complex balance tasks, but the underlying neural mechanisms are not fully understood yet. Here, we combined broad scale brain connectivity fMRI at rest and spinal excitability measurements during movement. Six weeks of slackline training improved the capability to walk on a slackline which was paralleled by functional connectivity changes in brain regions associated with posture and balance control and by task-specific changes of spinal excitability. Importantly, the performance of trainees was not better than control participants in a different, untrained balance task. In conclusion, slackline training induced large-scale neuroplasticity which solely transferred into highly task specific performance improvements.

1. Introduction

The seemingly simple act of ensuring an upright posture without falling during everyday activities like standing or walking is often taken for granted. Although humans are able to perform these balance tasks without much thought, the sensorimotor system that controls body orientation and ensures postural balance has to integrate a large number of signals of diverse sensory systems in order to coordinate appropriate motor commands. While postural balance required for everyday activities is mostly acquired during childhood and adolescence (Assaiante, 1998), we are still able to learn unusual or even difficult balance tasks, such as walking over a slackline, later in life. A consolidated knowledge of the underlying neural mechanisms seems to be essential for a deeper understanding of motor learning in general as well as for facilitating learning processes in health and disease.

Several structures within the central nervous system (CNS), including the cerebral cortex, cerebellum, basal ganglia, brainstem and spinal cord, have been shown to contribute to improved postural balance after training (Drijkoningen et al., 2015; Sehm et al., 2014; Taube et al., 2007; Taubert et al., 2010, 2011). Recently, Paillard (2017) and Aman and colleagues (Aman et al., 2014) reviewed the accumulating evidence for structural plasticity in the brain in healthy subjects and cortical reorganization in patients suffering from proprioceptive impairments after balance training. They concluded that this kind of training is able to induce a great amount of structural plasticity while improving postural balance. Although there is mounting evidence for the existence of a complex network mediating balance maintenance and control (Kirsch et al., 2018), most functional imaging work focussed on a subset of brain regions or employed parcellation approaches. Task-related functional MRI studies relied on vestibular stimulation (zu Eulenburg et al., 2012), mental imagery (Taubert et al., 2010) or pathological states (Gottlich et al., 2014; Riccelli et al., 2017), since it is difficult to manipulate postural control of the lower limbs within the scanner. Structural approaches like voxel-based morphometry are able to detect changes across the entire brain, but these methods require a large number of subjects and are not very sensitive, since they rely on grey matter changes. Here we employed task-free functional MRI

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https://doi.org/10.1016/j.neuroimage.2019.116061
Received 21 November 2018; Received in revised form 17 July 2019; Accepted 27 July 2019
Available online xxxx

to investigate intrinsic functional connectivity in healthy subjects before and after six weeks of slackline balance training. Connectivity analyses were carried out at the voxel level, thus enabling more detailed insights into the patterns of network changes through enhanced spatial localization ability (Hayasaka and Laurienti, 2010). .

There is solid evidence that, similar to the learning of a motor task (Henry, 1968; Schmidt and Lee, 1991), balance training induces only task-specific improvements in performance, i.e. the training of a certain balance task only improves the performance in the same task, but this improvement does not generalize to similar untrained tasks (Giboin et al., 2015; Kummel et al., 2016). This particularly applies to slackline training (Donath et al., 2017; Giboin et al., 2018a; Ringhof et al., 2018). The reasons for the lack of transfer to similar but untrained tasks are not known. A possible explanation is that neuroplasticity induced by the balance training is so specific to the task trained that the activation of the changed neural networks is functionally relevant only when performing the task tested. This hypothesis is supported by the fact that markers of such functional neuroplasticity, i.e. neural markers measured during or just before the execution of the trained task, have already been observed between different modalities of training. Indeed, when comparing balance training versus strength training (Beck et al., 2007; Schubert et al., 2008), or even two different kinds of strength training (Giboin et al., 2018b), a change of corticospinal excitability assessed with transcranial magnetic stimulation was observed but only when executing the trained tasks, not when executing the untrained tasks. It must be noted, however, that in these studies, the training modalities were very different from each other (Beck et al., 2007; Giboin et al., 2018b; Schubert et al., 2008). A strong functional marker of balance training-induced neuroplasticity is the H-reflex. The H-reflex method can track plasticity at the spinal level (Nielsen et al., 1993; Wolpaw, 1987), allowing a task-specific functional assessment of the involved neuronal networks (Zehr, 2002), and several studies have observed a reduction in H-reflex amplitude following balance training (Gruber et al., 2007; Keller et al., 2012; Trimble and Koceja, 1994). However, in these studies, due to methodological limitations, it was not possible to detect task specific neuroplasticity.

Therefore, in the present study, we hypothesized that training to walk on a slackline for 6 weeks would induce more task-specific than generalizable effects on behaviour. We tested this hypothesis by measuring performance pre- and post-training during the trained (slackline) and an untrained (tilt-board) balance task. To explain the task-specific effect, we measured H-reflexes in the Soleus muscle (Sol) of the right leg while the subjects were stepping onto the slackline or the tilt-board pre- and post-training. To overcome the limitations associated with H-reflex measurements during movement (Zehr, 2002), we used an innovative experimental paradigm controlling for ankle and knee joint angles, muscle background activities and the stochastic proprioceptive feedback during the balance tasks.

To sum up, it is known that various brain structures show changes after the learning of a new balance task, and that the behavioural changes observed after balance training are highly task-specific. In the present study, we investigate the neural correlates of learning a balance task by combining imaging techniques and electrophysiological methods. The combination of these methods allows us to analyse changes in connectivity between various brain structures within the cortex during rest as well as changes in the spinal excitability during the execution of the trained and an untrained balance task.

2. Methods

2.1. Data statement

Data and code are available upon direct request.

2.2. Participants

All experiments were approved by the ethics committee of the University Konstanz and conducted in accordance with the declaration of Helsinki. Forty-seven young healthy participants joined the study after giving written informed consent. Three participants dropped out from the study for reasons unknown to the investigators (Training: N = 22, 10 women, 25 ± 4 years old, 69 ± 12 kg, 173 ± 10 cm; Control: N = 22, 14 women, 22 ± 2 years old, 70 ± 12 kg, 175 ± 9 cm). Thirty-five subjects participated in the H-reflex measurements, but 5 were excluded from the analyses (Training: N = 17, 7 women, 25 ± 4 years old, 72 ± 12 kg, 175 ± 8 cm; Control: N = 13, 10 women, 22 ± 2 years old, 71 ± 11 kg, 174 ± 8 cm).

Participants were screened with questionnaires to be right leg dominant, free of pain and injuries in the lower limbs, naive to any balance training, and compatible with safety constraints of MRI. Participants were required to not perform any balance training and were asked to maintain their ordinary physical activity behaviour during the whole duration of the study.

2.3. Sampling plan

The sampling plan was not driven by an a-priori power analysis but by previous experience with the methods used (H-reflex and MRI) and by experimental constraints. The largest experimental constraints were the available time-slots for the MRI session at the clinic, and the capacity of our lab to manage at the same time the neurophysiological measurements and the training. We estimated that around 50 subjects would be the highest we could sample. We initially planned to sample 48 subjects with 20 in the control group and 28 in the training group to compensate for eventual drop outs. We were able to sample 47 subjects in the given time, with only 3 drop outs. We deviated from the initial plan by increasing the number of subjects in the control group to match groups (N = 22 per group).

2.4. Study design

The study had a pre-post-training measurements design (see Fig. 1). Pre- and post-training sessions of MRI and neurophysiological measurements were separated by 6 weeks of training. The MRI session was always conducted before the neurophysiological experiments, and both were done during the same week with at least one day in between. Participants were divided into a control and a training group. The division into groups was pseudo-randomized, aiming to match pre-training slackline and tilt-board balance performance between groups.

2.5. Slackline training

The training group followed a six-week training program, consisting of two sessions of 45 min per week, separated by at least 48 h of rest. All training sessions were supervised and conducted on fixed slacklines (4 m long, 45 mm wide, Slackline Tools). Every session started with a warm-up of 5 min (rotation, flexion and extension of all leg joints). The training program is enclosed as supplementary material.

2.6. Balance performance assessments

We tested balance performance of every participant on a slackline (Classic Line X13, Gibbons) and on a tilt-board (board with five degrees of freedom, Sensoboard, Sensosports GmbH). The tests were performed at the beginning of the experimental session, without any familiarisation trials. Both tasks were done twice, in a counter-balanced order, with 1 min of rest between each trial. The slackline task consisted in doing as many steps as possible on it, hands on the hip, and starting with the right foot from an elevated platform at the beginning of the line. The participant had to stand on one leg at least for 2 s before starting the next step. To make the standing time safe, the investigator checked the time and gave the participant a go signal for each step. For a valid step the participant had to stand at least 2s on one leg. Performance for the

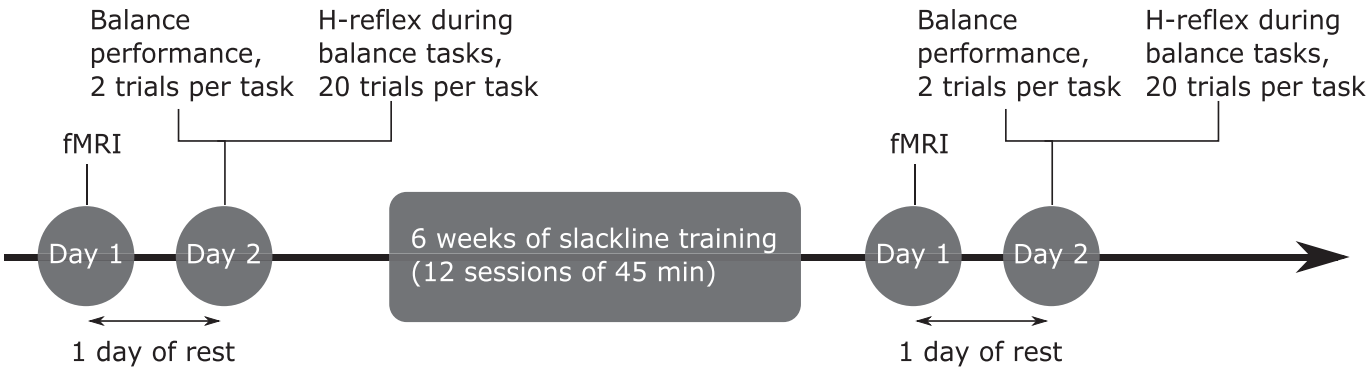

Fig. 1. Experimental timeline. The training and the control group performed pre- and post-training measurements consisting of one fMRI and one neurophysiological measurement session separated by at least one day. The MRI session always preceded the neurophysiological session.

slackline task was defined as the number of steps taken. The tilt-board task consisted of performing a one-leg stance on the tilt-board (right leg), hands on the hips and starting from an elevated platform. Performance for the tilt-board task was defined as the time at equilibrium, i.e. the time from the touch-down of the participant's foot on the tilt-board to the time when one side of the tilt-board or the participant touched the ground. The time at equilibrium was measured with a stopwatch.

2.7. MRI data acquisition

All imaging data were acquired on a Siemens Magnetom Skyra 3T MRI scanner (Siemens, Erlangen/Germany) with a 32-channel head coil. A high-resolution, T1-weighted structural scan was obtained for anatomical reference using a 3D-MPRAGE sequence (TE = 7.21 ms, TR = 2700 ms, TI = 1100 ms, flip angle = 7°, voxel size = 1 mm^3). Two runs of resting-state fMRI data were acquired using an echo-planar imaging (EPI) sequence (TE = 30 ms, TR = 2710 ms, flip angle = 80°, voxel size = 3 × 3 × 3 mm^3) sensitive to blood oxygen level-dependent (BOLD) contrast. Forty-eight axial slices were obtained parallel to the intercommissural (AC-PC) line (matrix size: 80 × 80). A total of 400 vol per subject (200 vol per run) were acquired. Participants were instructed to rest quietly with their eyes open during resting-state fMRI acquisition. To address the problem of geometric distortions in EPI caused by magnetic field inhomogeneity, a B0 field map was acquired prior to the EPI sequence using a double-echo gradient recall echo (GRE) sequence (TE 1/2 = 4.92 ms/7.38 ms, TR = 675 ms, flip angle = 60°, voxel size = 3 × 3 × 3 mm^3).

2.8. MRI data preprocessing

For each participant, structural images were skull-stripped (Smith, 2002) and warped to MNI space using FLIRT (Jenkinson et al., 2002) and FNIRT (Andersson et al., 2010) (T1-to-MNI registration). Functional images from each of the two resting-state runs were despiked, corrected for time differences in slice acquisition, and realigned to the mean functional image using 6 degrees of freedom rigid body transformations to compensate for head motion (Jenkinson et al., 2002). Geometric distortions induced by magnetic field inhomogeneity were corrected based on the GRE field map, and the EPI data were registered to the corresponding structural scan (T1). EPI distortion correction and EPI-to-T1 registration were performed simultaneously using FSL epi_reg. The spatial transformations from motion correction, EPI distortion correction, EPI-to-T1 registration, and T1-to-MNI registration were combined into a single warp to reduce interpolation-induced blurring (Glasser et al., 2013). Using this warp, the despiked and slice time corrected functional data were transformed from native to standard space in one resampling step. The resulting images were spatially smoothed using a Gaussian kernel (6 mm FWHM) to improve the signal-to-noise ratio and to further accommodate inter-individual anatomic variations. Confound regression was performed using 12 parameters (the 6 parameters from the motion correction step and their temporal derivatives). To account for low frequency intensity drifts and high frequency noise, the data were bandpass-filtered (0.01–0.1 Hz).

2.9. H-reflex measurements

2.9.1. Electromyography

EMG from the right leg M. Soleus (Sol), M. Tibialis Anterior (TA), M. Vastus Lateralis (VL) and M. Biceps Femoris (BF) were collected with surface EMG electrodes (Trigno wireless system, Delsys), band pass filtered (20–450 Hz), sampled (2000 Hz, Power1401, Cambridge Electronic Design) and recorded for online (Signal Software 5.08, Cambridge Electronic Design) and a posteriori analysis. EMG electrodes were taped over the muscle belly (shaved, abraded with sandpaper and cleaned with alcohol). The emplacement of the EMG electrodes was done in relation to anatomic landmarks and photographed to ensure similar electrode positions in the pre- and post-training measurements.

To normalise the background EMG, maximal voluntary isometric contractions of each muscle were performed for Sol and TA in an ankle ergometer with the knee fixed and for VL and BF in a custom-made chair with the hip, torso and right ankle of the participant strapped to the chair.

2.9.2. Motion capture

We measured kinematics of the right leg and the timing of the touchdown on the slackline and tilt-board with a motion capture system (Vicon Nexus, 12 T40s cameras, 200 Hz). Markers were fixed on the distal part of the tilt-board, on the slackline 1 m behind the elevated platform, as well as over the hallux, fifth metatarsal bone, lateral malleolus, lateral knee joint center and greater trochanter of the subject's right leg.

2.9.3. Stimulation triggering

Participants were standing on a platform towering above either the slackline or the tilt-board (Fig. 2). At the investigator signal, the participant, hands akimbo, had to step onto the balance device and perform a 2 s one-leg stance on it before returning to the platform. Note that the distance and the height of the platform with respect to the balance device was identical for the slackline and the tilt-board. To trigger stimulation, we fixed a light barrier system (Optogait, Microgate, Bolzano, Italy) 1 cm above the slackline or the tilt-board, sending a TTL signal to the sampling system as soon as the foot of the subject crossed it. First, the participant had to step 3 times onto the tilt-board and the slackline to calculate the optimal stimulation delay for both balance devices, i.e. ensuring the stimulation in between 100 ms before and 20 ms after the touchdown. Then, Mmax and H-reflexes were measured while the subject stepped onto the slackline or the tilt-board (random but counterbalanced task order, same order pre- and post-training).

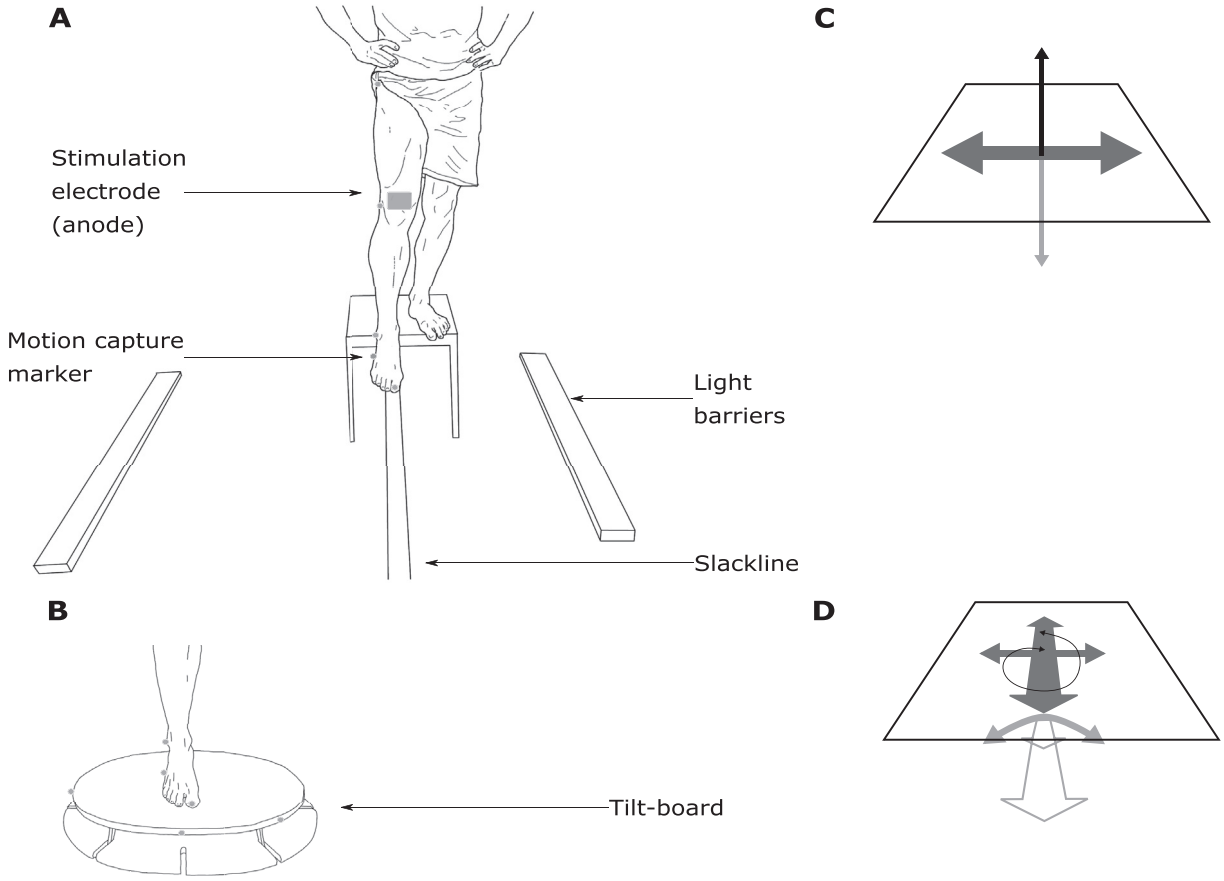

Fig. 2. Experimental set-up for H-reflex measurements. Participants stepped from an elevated platform toward the slackline (A) or the tilt-board (B) to perform a one leg stance for 2 s. The peripheral nerve stimulation was triggered by the foot crossing the light grid. The delay of stimulation has been adjusted individually. Knee and ankle angles were controlled with motion capture around touchdown. Panels C and D depict the main degrees of freedom of the slackline and tilt-board, respectively.

2.9.4. H-reflexes

H-reflexes were evoked in Sol, with the smallest response possible in the TA, by stimulating the tibial nerve (stimulator DS7A, Digitimer) with the cathode (copper, circular, 2 cm diameter, wrapped in a water-soaked sponge) fixed in the fossa poplitea and the anode (copper, 7×5 cm, wrapped in a soaked sponge) fixed over the patella. To minimise motor learning before actual measurements, all calibration procedures were done with the greatest economy in steps done on balance devices. First, a recruitment curve was done at rest, with the participant sitting on a chair and the right leg positioned with a knee angle of 120°. Then, Mmax was assessed during the first few steps on the balance device. Next, stimulation intensity was adjusted as follows: i) in the pre-training measurements, H-reflex was on the ascending part of the response/intensity curve, H-reflex size (normalised to Mmax) was equal to H-reflex size obtained while walking on the other balance task, and the M-wave adjusted to around 10% Mmax. ii) In the post-training measurements, H-reflex was on the ascending part of the response/intensity curve, M-wave (normalised to Mmax) and adjusted to M-wave amplitude used in the pre-training measurement. Twenty steps and stimulations were done, with a rest of 6–10 s in between each step. The same procedure was then done with the other balance task.

2.10. Analysis

2.10.1. Angle calculation

For each subject, the angles of the right knee and ankle joints in the sagittal plane at touchdown were calculated for each stimulation during each task and session. For that purpose, the kinematic data captured with the Vicon system was projected into the sagittal plane. The knee angle was calculated from the markers on the lateral malleolus, knee joint center and greater trochanter, and the ankle angle was calculated from the markers on the fifth metatarsal bone, lateral malleolus and knee joint center.

2.10.2. Background EMG

Background EMG was calculated as the root mean square (RMS) of an epoch of 50 ms taken before the stimulation. It was normalised to the RMS of an epoch of 200 ms taken at the highest EMG amplitude level during the isometric maximal voluntary contraction, for each muscle and each session.

2.10.3. H-reflexes

Stimulations given outside a window of 100 ms before to 20 ms after foot touchdown were removed from further analysis. We took great care in matching M-waves amplitude pre- and post-training during the experiment. Furthermore, to improve the comparison of the H-reflex amplitudes across time, we filtered stimulations accordingly to the M-wave amplitude with the following process: for each subject, M-waves amplitude post-training outside the mean M-wave amplitude ± 1.96 standard deviations pre-training were removed, and M-waves amplitude pre-training outside the mean M-wave amplitude ± 1.96 standard deviations post-training were also removed. The amplitude of H-reflexes

induced by the remaining stimulations were normalised to Mmax. Five subjects were fully removed due to all the stimulations being given outside of the touchdown window (3 subjects) or post training M-waves were outside the defined window (see procedure of M-wave amplitude matching) (2 subjects had all M-waves outside the defined window). Two subjects had stimulations remaining only for 1 task.

2.10.4. Statistics for performance and H-reflex

To assess changes following training in the slackline and tilt-board performance, H-reflex and M-wave amplitude, ankle and knee angles and background EMG, we fitted Bayesian linear mixed models (BLMM) with the *brms* package in R (Bürkner, 2017). Importantly, Bayesian statistics perform well with small sample size and with complex models such as mixed models. Bayesian statistics provide a distribution of probabilities that the given parameters estimates are contained in the distribution interval (credible interval). The interpretation of credible interval is intuitive and also allows researchers to assess the likelihood of no effect (Kruschke, 2013). Analyses were done at the trial level nested within participants (1655 trials after filtering according to M-wave amplitude for H-reflexes, and 352 trials for balance performance) (Moen et al., 2016). To be able to compare performance between the two different tasks, performance data were centred and scaled. We assessed normality of data with QQ-plots, since we wanted to fit data with Gaussian family models. H-reflex data were thus transformed to reduce skewness (square root of the H-reflex amplitude). M-waves were log transformed and sol, TA and BF background EMG were squared root transformed to reach a normal distribution. For the balance performance, no transformation was more satisfying than the non-transformed data. We indicate to the reader that this set of data is far from a normal distribution and this point must be taken into consideration when interpreting the model estimates. However, given the clear results observed, we believe that overall interpretations remain correct. For the H-reflex and the balance performance we fitted a model with an interaction between time, task and group (constant effects), with varying intercepts by-subjects and varying slopes by-subject for the main within-subject effects and interaction (response variable ~ group × task × time + (task × time | subject)). This way, the error structure of the models was maximized, reducing the type I error probability (Barr et al., 2013). We used the non-informative conservative priors for the population estimates (priors given by default by the package). We used 4 MCMC with 2000 iterations each (1000 for warm-up). The convergence of each model parameter estimated was monitored and the posterior distribution was compared to data distribution. First, we tested whether there was an interaction between group, task and time by comparing the fit of the previous model with a model without interaction (variable ~ group + task + time + (task + time | subject)). Models were compared with the LOO() function (leave-one-out cross-validation), where the smaller the leave-one-out information criterion (LOOIC), the better the model fit to the data (Vehtari et al., 2017). Then, because the contrasts given by the model output with the function *summary()* do not answer our hypothesis (see Table 2 legends and Results section for the interpretation of the output), we tested specific hypothesis with the *brms hypothesis()* function and applied contrasts by group, task and time on the Bayesian model with the R package *emmeans* (https://cran.r-project.org/web/packages/emmeans/index.html). Indeed, our hypothesis was: there is an increase in performance and a decrease in H-reflex amplitude after training, but only in the training group and only in the trained task (implying no changes for all other condition levels). For control measurements (e.g. M-waves, background EMG and angles), we tested whether there was a difference pre and post training, between tasks or between groups (response variable ~ group + time + task + (time + task |subject).

2.10.5. Functional connectivity analysis and statistics

For each subject and session, the two runs of preprocessed resting-state fMRI data were temporally concatenated before a voxel-level connectivity graph, or dense connectome (Akil et al., 2011; Marcus et al., 2011), was constructed. To that end, gray matter voxels were defined as nodes and internodal functional connectivity was estimated in terms of Pearson correlation between the nodes' associated time series. Subsequently, the Fisher *z*-transformation was applied to each of the correlation values.

To assess pre-post differences in connectivity between pre- and post-training measurements in the training group that are also accompanied by a between-group difference in pre-post differences, we first computed edge-level difference-in-differences and paired sample *t* statistics based on the connectomes from both groups and the training group, respectively. The resulting graphs of statistics G_{did} and $G_{trn,\ pre\text{-}post}$ were both pruned using an edge-level threshold of $\vartheta_p = 0.01$. $G_{trn,\ pre\text{-}post}$ was then pruned further to retain only those edges that also exist in G_{did}. Based on the directions of the pre-post changes in the training group, $G_{trn,\ pre\text{-}post}$ was then partitioned into two subgraphs corresponding to decreases ($G_{trn,\ pre>post}$) and increases ($G_{trn,\ pre<post}$) in connectivity, respectively.

Degree centrality was computed for both of these graphs resulting in two degree maps. The degree *k* of a node *v* is the number of node pairs *(v,w)* in a graph *G*, where *w* can be any node other than *v*. Each degree map was thresholded using a cluster-forming threshold of $\vartheta_k = 500$.

This procedure (compute and prune G_{did}, prune $G_{trn,\ pre\text{-}post}$ based on G_{did}, partition $G_{trn,\ pre\text{-}post}$ into $G_{trn,\ pre>post}$ and $G_{trn,\ pre<post}$, compute the degree maps) was repeated 1000 times based on random relabelings of the data to approximate the permutation distribution of the maximal cluster mass under the null hypothesis of no differences for each of the degree maps (each relabeling was conducted such that the order of the two measurements and the group membership was randomly determined for each subject). For each map, cluster-level *p* values were derived from the permutation distribution and multiplied by 2 because of multiple testing due to the two directions. Finally, clusters with a corrected *p* value < 0.05 were deemed significant.

2.11. Control measurements

To track task-specific neuroplasticity induced by the training, it was necessary to elicit potentials during the relevant tasks, i.e. while walking on the slackline or standing on the tilt-board. However, such practice may provide inadequate data interpretation in training studies. Indeed, the contractions of leg muscles may modify the distance between the nerve and the stimulation electrode. The increased, or reduced distance will affect the portion of Ia afferent fibres stimulated and consequently, the amplitude of the H-reflex. To ensure a similar stimulation of the Ia afferents, it is necessary to use a stimulation intensity able to induce a direct motor response (M-wave) and to control that the amplitude of the M-wave remained stable across sessions (Zehr, 2002). Moreover, as expected, the slackline training will modify movement behaviour, e.g. different posture and smaller movement amplitude while standing on the slackline (Keller et al., 2012). Yet, H-reflexes are sensitive to kinematic changes (Zehr, 2002). Thus, when observing modulation of H-reflexes after training, the movement during which potentials are elicited must remain identical pre- and post-training. Otherwise, it remains unclear whether the modulation of the potential size is caused by alterations in the movement kinematics or by neuroplasticity induced by the training. Results are displayed in Table 1. BLMM suggested that there was most probably no effect of group (posterior estimates [95% lower Credible Interval, 95% upper Credible Interval], 0.06 [-0.51, 0.62), time (0.04 [-0.02, 0.09]), or tasks (−0.06 [-0.27, 0.16]) in the log of M-wave amplitude (base levels being time pre, group control and task tilt board).

We controlled the muscle activity pre- and post-training by monitoring EMG normalized to the EMG obtained during a maximal isometric voluntary contraction (Table 1). The BLMMs indicate no credible effect of time or group (results not displayed). However, a difference between tasks could be seen for the TA (−0.47 [-0.7, −0.26]), the VL (−1.17 [-2.08, −0.3]) and the BF (−0.28 [-0.39, −0.18]). We explain these differences by the limb position just before stepping on balance device (more with the heel first on the tilt board than on the slackline).

Table 1
Mean M-wave, leg angles and EMGs pre- and post-training during H-reflex measurements. M-wave (in % Mmax, mean ± standard deviation) measured pre- and post-training in both task and for both groups. Ankle and knee angles (in degrees) of the right leg measured with motion capture at stimulation time while walking on the slackline or the tilt-board. RMS EMG measured before stimulation and normalized to EMG (%) obtained during a maximal isometric voluntary contraction of the relevant muscle pre- and post-training.

M-wave	Slackline		Tilt-board	
	Pre	Post	Pre	Post
Train	11.7 ± 11.3	10.7 ± 10	11.7 ± 11.3	10.6 ± 10.7
Con	8.6 ± 6.9	10.3 ± 10	8.6 ± 6.9	10.3 ± 10
Angle	Slackline		Tilt-board	
	Ankle	Knee	Ankle	Knee
Train PRE	139 ± 10	158 ± 8	138 ± 7	158 ± 9
Train POST	141 ± 11	162 ± 7	136 ± 10	162 ± 5
Con PRE	133 ± 11	155 ± 9	132 ± 11	158 ± 10
Con POST	141 ± 7	158 ± 9	136 ± 20	160 ± 10
EMG	Slackline			
	Sol	TA	VL	BF
Train PRE	14.7 ± 6	9.2 ± 6	13 ± 9	15.2 ± 12
Train POST	14.9 ± 9	7.6 ± 4	11.5 ± 6	20 ± 14
Con PRE	17 ± 13	10.4 ± 4	15.7 ± 13	14 ± 10
Con POST	22 ± 12	10 ± 7	10.6 ± 11	13.8 ± 12
EMG	Tilt-board			
	Sol	TA	VL	BF
Train PRE	15.4 ± 6	13.5 ± 10	12.4 ± 7	16.5 ± 12
Train POST	16.7 ± 9	10.4 ± 7	13.9 ± 9	23.3 ± 14
Con PRE	16.4 ± 12	15.8 ± 9	15.7 ± 13	16.3 ± 10
Con POST	21.7 ± 11	14.7 ± 12	14.5 ± 22	19.1 ± 15

With motion capture, we were able to control for the leg position at the time of H-reflex stimulation by measuring the ankle and knee angles while stepping on the tilt-board or the slackline pre- and post-training (Table 1). There was no credible effect of time, group or task for the knee angle and no credible effect of time or group for the ankle angle (results not displayed). However, there was an effect of task on the ankle angle (2.40 [0.29, 4.47]), possibly due to the different foot position at the approach of the balance device (to put in relation with the background EMG results). Taken together, these control observations indicate that a change observed in the H-reflex would not come from differences in biomechanical constraints.

3. Results

3.1. Balance performance

We determined balance performance in a control (Con, N = 22) and a training group (Train, N = 22) before and after 6 weeks of slackline training (12 sessions of 45 min). We measured the number of steps before losing equilibrium on a slackline (trained task) and the time before losing equilibrium in one-leg stance on a tilt-board (untrained task). Performance results are displayed in Fig. 3A and B. To be able to compare tasks between them, performance was centred and scaled. The output from the Bayesian LMM is displayed in Table 2. The model without interaction had a higher LOOIC than the model with interaction (960 ± 88 versus 933 ± 88, difference of 27 ± 25), indicating that there was probably an interaction effect between group, task and time. The output of the interaction model indicated that the estimate for groupTraining:taskSlackline:timePost was most probably different from zero. This indicated that the effect groupTraining:taskSlackline was higher at time Post compared to time Pre. The effect groupTraining:taskSlackline indicated the interaction effect between the training group and the task slackline compared to baseline. The difference of performance for the training group on the slackline pre- and post-training can be estimated by adding the groupTraining:taskSlackline:timePost effect to the timePost, groupTraining:timePost, and taskSlackline:timePost effects. Therefore, the estimates given by this particular treatment contrast did not answer our hypothesis, which was that after training we would observe an increase in performance, but only for the training group and only for the task trained. The contrast by group, task and time indicated a clear difference of performance on the slackline for the training group between pre and post (Fig. 3C). The hypothesis testing that performance on the slackline for the training group was higher at time post than at time pre gave an estimate of 1.08 [0.75, Inf] with an evidence ratio of infinity. The evidence ratio corresponds to the ratio between the posterior probability of the hypothesis performance slackline training post > slackline training pre and the alternative hypothesis. There was most probably no difference of performance within the same task and within the same group across time.

3.2. MRI

In the training group, the comparison between the pre- and post-training measurement revealed increases of functional connectivity in various cortical and subcortical brain structures. Cortical areas exhibiting increased connectivity were the bilateral premotor and primary motor cortex, the primary and secondary somatosensory cortex, insula, the posterior cingulate and superior parietal cortex, the superior middle and the inferior temporal cortex. Importantly, connectivity increases were also observed in subcortical structures like the right amygdala and hippocampus, bilateral caudate nucleus, globus pallidum, claustrum and the pulvinar as well as in the medial and lateral cerebellum, and in the brainstem (see Fig. 4). The opposite comparison did not reveal any decreases in connectivity. Most importantly, we did not observe any significant changes (neither increases nor decreases) in connectivity between the two measurement time points in the control group.

3.3. H-reflex

We have measured, pre- and post-training, H-reflex amplitudes in the soleus muscle while the participants were stepping from a stable platform toward the slackline (trained task) and towards the tilt-board (untrained task). In both tasks the participants were instructed to perform a one-leg stance for 2 s on the slackline or the tilt-board respectively (N = 30, 13 for the control group and 17 for the training group. More specifically, 12 for the control group and 17 for the training group for the tilt-board task, and 13 for the control group and 16 for the training group for the slackline task). The results are plotted in Fig. 5A and B. The model without interaction had a higher LOOIC than the model with interaction (4756 ± 69 versus 4643 ± 68, difference of 113 ± 23), indicating that there was most probably an interaction effect between group, task and time. The output of the interaction model obtained with the *summary()* function indicated that none of the displayed estimates tested against the baseline (i.e. control, tilt board and pre) are credibly different from zero (Table 2). In the same way as the performance results, this particular treatment contrast did not allow us to verify directly our hypothesis (i.e. the H-reflex amplitude is decreased after training but only in the training group and only in the trained task). The hypothesis testing that the square root amplitude of H-reflex was higher in the training group during the slackline task pre-training than post-training gave an estimate of 0.92 [0.28, Inf] and an evidence ratio of 94.2. Additionally, the contrasts at group, task and time level indicated no clear other difference in the H-reflex amplitude (see Fig. 5C).

4. Discussion

Six weeks of slackline training induced increases of connectivity in a widespread network of cortical and subcortical areas that are tightly related to movement planning, preparation, execution, evaluation and

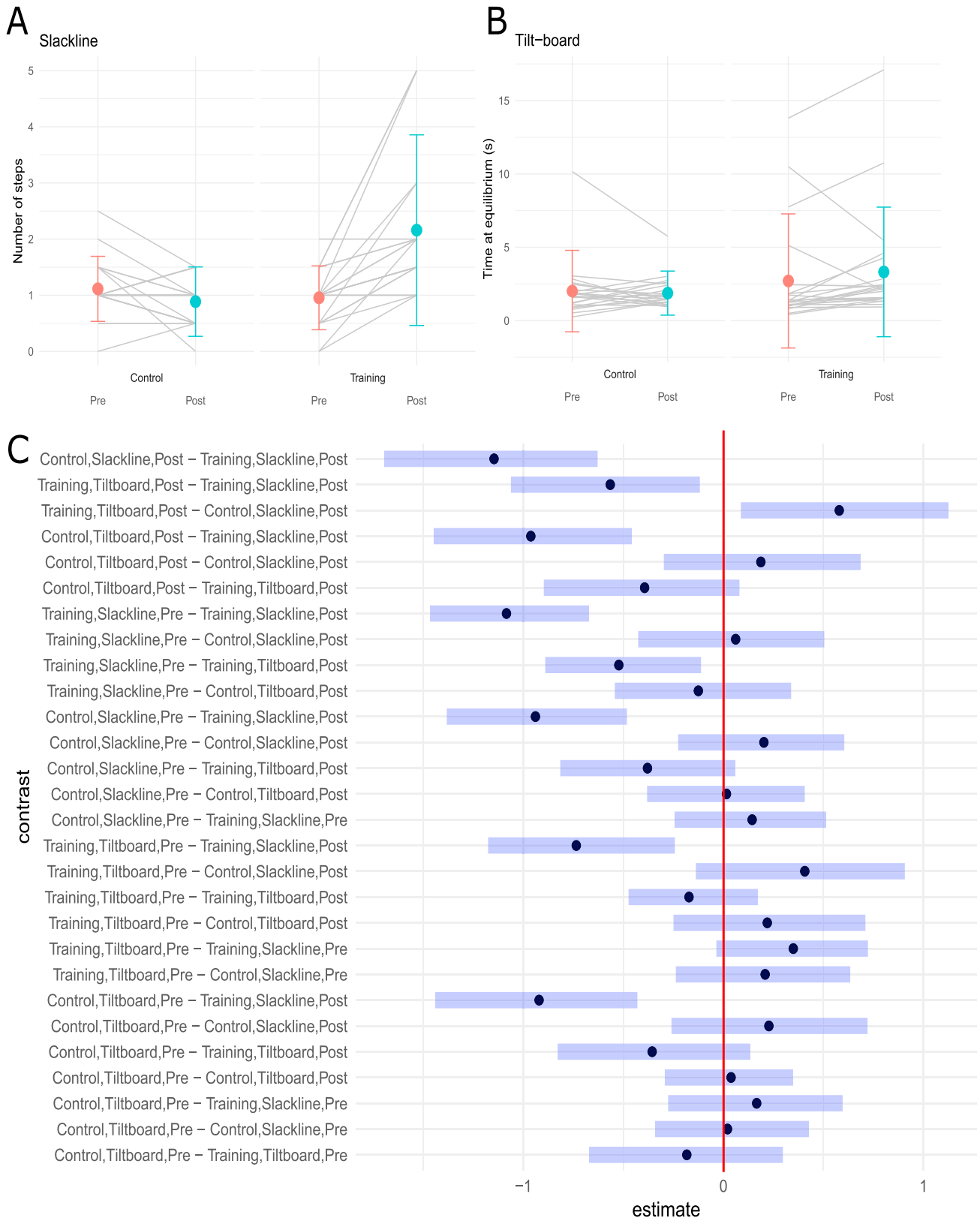

Fig. 3. Behavioural results. N = 44, 22 subjects per group. A) Performance on the slackline task (number of steps) pre- and post-training for the training and control group. B) Performance on the tilt-board (time at equilibrium in s). For A and B the grey lines correspond to the mean individual variation of performance pre- to post-training (mean of 2 trials). It must be noted that many of these lines are superposed, especially in the case of the slackline task. The large dots represent the group means and error bars represent the standard deviations. C) Posterior contrasts by group, task and time. Points represent mean estimate and blue error bars represent the 95% credible interval.

Table 2
Model outputs for balance performance and H-reflex amplitude. Estimates of the posterior distribution of the mean of constant effects and standard deviation of varying effects (estimate, standard deviation, 95% credible interval lower and upper bounds) given by the function *summary()* for the centred and scaled balance performance and the square root of the H-reflex amplitude. The estimates are tested against the base level (Intercept), which corresponds to the mean of the dependant variable with the three base levels (Control, Pre, Tilt board). Thus, as an example, for the H-reflex amplitude, the estimate of groupTraining indicates the difference in H-reflex amplitude between the Intercept and the training group when the task is the Tilt board and time is Pre.

	Balance performance (centred and scaled)			
	Estimate	Std. Error	Lower 95%	Upper 95%
Intercept	−0.126	0.176	−0.470	0.223
groupTraining	0.186	0.249	−0.301	0.67
taskSlackline	−0.022	0.198	−0.417	0.357
timePost	−0.039	0.167	−0.365	0.281
groupTraining:taskSlackline	−0.328	0.275	−0.854	0.217
groupTraining:timePost	0.209	0.237	−0.259	0.675
taskSlackline:timePost	−0.164	0.271	−0.681	0.376
groupTraining:taskSlackline:timePost	1.079	0.38	0.334	1.816
sd(Intercept) subject	0.622	0.101	0.438	0.839
sd(taskSlackline) subject	0.492	0.138	0.221	0.773
sd(timePost) subject	0.114	0.088	0.003	0.324
sd(taskSlackline:timePost) subject	0.597	0.184	0.248	0.973
	H-reflex amplitude (squared root transform)			
	Estimate	Std. Error	Lower 95%	Upper 95%
Intercept	4.661	0.402	3.883	5.435
groupTraining	0.319	0.549	−0.763	1.408
taskSlackline	−0.081	0.249	−0.573	0.415
timePost	−0.049	0.407	−0.834	0.772
groupTraining:taskSlackline	0.426	0.332	−0.229	1.072
groupTraining:timePost	−0.037	0.554	−1.136	1.062
taskSlackline:timePost	−0.179	0.338	−0.848	0.492
groupTraining:taskSlackline:timePost	−0.657	0.454	−1.559	0.226
sd(Intercept) subject	1.444	0.217	1.075	1.933
sd(taskSlackline) subject	0.772	0.147	0.521	1.097
sd(timePost) subject	1.465	0.232	1.079	2.032
sd(taskSlackline:timePost) subject	1.059	0.198	0.721	1.495

correction as well as to some extent to motor learning. The increased neural connectivity was associated with highly task-specific performance improvements in the trained but not in the untrained balance task. These task-specific performance improvements were accompanied by specific changes in spinal excitability of the Ia afferent pathways during execution of the balance task.

As expected (Donath et al., 2017; Giboin et al., 2018a; Ringhof et al., 2018), the 6 weeks of slackline training increased the ability of participants to walk on the slackline. At the cortical level, premotor, primary motor and somatosensory cortices showed training-induced connectivity increases. These brain regions are deeply involved in the planning and execution of movement and postural regulation of the trunk and extremity muscles that are also required to maintain balance on the slackline. Another brain structure belonging to the training-induced connectivity increases network was the cerebellum. Any self-produced movement relies on a descending motor command that is accompanied by an internal representation in the cerebellum, also known as efference copy, used to anticipate sensory feedback from that movement. This signal, called corollary discharge, is compared with the actual sensory feedback (Holst and Mittelstaedt, 1950). Using this signal (Jeannerod, 2003) the cerebellum is critically involved in movement correction ensuring precision, which is mandatory in the maintenance of balance (Ilg and Timmann, 2013; Jahn et al., 2004; Konczak et al., 2005; Morton and Bastian, 2004; Schoch et al., 2010; Taube et al., 2015). Especially the medial part of the cerebellum, the spinocerebellum, receives afferent proprioceptive information and has been strongly associated with the maintenance of posture (Kelly and Shanley, 2016; Lam et al., 2016). Moreover, body sway considerably increases after inactivation of the vermis (Colnaghi et al., 2017), demonstrating the distinct role of this structure for balance regulation. In the current work the medial and lateral parts of the cerebellum exhibited training-induced increases in connectivity, which is perfectly in line with the eminent role of the cerebellum in the maintenance of balance and posture (Drijkoningen et al., 2016). Further increases in connectivity were also observed in the insula, in the parietal cortices as well as in the thalamus. These regions were described to form a neural network that supports interoception (Critchley et al., 2004), which is crucial in the maintenance of balance necessary for standing and even more for walking on a slackline. Training-induced increases of functional connectivity were also observed in subcortical areas such as the right amygdala and hippocampus. These brain areas are not necessarily directly related to motor learning or the maintenance of posture. Nevertheless, activity in these areas was reported to change as a function of exercise (Maass et al., 2015), which would be in line with the current results since the slackline training performed in the current study can be considered as a form of physical exercise. The thalamus also exhibited a training-induced increase of connectivity. This is also well in line with the role of the thalamus in maintaining balance (Ramirez-Zamora et al., 2016). Importantly, the slackline training also induced changes in connectivity in areas of the basal ganglia (bilateral caudate nucleus, globus pallidum, claustrum). These areas are tightly related to motor control and execution, to postural control, and were shown to be responsible for motor learning and especially for the transduction of the learned skills into automaticity (Aron and Poldrack, 2006; Ashby et al., 2010; Boisgontier et al., 2017; Moors and De Houwer, 2006). Furthermore, changes in brainstem connectivity were also observed. This is well in line with previous studies showing that the brainstem, and more particularly the pedunculopontine nuclei, is related to balance and gait control (Boisgontier et al., 2017; Lau et al., 2015).

In the present study, we exclusively observed increases in functional connectivity in a widespread network of cortical and subcortical brain areas to be the functional correlate of training-induced changes of the ability to maintain balance and posture on a slackline. Most fMRI studies found training- or learning-induced activity decreases in the same regions (Lehericy et al., 2005; Poldrack et al., 2005; Ruffieux et al., 2018; Wu et al., 2004). It has to be emphasized that the observation of activity decreases in previous studies is not necessarily inconsistent with the results of the present study. Quite the contrary, the observed increase in connectivity may have led to a more efficient processing in the affected neural networks and thereby could explain the reduction of neural activity required for a trained task or action.

Despite the large-scale changes in connectivity after the training, the performance of trainee participants was not better than control participants in the untrained balance task. Although this behavioural result is in line with previous studies (Giboin et al., 2015, 2018a; Ringhof et al., 2018) and meta-analysis (Donath et al., 2017; Kummel et al., 2016), this is the first time that a study demonstrates at the same time task-specific performance improvement and connectivity changes in multiple structures traditionally associated with balance, posture, and motor control. Therefore, participants with the large training-induced changes in connectivity in cortical and subcortical structures related to balance performance, did not perform better in an untrained balance task than participants who do not share these neural changes. In order to explain this expected issue, we measured spinal excitability during task execution with the H-reflex method. We observed that a task-specific decrease in H-reflex amplitude was accompanying the task-specific increase in performance following training. The decrease in H-reflex after balance training is in line with previous studies (Gruber et al., 2007; Keller et al., 2012; Trimble and Koceja, 1994). However, the present study is the very first to show that the decrease can be task-specific since it was exclusively observed for the trained task. By measuring during the preparatory phase at the very onset of the task we circumvented the influence of training-induced kinematic modifications that were expected to happen

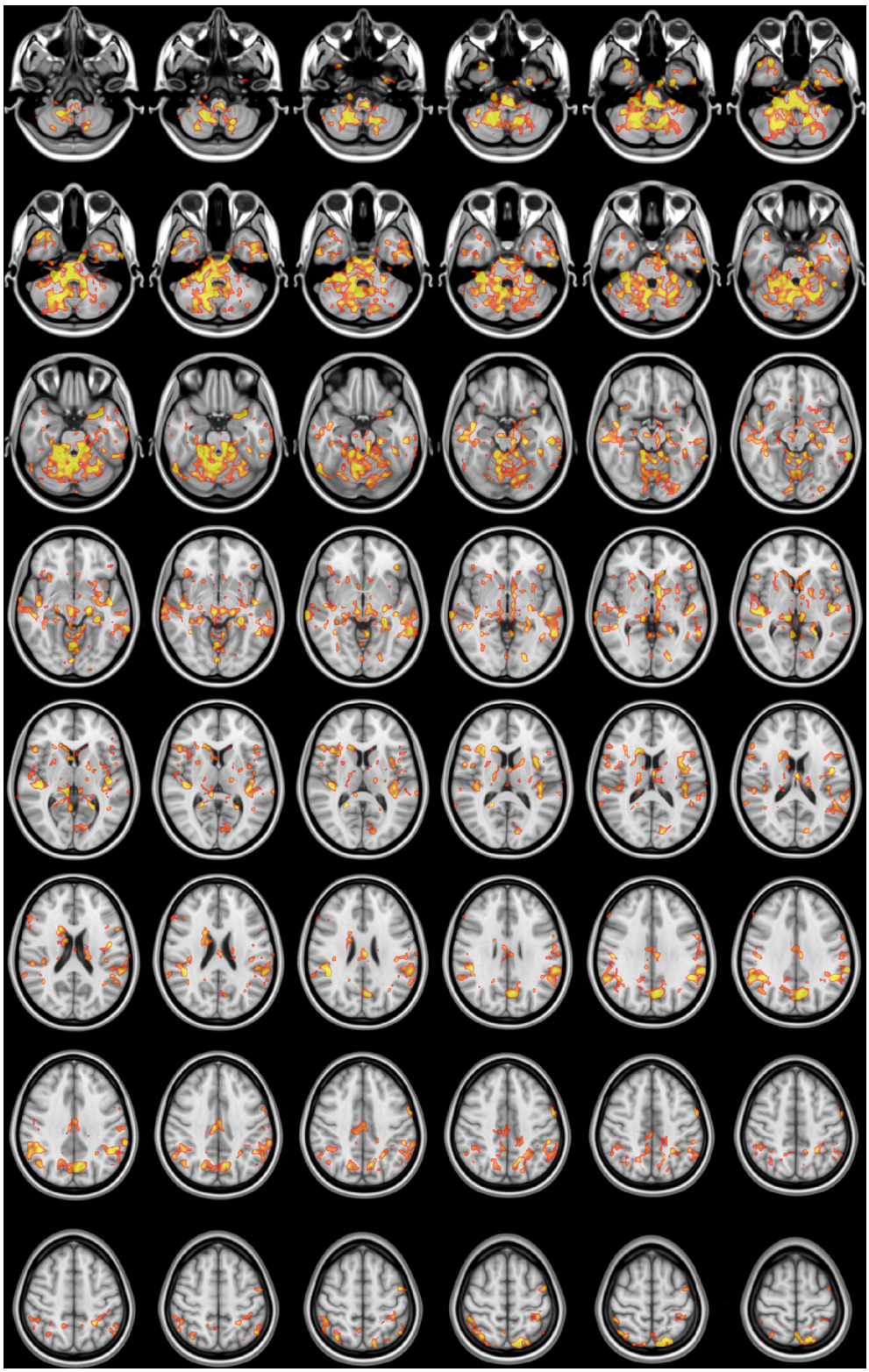

Fig. 4. Training-induced increases in connectivity. The degree k of the node/voxels in $G_{trn,\ pre\text{-}post}$ is superimposed on MNI T1 slices in order to map significant clusters of training-induced connectivity increases ($p < 0.05$).

during the task, which may influence the size of the reflex (Zehr, 2002). Indeed, the behavioural results indicate that there was less sway after the training on the slackline and thus a change in the H-reflex amplitude might have not necessarily reflected a change in spinal excitability but just an altered mechanical situation that goes along with an improved task-performance. In the present study we overcame such mechanical corruptions between pre and post measurements and additionally avoided impaired H-reflex measurements by proprioceptive input associated with the balancing task. Therefore, we can assume that the observed decrease in H-reflex amplitude indeed reflects training-induced functional neuroplasticity. We suggest that the task-specific H-reflex modulation was induced by a training-induced increase in presynaptic

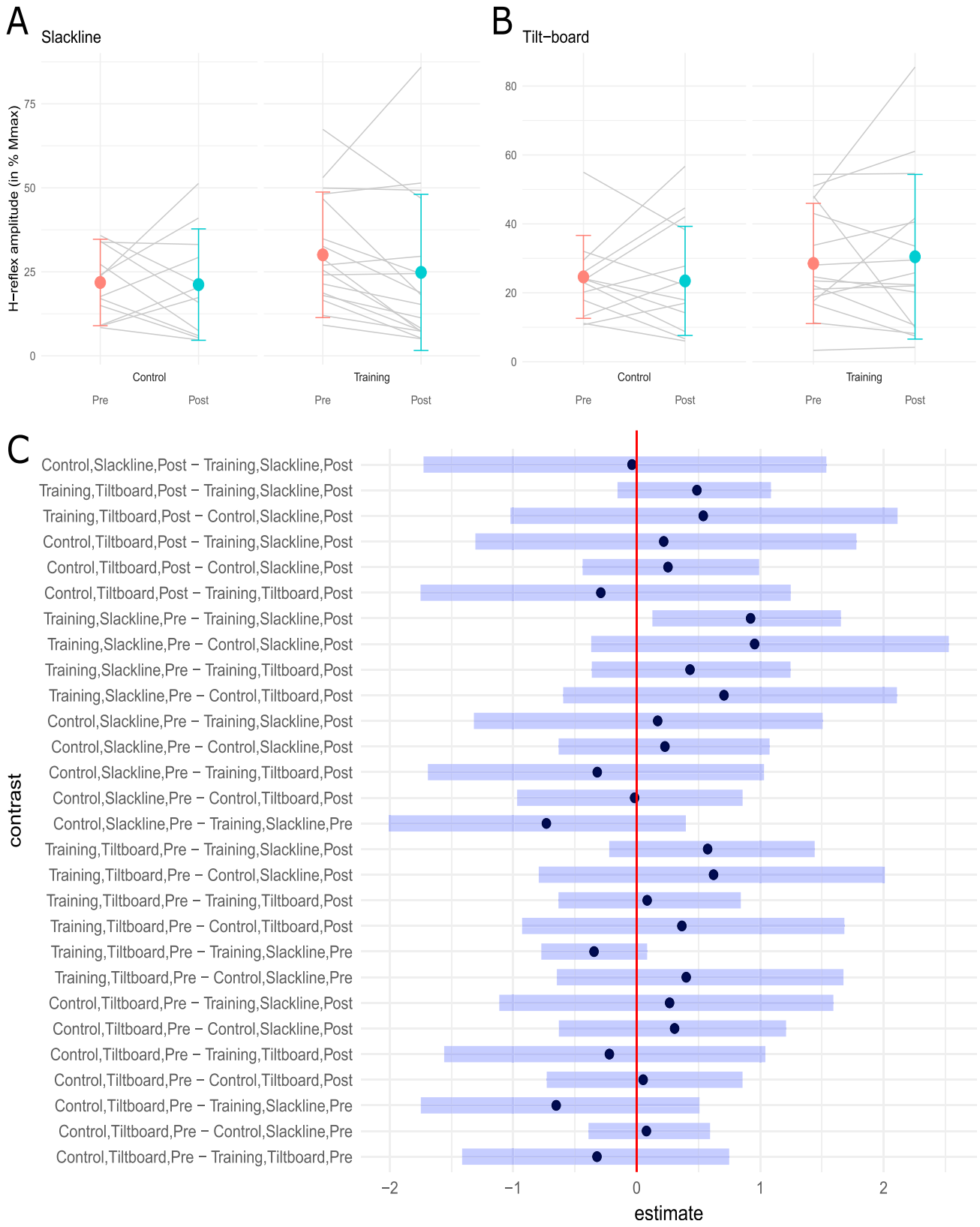

Fig. 5. H-reflex results. N = 30, 13 for the control group and 17 for the training group. More specifically, 12 for the control group and 17 for the training group for the tilt-board task, and 13 for the control group and 16 for the training group for the slackline task. A) and B) The large dots correspond to the mean H-reflex amplitudes normalized to Mmax while walking on the slackline (A) or the tilt-board (B) for the training and control group. The grey lines correspond to the mean individual variation in H-reflex amplitude pre- to post-training. Error bars represent standard deviations. C) Posterior contrasts by group, task and time. Points represent mean estimate and blue error bars represent the 95% credible interval.

inhibition. Indeed, presynaptic inhibition is exerted mainly via the descending control of spinal interneurons. This descending control seems to be pre-programmed according to the task to be performed (Pierrot--Deseilligny and Burke, 2012) and appears to be also reflected in the functional connectivity changes in cortical-subcortical motor control networks observed in the current study. It must be noted that there could be a difference of H-reflex amplitude pre-training between tasks in the training group (with a higher amplitude on the slackline task, see Fig. 5). It is known that a higher H-reflex amplitude (up to a certain level) is more sensitive to pre- and post-synaptic inhibition (Crone et al., 1990). Therefore, one could suggest that the absence of H-reflex reduction during the tilt-board task post-training in the training group could be due to a lower sensitivity to inhibition and not due to a task-specific modulation. This seems rather unlikely because the pre-training difference in H-reflex amplitude between tasks remained relatively small (around 3 point of normalized amplitude), and would therefore not mask entirely an inhibition effect.

The observation of functional plasticity, i.e. during the execution of the task, strongly suggests that the training-induced cerebral connectivity changes observed with fMRI also reflect to some extent functional neuronal adaptations. The increase of connectivity in the basal ganglia, which presumably indicates a higher automaticity of task execution (Aron and Poldrack, 2006; Ashby et al., 2010; Moors and De Houwer, 2006), is well in line with a reduction of the H-reflex that may reflect a decrease of proprioceptive feedback efficiency toward motoneurons at the onset of the task (reducing reflex responses), and thus the transition to a more feedforward task execution (Seidler et al., 2004). Indeed, during the learning process, the stereotyped reflex response may become detrimental to the performance of such a fine task that is to balance on a slackline. Reflexes could contaminate a much more optimized learned motor command, or even prevent fine learning adjustments. Therefore, in the training group, after the 6 weeks of training, the non-reduced H-reflex during the untrained task execution may indicate that the feedforward and feedback component proportion of the motor command is similar to the control group. This implies that the training induced neural changes leading to the better performance on the slackline are not used during the execution of untrained tasks. These results strongly support the concept that balance should be seen as a sum of specific skills and not as a general ability (Giboin et al., 2015). It should be noted, though, that the two tasks used in the present study were different in their degrees of freedom, which might partly explain why the skills learned during the training were not transferred to the untrained task. The present observation does not exclude that some balance skills (e.g. a particular hip strategy) can be shared across many different tasks. Actually, it has been shown that in the case of very similar tasks, such as walking on slacklines with different slack or width, trained balance skills were most probably shared (Giboin et al., 2018a). In addition, MRI based methods have the issue that subjects are lying in supine position while the H-reflex measurement here was performed in vertical position. Nevertheless, the balance performance generalization/transfer from a trained to an untrained task should not be expected. This is an important issue with regard to neuro-rehabilitation and training strategies aiming to reduce falls occurrence. In the absence of generalization, required or lost balance skills need to be trained specifically one by one.

There is currently a debate in regard to how and how much motor learning can generalize, see for examples (Krakauer et al., 2006; Rochet-Capellan et al., 2012). The present results lend support to the concept that motor learning generalizes poorly. However, it must be noted that most motor learning studies are conducted using upper body tasks, whereas balance training tasks are performed using the whole body and are possibly under less direct cortico-motoneuronal control than visuomotor hand reaching tasks. This implies that potentially different neural structures are recruited and that different neural processes are at work. Further, many studies focus primarily on motor adaptations (i.e. training and generalization testing in the same session) rather than longer term motor learning (i.e. as presently), where again, different neural structures could be involved (Doyon and Benali, 2005). The difference in the neural control structures could partly explain why the learning of certain types of tasks (e.g. visuomotor hand reaching tasks vs. balance tasks) at different stages of learning (e.g. short-term versus longer-term) generalize better than others.

In conclusion, only twelve training sessions of 45 min over six weeks on a slackline induced considerable neuroplasticity at brain and spinal level. This shows that the learning of such a complex balance task modulates the connectivity within a widespread neural network of cortical, subcortical and spinal regions that underlies performance improvements after balance training. Importantly, there was no performance transfer to an untrained balance task, strongly arguing for the specificity of the balance training-induced neural plasticity observed here.

Funding

This work was not supported by funding.

Acknowledgements

The authors have no direct or indirect conflicts of interest in the present work.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.neuroimage.2019.116061.

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