Can local vibration alter the contribution of persistent inward currents to human motoneuron firing ?

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Vibration-induced depression in spinal loop excitability revisited

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Key points

- While it has been well described that prolonged vibration locally applied to a muscle or its tendon (up to 1 h) decreases spinal loop excitability between homonymous Ia afferents and motoneurons, the involved mechanisms are not fully understood.
- By combining electrophysiological methods, this study aimed to provide new insights into the mechanisms involved in soleus decreased spinal excitability after prolonged local vibration.
- We report that prolonged vibration induces a decrease in motoneuron excitability rather than an increase in presynaptic mechanisms (as commonly hypothesized in the current literature).
- The present results may help to design appropriate clinical intervention and could reinforce the interest in vibration as a treatment for spastic patients who are characterized by spinal hyper-excitability responsible for spasms and long-lasting reflexes.

Abstract The mechanisms that can explain the decreased spinal loop excitability in response to prolonged local vibration (LV), as assessed by the H-reflex, remain to be precisely determined. This study provides new insights into how prolonged Achilles' tendon LV (30 min, 100 Hz) acutely interacts with the spinal circuitry. The roles of presynaptic inhibition exerted on Ia afferents (Experiment A, $n = 15$), neurotransmitter release at the synapse level (Experiment B, $n = 11$) and motoneuron excitability (Experiment C, $n = 11$) were investigated in soleus. Modulation of presynaptic inhibition was assessed by conditioning the soleus H-reflex (tibial nerve electrical stimulation) with fibular nerve (D1 inhibition) and femoral nerve (heteronymous facilitation, HF) electrical stimulations. Potential vibration-induced changes in neurotransmitter depletion at the Ia afferent terminals was assessed through paired stimulations applied over the tibial nerve (HD). Intrinsic motoneuron excitability was assessed with thoracic motor evoked potentials (TMEPs) in response to electrical stimulation over the thoracic spine. Non-conditioned H-reflex

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was depressed by ∼60% after LV ($P < 0.001$), while D1 and HF H-reflexes increased by ∼75% after LV ($P = 0.03$ and 0.06, respectively). In Experiment B, HD remained unchanged after LV ($P = 0.80$). In Experiment C, TMEPs were reduced by ∼13% after LV ($P = 0.01$). Overall, presynaptic mechanisms do not seem to be involved in the depression of spinal excitability after LV. It rather seems to rely, at least in part, on a decrease in intrinsic motoneuron excitability. These results may have implications in reducing spinal hyper-excitability in spastic patients.

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Introduction

Vibration is a powerful stimulus to activate Ia afferents originating from muscle spindles (Burke, 1980). When applied locally to a relaxed muscle or its tendon, the so-called local vibration (LV) increases muscle spindle discharge projecting onto α-motoneurons and concomitantly decreases the monosynaptic reflexes, a mechanism known as the vibration paradox (Desmedt & Godaux, 1978). Interestingly, when applied for a prolonged (20–60 min) duration, LV also acutely decreases spinal loop excitability after the cessation of the vibration, as assessed by the Hoffmann (H)-reflex (e.g. Ushiyama *et al.* 2005; Fry & Folland, 2014; Farabet *et al.* 2016). Because of repetitive activation of Ia afferents during LV (Burke, 1980), the main mechanism involved has been postulated to be due to an attenuation of Ia afferent inputs onto spinal motoneurons (Bongiovanni *et al.* 1990). Since the H-reflex is evoked by electrical stimulation of a nerve trunk, the LV-induced decreased H-reflex could be explained by an increased firing threshold of Ia afferent axons (Hayward *et al.* 1986). However, this hypothesis is not supported by findings of unchanged current required to elicit maximal H-reflex amplitude after LV (Fry & Folland, 2014). Another possibility is the neurotransmitter depletion at the Ia afferent terminals, i.e. homosynaptic post-activation depression (HD), due to repetitive Ia afferent activation by vibrations (Curtis & Eccles, 1960). HD can be tested by assessing the amplitude of the depression in H-reflex evoked immediately after a conditioning one (Rothwell *et al.* 1986). Finally, Ia afferent inputs onto motoneurons may decrease as a result of increased presynaptic inhibition (Hultborn *et al.* 1987*a*,*b*) through activation of GABAergic primary afferent depolarization (PAD) interneurons (Rudomin & Schmidt, 1999). Its contribution to depressed soleus (SOL) H-reflexes after LV has been proposed as the main mechanism although it has never been directly investigated. To do so, H-reflex conditioning techniques can be employed, i.e. D1 inhibition (Mizuno *et al.* 1971) and heteronymous Ia facilitation (HF) (Hultborn *et al.* 1987*a*). In addition to presynaptic inhibition, H-reflex amplitude also depends on intrinsic motoneuron excitability (Schieppati, 1987). To date, the most direct method to test motoneuron excitability to synaptic inputs is to electrically stimulate the descending spinal tracts (i.e. below the motor cortex) at the mastoid (cervicomedullary motor evoked potential, CMEP) or thoracic (α-motoneuron, TMEP) levels, being a more reliable approach than F-wave (McNeil *et al.* 2013).

The exact mechanisms by which LV depresses the H-reflex remain to be precisely determined. To date, the aforementioned mechanisms have been only partially investigated for SOL (HD, Ekblom & Thorstensson, 2011; presynaptic inhibition, Lapole *et al.* 2012*b*), knee extensors (Ia firing threshold, Fry & Folland, 2014; motoneuron excitability through TMEPs, Souron *et al.* 2017*a*) and first dorsal interosseous (motoneuron excitability through F-waves, Christova *et al.* 2011) muscles. Besides the fact that no study concomitantly investigated these mechanisms, the heterogeneity in the tested muscles, experimental procedures and LV characteristics among these studies prevent a full comprehension of the mechanisms involved in the spinal loop depression after the cessation of LV (LV post-effect).

The aim of this study was therefore to provide new insights into the mechanisms involved in LV post-effect in SOL spinal excitability after prolonged LV, with the aim to better understand previous findings about acute spinal alterations in response to Achilles' tendon LV (Lapole *et al.* 2012*a*,*b*). A better definition of how LV acutely interacts with the spinal circuitry is crucial in order to optimize its effects, especially when LV is used to trigger long-term adaptations leading to improved motor performance (for review, see Souron *et al.* 2017*b*). The main strength of the present work was to concomitantly investigate, in the same muscle, the role of PAD interneuron functioning (i.e. D1 inhibition and HF), neurotransmitter release at the synapse level (i.e. HD) and motoneuron excitability (i.e. TMEPs).

Methods

Ethical approval

Each of the participants was informed about the possible risks and discomfort, and gave written consent to participate. This study conformed to standards from the

latest revision of the *Declaration of Helsinki* (except for registration in a database) and was approved by the local research ethics committees (CPP Sud Est I NCT02668224).

Study design

Three separate experiments were performed to investigate the effects of a 30 min prolonged LV exposure to the Achilles' tendon on SOL presynaptic inhibition (Experiment A; $n = 15$), HD (Experiment B; $n = 11$) and motoneuron excitability (Experiment C; $n = 11$). A flowchart of the experimental design is displayed in Fig. 1 to show how subjects were recruited depending on the experiment. Subjects were different for each experiment except for six subjects who participated in both Experiments A and C. It should be noted that Experiments A and C were performed in one laboratory, and Experiment B in another. None of the subjects had acute or chronic neurological disorders and trauma. Subjects were asked to refrain, for 24 h before testing, from strenuous and unaccustomed physical activity to avoid confounding factors associated with muscle fatigue or damage. In each experiment, neurophysiological parameters were recorded before (PRE) and immediately after (POST) LV on the right leg. All the POST measurements were performed within 3 min after the end of LV. This allowed us to ensure that spinal excitability was effectively decreased for all our measurements since ∼20 min are necessary for a complete recovery (Ushiyama *et al.* 2005).

Experimental design

Experiment A: presynaptic inhibition. Fifteen subjects (5 females; age: 23 ± 3 years; height: 175 ± 8 cm; weight: 68 ± 13 kg) participated in this experiment. LV post-effect on SOL Ia presynaptic inhibition was investigated by comparing results from two conditioning methods of the H-reflex. The D1 inhibition method (Mizuno *et al.* 1971) consists of activating PAD interneurons acting on SOL Ia afferent terminals by a conditioning stimulation applied to the fibular nerve (Fig. 2*A*). An increased level of presynaptic inhibition due to LV should lead to greater responsiveness of PAD interneurons to the conditioning stimulation, reducing the amplitude of the conditioned H-reflex when compared to the non-conditioned reflex (test reflex). The heteronymous Ia facilitation (HF) method assesses the monosynaptic facilitatory effect of a femoral nerve stimulation on the SOL H-reflex amplitude (Fig. 2*B*) (Hultborn *et al.* 1987*a*). An increase in presynaptic inhibition through PAD interneurons converging on femoral Ia afferents should decrease the strength of the excitatory inputs

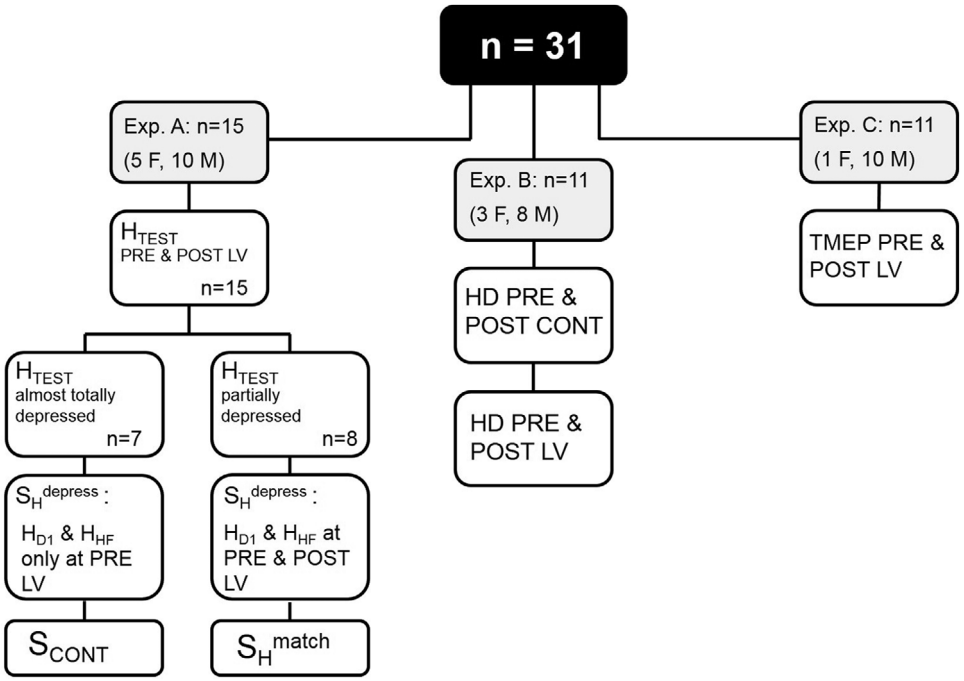

Figure 1. Flow diagram representing experimental design
Note that 6 subjects participated in both Experiment A and C. CONT: control; F: female; HD: homosynaptic post-activation depression; H_{D1}: conditioned H-reflex by a fibular nerve stimulation; H_{HF}: conditioned H-reflex by a femoral nerve stimulation; H_{TEST}: non-conditioned H-reflex; LV: local vibration; M: male; S_{CONT}: control session of Experiment A; $S_H^{depress}$: session with POST measurements performed on a depressed H-reflex; S_H^{match}: session with POST measurements performed with an H-reflex amplitude being the same as PRE; TMEP: thoracic motor evoked potential.

from femoral Ia afferents on SOL motoneurons, and thereby depresses the conditioned H-reflex amplitude. It is recommended that these two methods are combined to avoid the possible drawback associated with changes in the recruitment gain of the reflex (Crone *et al.* 1990) and a possible occlusion at the PAD interneuron level in the D1 method (Baudry & Duchateau, 2012). The experimental procedures for Experiment A are displayed in Fig. 3*A*. As the size of the unconditioned H-reflex may influence its sensitivity to excitatory and inhibitory inputs (Johannsson *et al.* 2015), our experimental protocol included two sessions: $1/S_H^{depress}$, where POST measurements were performed on a depressed H-reflex, and $2/S_H^{match}$, where POST measurements were performed with an H-reflex amplitude being the same as PRE (see below for further explanations).

$S_H^{depress}$ was dedicated to the investigation of the effects of LV on Ia afferent presynaptic inhibition without consideration of the LV-induced depression in the non-conditioned H-reflex. The recruitment curves for SOL H-reflex and M-wave were first determined at rest by incrementally increasing the stimulus intensity by steps of 0.5–1.0 mA, with five stimulations delivered for each step and an interstimulus delay of 5–10 s (Burke *et al.* 1989). Using the recruitment curves, we then determined (i) the stimulus intensity required to obtain an H-reflex with an amplitude of 50% of its maximal amplitude, and (ii) the stimulus intensity associated with the maximal M-wave (M_{MAX}). The latter was then increased by 30% to confirm supramaximality. Ten non-conditioned H-reflexes (H_{TEST}) and three M_{MAX} were recorded on the relaxed SOL PRE and POST LV (Fig. 3*A*), with H_{TEST} peak-to-peak amplitude being expressed as a percentage of the mean M_{MAX} amplitude. The intensity of electrical tibial nerve stimulation to evoke H_{TEST} was kept constant between PRE and POST and the amplitude of the M-wave preceding H_{TEST} was recorded (and expressed relative to M_{MAX}) to ensure that the effective stimulation remained the same after LV. Then, POST measurements of presynaptic inhibition were performed with a depressed H_{TEST}. Note that seven subjects exhibited an almost total suppression of the H_{TEST} after LV (i.e. depression of more than 95% of the H_{TEST} obtained at PRE; see the Results section) and it was not possible for them to perform D1 and HF at POST LV.

Regarding the D1 method, we first determined the intensity of the conditioning fibular nerve stimulation set at 130% of the tibialis anterior motor threshold, i.e. the lowest intensity that evoked at least three M-waves out of five stimulations (mean M-waves were 0.68 ± 0.36 mV and 0.59 ± 0.33 mV for $S_H^{depress}$ and S_H^{match} sessions, respectively). Then the SOL H-reflex (using the stimulation intensity determined for H_{TEST}) was conditioned by a prior stimulation of the fibular nerve (Mizuno *et al.* 1971; Hultborn *et al.* 1987*b*) with an interstimulus interval of 20 ms, reported as the most effective delay to ensure a large inhibitory effect on the conditioned H-reflex (Grospretre *et al.* 2018). Ten

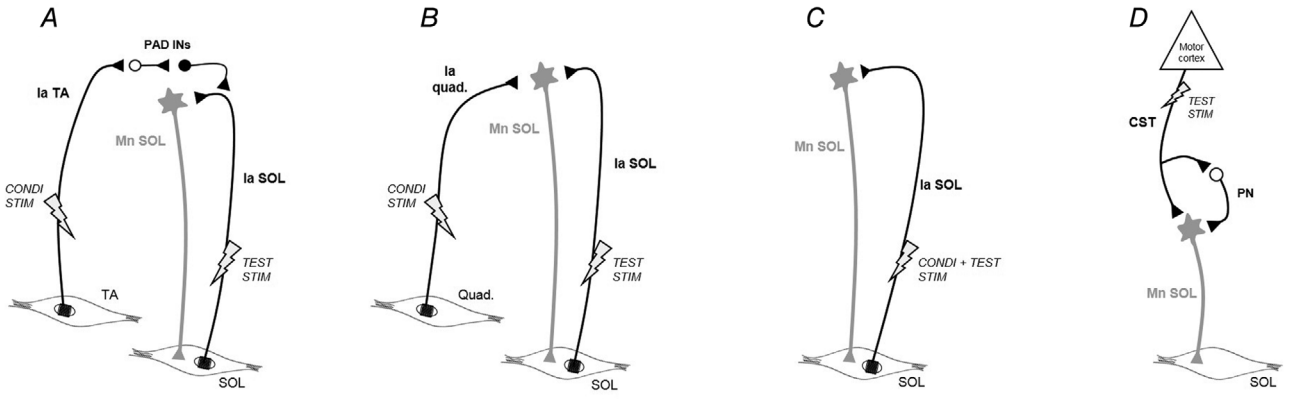

Figure 2. Schematic representation of the pathways involved in the recorded responses
A, schematic representation of the pathways involved in D1 inhibition. A conditioning stimulus applied to the fibular nerve (CONDI STIM) activates primary afferent depolarization interneurons (PAD INs) acting on soleus Ia afferents (Ia SOL), reducing the amplitude of the conditioned H-reflex (H_{D1}). *B*, schematic representation of the pathways involved in heteronymous facilitation. A conditioning stimulus applied to the femoral nerve (CONDI STIM) facilitates the amplitude of the conditioned H-reflex (H_{HF}) through a monosynaptic connection between the Ia afferents of the quadriceps (Ia quad) and the motoneuron pool of the soleus muscle (Mn SOL). *C*, schematic representation of the pathway involved in homosynaptic post-activation depression. The repetitive activation of Ia–α-motoneuron synapse through paired stimuli (CONDI STIM then TEST STIM) depresses the amplitude of the conditioned H-reflex under the influence of neurotransmitter depletion. *D*, schematic representation of the pathway involved in the recording of the TMEPs. The electrical stimulation over the thoracic spine (TEST STIM) evokes a single volley in the corticospinal tract (CST) that activates the α-motoneuron through oligosynaptic connections involving propriospinal neurons (PN).

conditioned H-reflexes (H_{D1}) were recorded at 5–10 s intervals for PRE and POST measurements (Fig. 3*A*). Mean H_{D1} peak-to-peak amplitude was expressed as a percentage of the corresponding H_{TEST} amplitude.

For the HF method (Fig. 2*B*), we first determined the intensity of the conditioning femoral nerve stimulation that was set at 130% of the vastus lateralis motor threshold. Contrary to D1, the femoral (i.e. conditioning) stimulation was delivered after the tibial nerve stimulation because of the shorter neural pathway of the heteronymous femoral Ia afferent pathway compared with the homonymous Ia afferent pathway (Johannsson *et al.* 2015). Such conditioning stimulation should facilitate the SOL H-reflex because of heteronymous excitatory Ia afferent projections. We determined the onset of H-reflex facilitation by changing the delay between the test (i.e. tibial nerve) and conditioning (i.e. femoral nerve) stimulations by 1 ms steps from –9 ms to –1 ms (Baudry & Enoka, 2009; Johannsson *et al.* 2015). Assessing the onset of the facilitation is mandatory to reduce the contamination of the monosynaptic heteronymous facilitation by polysynaptic excitatory inputs (Baudry & Enoka, 2009). Five trials were then performed for each interstimulus interval and the optimal interval was determined as the one that induced the greatest facilitation in SOL H-reflex relative to the unconditioned H-reflex previously obtained (H_{TEST}). The onset of facilitation was defined as the delay inducing the greatest conditioned H-reflex. Ten conditioned H-reflexes (H_{HF}) were recorded at 5–10 s intervals for PRE and POST measurements (Fig. 3*A*). Mean H_{HF} peak-to-peak amplitude was expressed as a percentage of the corresponding H_{TEST} amplitude.

As previously mentioned, presynaptic inhibition was investigated in this first testing session by keeping the same effective stimulation intensity of the tibial nerve for PRE and POST measurements. Then, because of the LV-induced depression in H-reflex amplitude, we

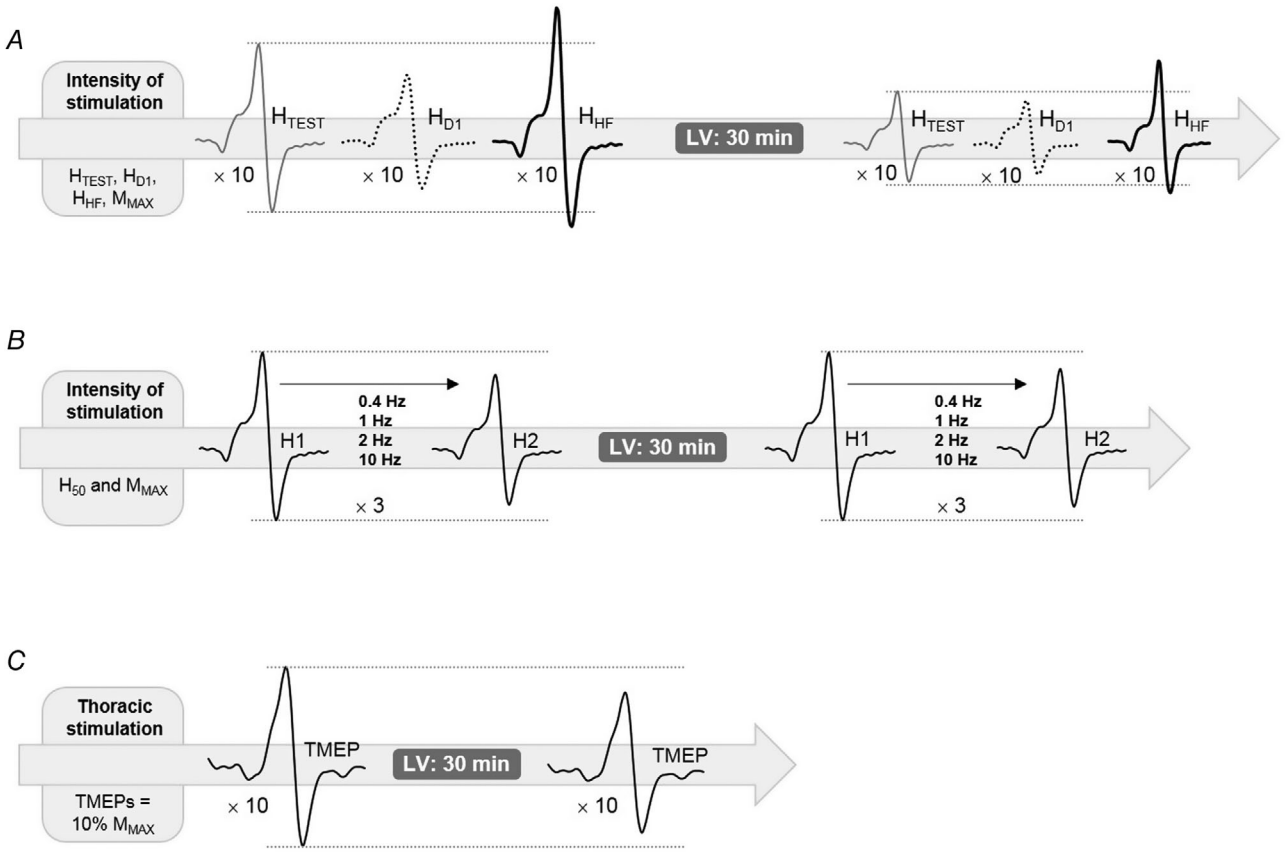

Figure 3. Schematic representation of the experimental procedures for Experiments A, B and C
A, non-conditioned (H_{TEST}) and conditioned (H_{D1} and H_{HF} conditioned by stimulation of fibular and femoral nerves, respectively) soleus (SOL) H-reflexes. Three different sessions were performed, i.e. $S_H^{depress}$ (POST measurements performed on a depressed H-reflex), S_H^{match} (POST measurements performed with an H-reflex amplitude being the same as PRE) and S_{CONT} (control session). *B*, non-conditioned (H_1) and conditioned (H_2) SOL H-reflexes were evoked by tibial nerve stimulations using various frequencies, i.e. 0.4, 1, 2 and 10 Hz. *C*, SOL motoneuron excitability tested by recording thoracic motor evoked potentials (TMEPs) during a submaximal voluntary contraction at 30% MVC. All tests were performed before and after a 30 min local vibration (LV) period.

cannot ascertain that our results concerning presynaptic inhibition were not biased by decreased H_{TEST} amplitude in the eight tested subjects for POST measurements (Crone *et al.* 1990). To address this potential drawback, these eight subjects (4 females; age: 23 ± 2 years) participated in S_H^{match} during which the intensity of stimulation to evoke H_{TEST} was set up at POST to match the amplitude of the H_{TEST} obtained at PRE for same session.

The remaining seven subjects (1 woman; age: 24 ± 4 years) for whom we were not able to perform POST measurements for presynaptic inhibition were retested in a control session (no LV; S_{CONT}) to investigate the intra-session reliability of H_{TEST}, H_{D1} and H_{HF}, and to ensure that the prolonged sitting period imposed on the subjects did not affect H-reflex measurements.

Experiment B: homosynaptic post-activation depression. HD (Fig. 2*C*) was investigated in 11 subjects (3 females; age: 24 ± 4 years; height: 172 ± 13 cm; weight: 74 ± 15 kg) in two separate, randomly assigned, sessions, i.e. control (no LV) and LV. The input–output relations of the H-reflex and M-wave (the amplitude of the evoked potentials plotted against the stimulus intensity) were first determined by progressively increasing the stimulus intensity in steps of 0.5–1.0 mA (5 stimulations per step) until the M-wave amplitude reached a plateau (M_{MAX}). Thereafter, the stimulus intensity required to obtain an H-reflex with an amplitude of ∼50% of its maximal amplitude and the intensity associated with M_{MAX} (the latter one being increased by 30%) was determined. This intensity was adjusted after LV to obtain similar H-reflex amplitudes before and after LV. Thereafter, paired-stimuli with interstimulus intervals of 2.5 (0.4 Hz), 1 (1 Hz), 0.5 (2 Hz) and 0.1 s (10 Hz) were delivered in a counterbalanced order to assess HD while subjects remained relaxed (Fig. 3*B*). These interstimulus intervals were used to provide a more comprehensive understanding of the effects of LV on HD as the magnitude of HD is known to increase when the interstimulus interval is shortened (Stein *et al.* 2007), the HD underlying mechanisms possibly differing between long and short interstimulus intervals (Honig *et al.* 1983). Three pairs of stimuli for each interstimulus interval were delivered at least 10 s apart before and after LV. The peak-to-peak amplitudes of the two H-reflexes were measured from the unrectified EMG signal and normalized to the M_{MAX} amplitude, and the amplitude of the second reflex response (H_2) was expressed as a percentage of the amplitude of the first reflex response (H_1) within the same pair (H_2/H_1). Average values of the three pairs of stimuli recorded for each interstimulus interval were considered for further analysis.

Experiment C: motoneuron excitability. Motoneuron excitability was investigated in 11 subjects (1 woman; age: 26 ± 6 years; height: 178 ± 9 cm; weight: 77 ± 13 kg) using electrical stimulation of the descending corticospinal tract at the thoracic spine level to record thoracic motor evoked potentials (TMEPs) (McNeil *et al.* 2013). Thoracic rather than mastoid (i.e. CMEP) stimulations were used in this experiment since mastoid stimulations may be limited to informing about changes in lower limb muscles due to difficulties in evoking discernible responses (Ugawa *et al.* 1991, 1995). Thoracic stimulation is considered a more appropriate tool to examine motoneuron excitability changes in lower limbs (Martin *et al.* 2008). As such, this method provides the most direct assessment of the motoneuron pool's responsiveness to synaptic input because (i) a large proportion of the response is monosynaptic (Martin *et al.* 2008) and (ii) descending tracts are not influenced by presynaptic inhibition (Nielsen & Petersen, 1994). Motoneuron excitability was only investigated PRE and POST LV, i.e. no control condition was included to minimize the use of potentially painful stimuli (Martin *et al.* 2008).

In contrast with the first two experiments where H-reflexes were recorded at rest, TMEPs were recorded during submaximal voluntary plantarflexion at 30% maximal voluntary contraction (MVC; calibrated instrumented pedal; CS1060 300 Nm, FGP Sensors, Les Clayes Sous Bois, France) because it was not possible to evoke TMEPs in resting SOL for most of the subjects during pilot experiments. POST LV measurements were performed at the same absolute force as for PRE measurements.

After the determination at rest of the stimulus intensity associated with the maximal M-wave (M_{MAX}) by incrementally increasing stimulus intensity by steps of 10 mA at an interstimulus delay of 5–10 s, this intensity was further increased by 30% to ensure supramaximality. Three M_{MAX} were recorded during contraction for PRE and POST measurements. The intensity of stimulation of the corticospinal tract was determined by increasing intensity by steps of 50 mA until TMEPs amplitude was approximately 10% of the M_{MAX} obtained during contraction. When the optimal intensity was set, 10 TMEPs were recorded with an interstimulus delay of 5–10 s. The same stimulation intensity was used for PRE and POST measurements. TMEP peak-to-peak amplitudes were averaged PRE and POST LV and expressed as a percentage of the corresponding M_{MAX} amplitude. SOL root mean square (RMS) EMG was calculated over a 500 ms period before thoracic electrical stimulation and expressed as a percentage of M_{MAX} to give information on muscle activation at the time of stimulation. This ensured that TMEPs were recorded at the same level of muscle activation for PRE and POST measurements. The experimental design for Experiment C is displayed in Fig. 3*C*.

EMG recording

Experiments A and C. In Experiment A, electromyogram (EMG) was recorded from soleus (SOL), tibialis anterior (TA) and vastus lateralis (VL) muscles with pairs of self-adhesive surface electrodes (Meditrace 100; Covidien, Mansfield, MA, USA) in bipolar configuration with a 30 mm inter-electrode distance. SOL electrodes were placed 2 cm below the muscle–tendon junction of the gastrocnemii. TA electrodes were placed on the muscle belly parallel to the longitudinal axis of the muscle at one-third of the distance between the head of the fibula and the tip of the medial malleolus. VL electrodes were placed at a position two-thirds along the line from the anterior spina iliaca superior to the lateral side of the patella. The earth electrode was positioned on the patella. Low impedance (<5 kΩ) between electrodes was obtained by shaving and gently abrading the skin and then cleaning it with isopropyl alcohol. In Experiment C, the electrodes were only positioned on the SOL. Signals were amplified ($\times$5000) with an octal bio-amplifier (ML138, ADInstruments, Bella Vista, Australia), band-pass filtered (5–500 Hz) and analog-to-digitally converted at a sampling rate of 2000 Hz by a PowerLab System (16/30, ADInstruments). All data were analysed off-line with Labchart 8 software (ADInstruments).

Experiment B. The EMG signal was recorded from SOL with surface electrodes (silver–silver chloride electrodes, 8 mm diameter, 20 mm inter-electrode distance) placed after skin preparation. The electrodes were filled with gel and held on the skin by means of adhesive tape. Electrode positions were similar to those described above. The EMG signals were amplified ($\times$1000) and band-pass filtered (10–1000 Hz) prior to analog-to-digital sampling at 2 kHz (Power 1401, 16-bit resolution, Cambridge Electronic Design, Cambridge, UK) and then stored on a computer for further analysis. All data were analysed off-line with Spike 2 software (Cambridge Electronic Design).

Local vibration

In all experiments, LV was applied on the right Achilles' tendon for 30 min using a mechanical vibrator (VB 115, Techno Concept, Mane, France). LV was applied while the subjects were relaxed in a seated position, with knee and ankle angles of 120 and 90°, respectively. According to previous studies reporting that Ia afferents discharge synchronously with vibration frequencies up to 80–120 Hz (Roll & Vedel, 1982; Roll *et al.* 1989) and are sensitive to small vibration amplitude (Roll *et al.* 1989), a 100 Hz frequency and a 1 mm amplitude were used in this study, in line with our previous studies investigating the acute effects of prolonged LV (Farabet *et al.* 2016; Souron *et al.* 2017*a*).

Electrical stimulation

Experiment A. Electrical stimuli with maximal 400 V output voltage were applied to the tibial (1 ms duration) as well as the fibular and femoral (0.2 ms duration) nerves via constant current stimulators (DS7A and DS7AH, Digitimer, Welwyn Garden City, UK). For the tibial nerve, a bipolar bar stimulating electrode with 30 mm anode–cathode spacing (Bipolar Felt Pad Stimulating Electrode Part number E.SB020/4 mm, Digitimer) was placed at the level of the popliteal fossa (Schieppati, 1987). The optimal stimulation site was defined as the site that elicited the larger H-reflex in the SOL with no concomitant response in TA (Johannsson *et al.* 2015). The fibular nerve (D1 inhibition; see below) was stimulated with the cathode (Meditrace 100) placed next to the fibular head and the anode (Durastick Plus; DJO Global, Vista, CA, USA) near the medial part of the tibia. The optimal stimulation site was defined as the site eliciting the greatest M-wave in TA for a given stimulus intensity. We further ensured that the stimulation maximized the activation of the TA with no activation of peroneal muscles (verified by palpation). The femoral nerve (HF; see below) was stimulated with the cathode (Meditrace 100) placed over the femoral triangle and the anode (Durastick Plus) positioned in the gluteal fold. The optimal location was defined as the site eliciting the greatest M-wave in VL for a given stimulus intensity.

Experiment B. Electrical stimuli (1 ms duration) applied to the tibial nerve were delivered via a constant current stimulator (DS7A, Digitimer) that was connected to two surface electrodes (silver–silver chloride electrodes of 8 mm diameter) attached to the skin at knee level of the right leg with adhesive tape. The cathode was placed in the popliteal fossa and the anode located just above the patella. The optimal site of stimulation was determined by moving a pen electrode (cathode) until the site eliciting the largest H-reflex amplitude in the SOL at a given intensity was identified.

Experiment C. Surface electrodes were placed between the spinous processes of T3 and T4 (cathode) and 5–10 cm above (anode) (Ugawa *et al.* 1991) using a constant-current stimulator (DS7AH; Digitmer) with 0.2 ms duration and 400 V maximal output voltage.

Statistical analysis

Statistical analyses were performed with Statistica software (StatSoft Inc., Tulsa, OK, USA). All descriptive statistics presented in the text, tables and figures are mean values $\pm$SD. Data normality was verified using the Shapiro–Wilk normality test. Student's paired t tests were used to compare PRE and POST measurements for all the recorded

Table 1. Reliability for spinal excitability and presynaptic inhibition-related parameters obtained in 7 subjects (S_{CONT})

	Mean ± SD		Intra-session		
	PRE	POST	CV	ICC	SEM
H_{TEST} (% M_{MAX})	22.1 ± 9.2	21.7 ± 9.9	4.5 ± 4.9	0.98	1.2
H_{D1} (% H_{TEST})	35.3 ± 20.6	40.7 ± 15.3	17.4 ± 18.3	0.94	4.4
H_{HF} (% H_{TEST})	109.3 ± 17.7	110.4 ± 16.1	4.2 ± 5.1	0.83	6.8
M_{MAX} (mV)	13.4 ± 2.2	13.6 ± 2.1	1.8 ± 0.8	0.98	0.3

Absolute data and CV are expressed as mean ± standard deviation. H_{TEST}: non-conditioned H-reflex; H_{D1}: SOL H-reflex conditioned by a stimulation of the fibular nerve; H_{HF}: SOL H-reflex conditioned by a stimulation of the femoral nerve; M_{MAX}: maximal M-wave recorded at rest; CV: coefficient of variation; ICC: intraclass correlation coefficient; SEM: standard error of the mean.

parameters, as well as to analyse the effect of conditioning the H-reflex in Experiment A. Intra-session reliability for H_{TEST}, D1 and HF in Experiment A was assessed using the intra-class correlation coefficient (ICC, with a two-way mixed-effects model based on single rater), standard error of the mean (SEM) and coefficient of variation (CV), as recommended by Hopkins (2000). The influence of LV on HD was assessed by three-way ANOVAs (session × time × interstimulus interval) with repeated measures design. For the paired *t* tests, the effect size (i.e. Cohen's *d*) was determined by calculating the mean difference between PRE and POST measurements, then dividing it by the pooled standard deviation. Values of $d = 0.2$, 0.5 and 0.8 should be interpreted as small, medium and large effects, respectively (Cohen, 1988). Eta squared (η^2) was calculated for significant ANOVAs as an estimate of effect size with small ($\eta^2 = 0.1$), medium ($\eta^2 = 0.25$), and large ($\eta^2 = 0.40$) effects. Statistical significance was set at $P < 0.05$.

Results

Experiment A: presynaptic inhibition

Reliability. The main values and intra-session reliability outcomes (i.e. CV, ICC and SEM) of H_{TEST}, H_{D1}, H_{HF} and M_{MAX} are presented in Table 1. Statistical *t* test analysis did not identify any significant variation between PRE and POST measurements for the 30 min resting period, nor for the H_{TEST} ($t_{(6)} = 0.54$; $P = 0.60$, $d = 0.04$), H_{D1} ($t_{(6)} = 2.11$; $P = 0.18$, $d = 0.29$) or H_{HF} ($t_{(6)} = 0.32$; $P = 0.75$, $d = 0.06$).

H_{TEST}.

$S_H{}^{depress}$. H_{TEST} was significantly reduced at POST (−77.2 ± 25.7%; $t_{(14)} = 9.49$, $P < 0.001$, $d = 2.38$). Seven out of the 15 subjects that participated in $S_H{}^{depress}$ presented a quasi-total extinction of H_{TEST} (−97.0 ± 1.4%; $t_{(6)} = 10.03$, $P < 0.001$, $d = 5.26$), while the remaining eight subjects presented a lower depression of H_{TEST} (−59.8 ± 24.0%; $t_{(7)} = 5.76$, $P < 0.001$, $d = 1.73$; Fig. 4*A*). There were no changes in the small M-wave amplitude that preceded H_{TEST} between PRE and POST measurements (2.5 ± 1.8% M_{MAX} *vs.* 2.9 ± 2.3% for PRE and POST, respectively; $t_{(14)} = 1.23$, $P = 0.23$, $d = 0.14$). Similarly, no changes were reported in M_{MAX} between PRE and POST measurements (10.6 ± 3.5 *vs.* 10.1 ± 3.8 mV for PRE and POST, respectively; $t_{(14)} = 1.71$, $P = 0.62$, $d = 0.18$).

$S_H{}^{match}$. For the eight tested subjects, no differences were reported for H_{TEST} between PRE (17.0 ± 8.0% M_{MAX}) and POST (18.0 ± 8.2% M_{MAX}) measurements ($t_{(7)} = 3.17$; $P = 0.40$, $d = 0.99$; Fig. 4*B*). No changes were reported in M_{MAX} between PRE and POST measurements (10.6 ± 3.3 *vs.* 10.2 ± 3.4 mV for PRE and POST, respectively; $t_{(7)} = 1.24$, $P = 0.81$, $d = 0.24$).

D1 inhibition (H_{D1}).

$S_H{}^{depress}$. At baseline, the conditioning stimulation over the peroneal nerve induced a significant inhibition in conditioned H_{D1} when compared with unconditioned H_{TEST} for the whole sample of subjects (39 ± 20% of H_{TEST}; $t_{(14)} = 9.21$, $P < 0.001$, $d = 1.99$). For the eight subjects for which the conditioned H_{D1} was recorded after LV, H_{D1} amplitude recorded at POST (74.8 ± 32.3%) was significantly increased when compared to PRE (47.5 ± 21.2%) (+73.1 ± 80.7%; $t_{(7)} = 2.54$; $P = 0.03$, $d = 0.99$; Fig. 4*A*). There were no changes in the small M-wave amplitude that preceded H_{D1} between PRE and POST measurements (2.4 ± 1.8% M_{MAX} *vs.* 2.5 ± 1.3% for PRE and POST, respectively; $t_{(7)} = 0.26$, $P = 0.79$, $d = 0.06$).

$S_H{}^{match}$. When compared with PRE (44.5 ± 78.6%), the amplitude of the conditioned H_{D1} recorded after LV (78.6 ± 16.8%) was significantly increased by 97.2 ± 80.6% ($n = 8$; $t_{(7)} = 5.75$, $P < 0.001$, $d = 2.14$; Fig. 4*B*).

Heteronymous facilitation (H_{HF}).

$S_H{}^{depress}$. Interval stimulation was −7.9 ± 1.0 ms. At baseline, the conditioned H_{HF} was significantly facilitated by the conditioning femoral nerve stimulation when

compared with unconditioned H_{TEST} ($n = 15$; 123 ± 34% of H_{TEST}; $t_{(14)} = 2.80$, $P = 0.01$, $d = 0.66$). For the eight subjects where the conditioned H_{HF} was recorded after LV, H_{HF} amplitude recorded after the LV period (218.4 ± 115.9%) tended to increase when compared to baseline values (129.2 ± 44.7%) (+75.2 ± 89.4%; $t_{(7)} = 2.54$; $P = 0.06$, $d = 0.01$; Fig. 4*A*). There were no changes in the small M-wave that preceded H_{HF} between PRE and POST measurements (2.4 ± 1.6% M_{MAX} *vs.* 2.5 ± 1.1% for PRE and POST, respectively; $t_{(7)} = 0.10$, $P = 0.92$, $d = 0.08$).

S_H^{match}. Interval stimulation was −7.6 ± 0.7 ms. At baseline, the conditioned H_{HF} was not significantly facilitated by the conditioning femoral nerve stimulation when compared with unconditioned H_{TEST} ($n = 8$; 120 ± 32% of H_{TEST}; $t_{(7)} = 1.34$, $P = 0.22$, $d = 0.33$). When compared with PRE, the amplitude of the conditioned H_{HF} recorded after the LV period (178.7 ± 51.7%) was significantly increased ($n = 8$; +49.7 ± 29.6%; $t_{(7)} = 4.60$; $P = 0.002$, $d = 1.35$; Fig. 4*B*).

Experiment B: homosynaptic post-activation depression

At baseline, the amplitude of the test H-reflex (H_1) was 39.3 ± 4.3% and 38.8 ± 4.3% M_{MAX} in the LV and control sessions, respectively. At POST, H_1 amplitude was similar to the values obtained at PRE for both LV (41.9 ± 4.4% M_{MAX}) and control (42.3 ± 4.4% M_{MAX}) sessions. The H_2/H_1 ratio decreased significantly with the decrease in the interstimulus interval ($P < 0.001$; $\eta = 4.3$; Fig. 5). However, there was no session ($P = 0.96$), time ($P = 0.17$), nor session × time interaction effect ($P = 0.80$) (Fig. 5). No changes were reported in the amplitude of M_{MAX} at PRE and POST measurements for both the LV (7.7 ± 1.1 and 7.4 ± 1.2 mV for PRE and POST measurements, respectively) and control (8.6 ± 1.1 and 7.8 ± 1.2 mV, respectively) sessions.

Experiment C: motoneuron excitability

No changes were reported in M_{MAX} between PRE and POST measurements (12.1 ± 3.9 *vs.* 11.7 ± 4.2 mV for PRE and POST, respectively; $t_{(10)} = 1.71$, $P = 0.52$, $d = 0.66$).

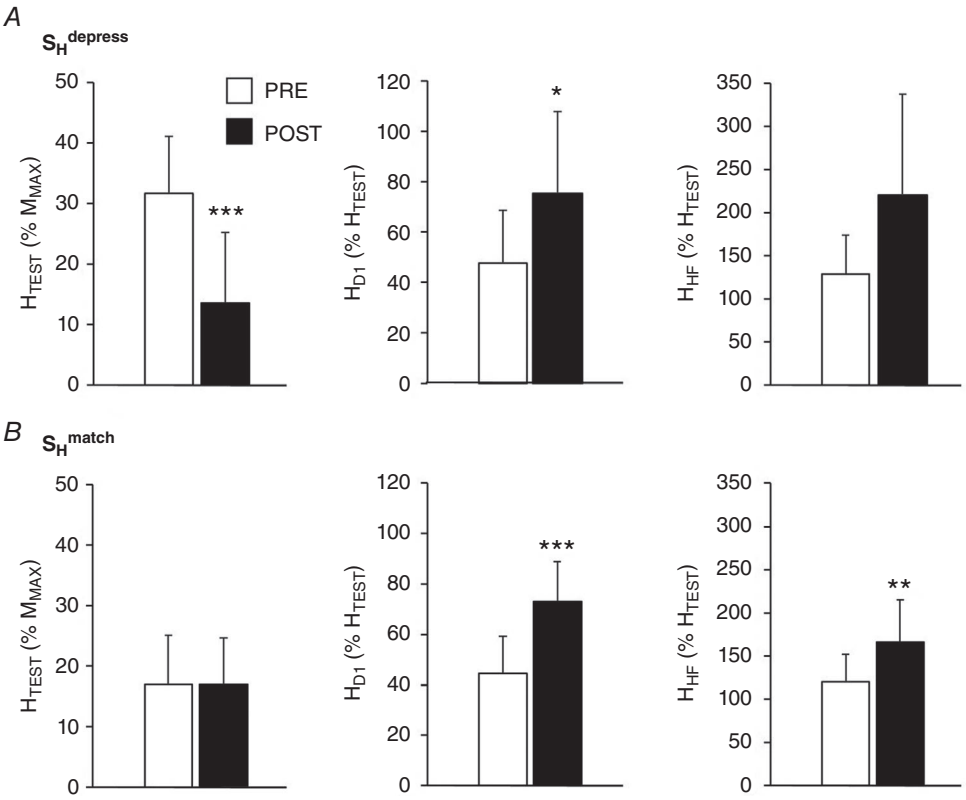

Figure 4. Non-conditioned (H_{TEST}) and conditioned (H_{D1} and H_{HF} conditioned by stimulation of fibular and femoral nerves, respectively) SOL H-reflexes recorded before (PRE) and after (POST) a 30 min resting or LV period
A, data ($n = 8$) for $S_H^{depress}$ where the electrical intensity to evoke H-reflexes was kept constant between a PRE and POST 30 min of LV. *B*, data ($n = 8$) for S_H^{match} where the electrical intensity to evoke H-reflexes was set at POST to match the amplitude of the H_{TEST} obtained at PRE.

TMEPs were significantly reduced by 12.9 ± 11.6% after the 30 min LV period ($t_{(10)} = 3.10$; $P = 0.01$, $d = 0.33$; Fig. 6). Normalized SOL EMG remained unchanged between PRE and POST measurements (0.94 ± 0.37% M_{MAX} *vs.* 0.95 ± 0.40% at PRE and POST, respectively; $t_{(11)} = 0.13$; $P = 0.89$, $d = 0.03$).

Discussion

This study aimed to provide new insights into the mechanisms involved in depressed spinal excitability after prolonged LV. The main results were that the H-reflex depression observed after LV was not related to an increase in presynaptic inhibition level (D1 and HF) nor

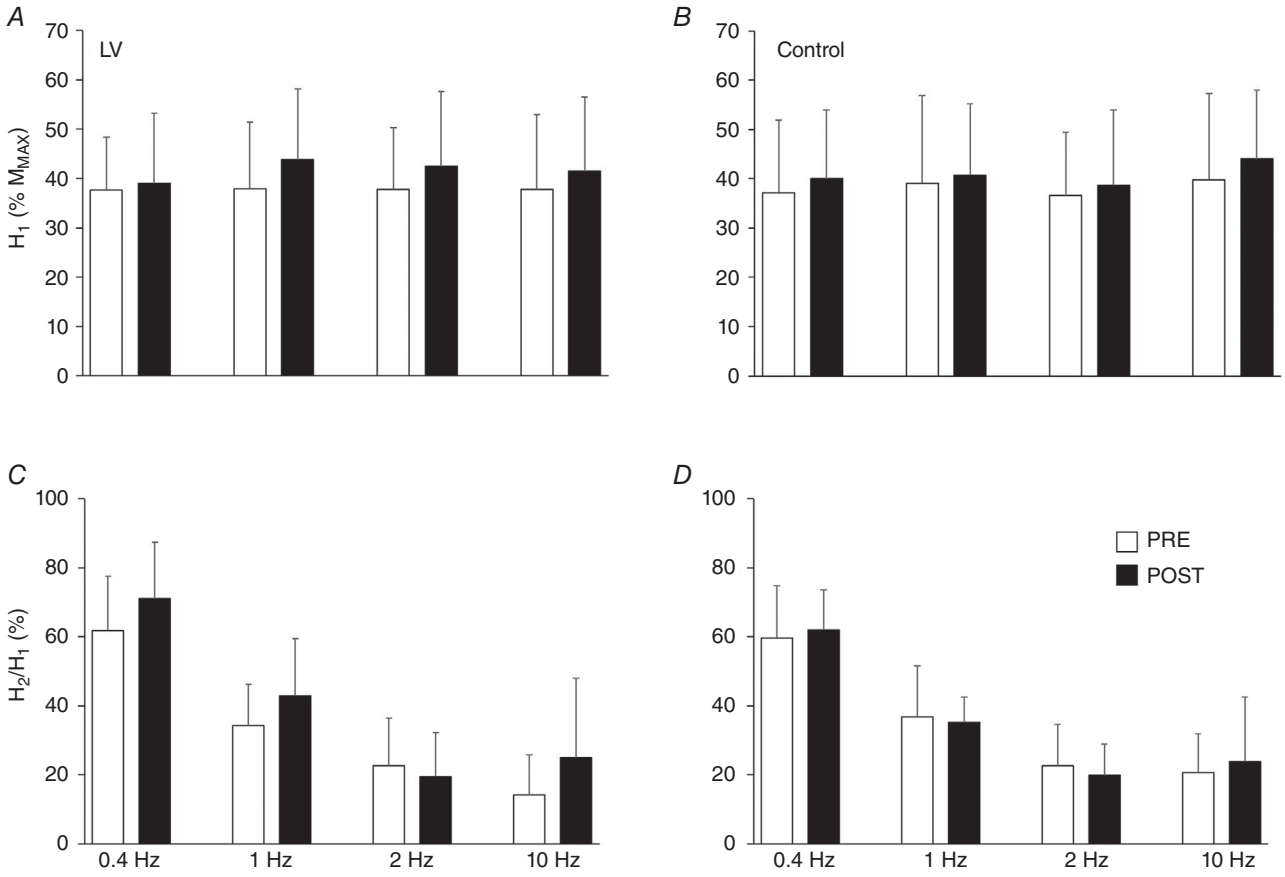

Figure 5. H-reflexes (H_1; *A* and *B*) and H_2/H_1 ratios (*C* and *D*) recorded before (PRE) and after (POST) local vibration (LV) or a 30 min rest period (Control)
Values are expressed as mean ± SD.

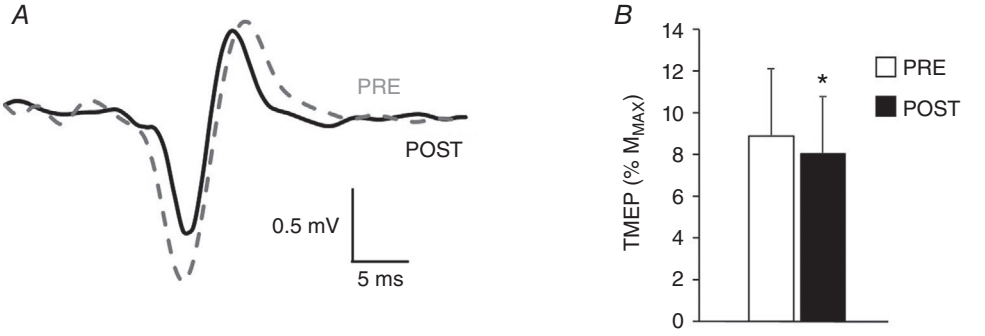

Figure 6. Thoracic motor evoked potential recordings
A, representative traces of thoracic motor evoked potentials (TMEPs) recorded before (PRE) and after (POST) the 30 min period of LV. *B*, data (mean values with standard deviation) for TMEP normalized to M_{MAX} recorded in 11 healthy young subjects for soleus muscle before (PRE; dashed line) and after (POST; continuous line) a 30 min LV period. *Significantly different from PRE at $P < 0.05$.

alterations in neurotransmitter release due to repetitive activation (HD), but was likely due to a decrease in intrinsic motoneuron excitability (TMEPs). These results are in contrast with the commonly accepted idea that the mechanisms responsible for the decrease in spinal excitability after LV are located at the presynaptic level. A model in Fig. 7 summarizes the current research findings and hypotheses.

Spinal plasticity at the presynaptic level in response to LV

The mean 77% decrease in H_{TEST} reported in this study confirmed the well-described capacity for prolonged LV to decrease spinal loop excitability (for review, see Souron *et al.* 2017*b*). While most authors suggested this was due to presynaptic inhibitory mechanisms, the originality of the present study was to directly investigate this hypothesis. In our protocol, we ascertained that our results were not biased by changes in the size of the unconditioned H-reflex that may influence its sensitivity to excitatory and inhibitory inputs (Johannsson *et al.* 2015) by testing these presynaptic mechanisms in two sessions with and without adjusting the size of the H-reflex after LV. The results were the same in both testing sessions with an increase in both H_{D1} and H_{HF} after LV (i.e. a decrease in presynaptic inhibition), contrasting with what the current literature hypothesized (Ushiyama *et al.* 2005; Ekblom & Thorstensson, 2011; Lapole *et al.* 2012*b*; Fry & Folland, 2014). These results could reflect a decrease in PAD interneuron excitability. PAD interneurons have a low discharge threshold compared to other neurons (Daniele & MacDermott, 2009) and are strongly activated by short-lasting LV, partly explaining the 'vibration paradox phenomenon' (Gillies *et al.* 1969; Hultborn *et al.* 1987*a*). We speculate that the prolonged activation of PAD interneurons during LV may decrease their excitability. Second, prolonged LV likely activated cutaneous receptors (Pantaleo *et al.* 1986; Munte *et al.* 1996), although to a lower degree than Ia afferents (Munte *et al.* 1996). Their activation may decrease presynaptic inhibition by inhibiting first-order interneurons involved in the pathway of presynaptic inhibition, thus reducing the strength of this mechanisms on SOL Ia afferents (Iles, 1996). However, it remains unknown whether presynaptic inhibition may continue to be reduced after repeated activation of cutaneous afferents as after LV. Third, it was

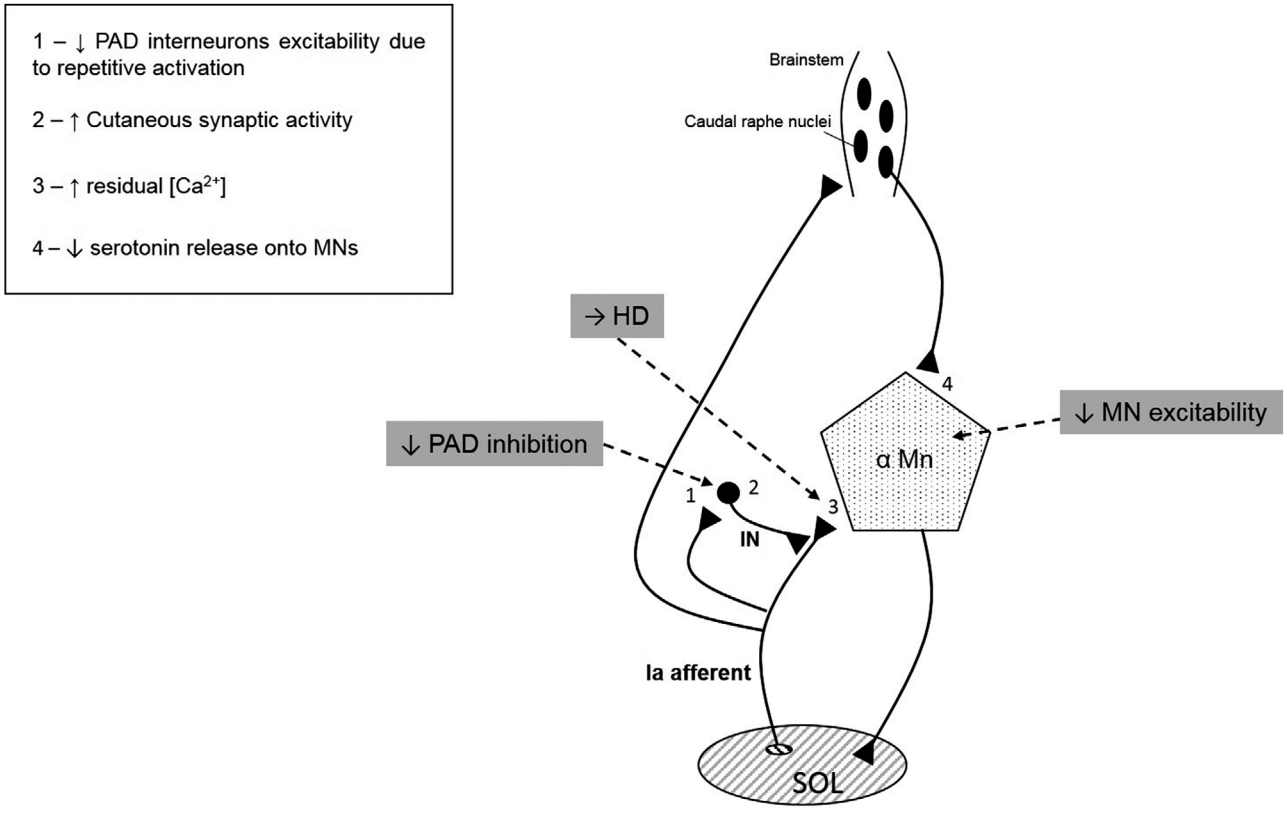

Figure 7. Schematic representation of experimental data (grey boxes) and hypothetical mechanisms involved in depressed spinal loop excitability after long-duration local vibration (white box)
α Mn: α-motoneuron; Ca^{2+}: calcium; HD: homosynaptic post-activation depression; IN: interneuron; MN: motoneuron; PAD: primary afferent depolarization; SOL: soleus

previously reported in cats that repetitive activation of Ia afferents by electrical stimulation (i.e. 5 pulses at 200 Hz) may transiently reduce their sensitivity to presynaptic inhibition (Enriquez-Denton *et al.* 2002). This may occur through an increased amount of residual calcium in the Ia afferent terminals after repetitive activations, so increasing transmitter release probability despite presynaptic inhibition (Enriquez-Denton *et al.* 2002). This transient increase in synaptic strength under the influence of calcium movements, i.e. the so-called post-tetanic potentiation known as a short-term presynaptic plasticity mechanism (Regehr, 2012), may in fact last seconds to minutes after a sustained high-frequency stimulation (the longer the stimulation the longer the potentiation). Although speculative, such an increase in residual calcium at the Ia afferent terminals level is conceivable after 30 min of high-frequency LV that strongly activates Ia afferents (Roll *et al.* 1989). This would provide a valuable explanation for the LV-induced decrease in presynaptic inhibition.

No changes in SOL HD were found in the present study after LV, as previously reported (Ekblom & Thorstensson, 2011). Altogether our results support the notion that the global depression in the spinal loop excitability after LV cannot be explained by increased presynaptic mechanisms acting on muscle spindle afferents. Furthermore, we suggest that Ia excitability remained unchanged, as previously demonstrated by others (Fry & Folland, 2014).

LV decreases motoneuron excitability

Because H-reflex amplitude also depends on motoneuron excitability, we further investigated postsynaptic mechanisms using electrical stimulation of the descending corticospinal tract at the thoracic spine level. A significant 13% decrease of SOL TMEPs was reported, indicating that motoneuron excitability was depressed after LV. While this contrasts with previous studies using F-wave measurements (Christova *et al.* 2011; Lapole *et al.* 2012*b*), a method known to provide a flawed measurement of motoneuron excitability (McNeil *et al.* 2013), this confirms our recent findings of a decrease in rectus femoris TMEPs after LV (Souron *et al.* 2017*a*). We acknowledge that the magnitude of LV-induced depressed motoneuron excitability reported here is largely lower than the global spinal loop excitability. Yet, both TMEP and H-reflex responses were of different size and so did not recruit the same proportion of motor units. Moreover, while the former was investigated during contraction, the latter was evaluated at rest. It is impossible to exclude that such methodological discrepancies (i.e. some parameters being investigated during contraction (TMEPs) *vs.* at rest (H_{TEST}, H_{D1}, H_{HF}, HD)) may have biased the interpretation we made about the present results. Nevertheless, we previously demonstrated that H-reflex recorded on the tibialis anterior during submaximal voluntary contraction (i.e. 10% MVC) also decreases after prolonged LV (Farabet *et al.* 2016). We are quite confident in the fact that similar results would have been observed in the present study if H-reflex had been evoked at 30% MVC submaximal contraction (i.e. same force level as TMEP). Yet, a direct comparison of H-reflex and TMEP recorded at the same level of central drive would provide more direct evidence regarding the influence of motoneuron excitability in decreased spinal excitability after prolonged LV.

Alterations in the excitability of the corticospinal tract are unlikely to explain our results of vibration-induced decreased TMEPs. For instance, fatiguing contractions failed to demonstrate impaired excitability of the corticospinal tract (Petersen *et al.* 2003; Giesebrecht *et al.* 2010) and impaired efficacy in synaptic transmission during strong contractions (Petersen *et al.* 2003), and LV is not thought to act through the corticospinal tract. Because TMEPs were recorded during contraction, the potential contribution of Ib inhibitory interneurons or Renshaw cells should not be ruled out. While it is still unclear how Ia afferents may influence Renshaw cell activity, it has been reported in cats that Ia converge onto Ib afferents leading to non-reciprocal group I inhibitory interneurons (Jankowska *et al.* 1981). Besides postsynaptic inhibitory mechanisms, our results may also suggest a reduction in intrinsic motoneuron excitability as postulated after repetitive motoneuron activation through fatiguing contractions (Johnson *et al.* 2004; McNeil *et al.* 2011). For instance, motoneuron excitability can be regulated intrinsically by dendritic persistent inward currents (Heckmann *et al.* 2005). These persistent inward currents are under the influence of descending neuromodulatory inputs from the brainstem originating from the caudal raphe nucleus for serotoninergic neurons and locus coeruleus for noradrenergic neurons (Heckman *et al.* 2009). These neurons are sending their axons down to the spinal motoneurons where their action is diffuse and non-specific (Johnson & Heckman, 2014). Serotonin release may increase motoneuron excitability through persistent inward currents when acting on 5-HT_2 receptors (identified on the dendrites and soma of motoneurons), while it may decrease it when spillover of serotonin leads to activation of 5-HT_{1A} receptors located on the axon initial segment of motoneurons (Taylor *et al.* 2016). Previous reports support the hypothesis that serotonin release may decrease with exercise (Fornal *et al.* 2006). Although speculative, it could be hypothesized that the same holds true for prolonged LV. Considering that caudal raphe neurons are sensitive to a variety of afferent stimuli such as electrical stimulation of hindlimb nerves (Moolenaar *et al.* 1976), one may suggest that prolonged activation of these neurons by LV may have led to changes in serotonin

release from the brainstem and thus a decrease in persistent inward currents to the motoneuron pool, and ultimately a decrease in motoneuron excitability. One should keep in mind, however, that there is no direct evidence for the role of serotonin in fatigue so far (Taylor *et al.* 2016), and this specific hypothesis to explain our results should be considered with caution. The present results give support to recent findings reporting a detrimental influence of long-duration LV exposure on motor unit firing properties, i.e. decrease in firing rates and increase in recruitment threshold (Barrera-Curiel *et al.* 2019).

Conclusions

This study provides new evidence that presynaptic mechanisms (i.e. modulations in PAD interneurons and/or neurotransmitter release at the Ia–α motoneuron synapse) are not involved in the depression of spinal excitability after LV. Rather, we suggest that the depressed spinal excitability relies on postsynaptic changes with potential decreased motoneuron excitability. It remains to be investigated how chronic LV may induce motoneuron plasticity to give more evidence on neural adaptations when LV is used as a training modality (Souron *et al.* 2017*b*).

These results may also allow a better understanding of plasticity in spinal circuitry of spastic patients, these patients being characterized by a spinal hyperexcitability responsible for muscle spasms and long-lasting reflexes (Nardone & Schieppati, 2005; Ritzmann *et al.* 2018). Our results could reinforce interest in the use of vibration as a therapy in those patients. It has been reported that muscle spasms and long-lasting reflexes characterizing spasticity are under the influence of large persistent inward currents that make the spinal cord hyperexcitable (Heckmann *et al.* 2005). Then, and although speculative, the use of vibration may reduce the influence of such persistent currents to improve the quality of life of spastic patients both in the short (e.g. reduced reflex excitability, spasticity and coordination deficits) and long (e.g. reduced muscle tone, improved movement ability, improved strength and gait) terms (Ritzmann *et al.* 2018). Further studies should now precisely determine how LV application may interact with persistent inward current in motoneurons.

References

Barrera-Curiel A, Colquhoun RJ, Hernandez-Sarabia JA & DeFreitas JM (2019). The effects of vibration-induced altered stretch reflex sensitivity on maximal motor unit firing properties. *J Neurophysiol* **121**, 2215–2221.

Baudry S & Duchateau J (2012). Age-related influence of vision and proprioception on Ia presynaptic inhibition in soleus muscle during upright stance. *J Physiol* **590**, 5541–5554.

Baudry S & Enoka RM (2009). Influence of load type on presynaptic modulation of Ia afferent input onto two synergist muscles. *Exp Brain Res* **199**, 83–88.

Bongiovanni LG, Hagbarth KE & Stjernberg L (1990). Prolonged muscle vibration reducing motor output in maximal voluntary contractions in man. *J Physiol* **423**, 15–26.

Burke D (1980). Muscle spindle activity induced by vibration in man: Implications for the tonic stretch reflex. In *Spinal and Supraspinal Mechanisms of Voluntary Motor Control and Locomotion*, ed. Desmedt JE, pp. 243–253. Karger, Basel.

Burke D, Adams RW & Skuse NF (1989). The effects of voluntary contraction on the H reflex of human limb muscles. *Brain* **112**, 417–433.

Christova M, Rafolt D, Golaszewski S & Gallasch E (2011). Outlasting corticomotor excitability changes induced by 25 Hz whole-hand mechanical stimulation. *Eur J Appl Physiol* **111**, 3051–3059.

Cohen J (1988). *Statistical Power Analysis for the Behavioral Sciences*. Erlbaum, Hillsdale, NJ, USA.

Crone C, Hultborn H, Mazieres L, Morin C, Nielsen J & Pierrot-Deseilligny E (1990). Sensitivity of monosynaptic test reflexes to facilitation and inhibition as a function of the test reflex size: a study in man and the cat. *Exp Brain Res* **81**, 35–45.

Curtis DR & Eccles JC (1960). Synaptic action during and after repetitive stimulation. *J Physiol* **150**, 374–398.

Daniele CA & MacDermott AB (2009). Low-threshold primary afferent drive onto GABAergic interneurons in the superficial dorsal horn of the mouse. *J Neurosci* **29**, 686–695.

Desmedt JE & Godaux E (1978). Mechanism of the vibration paradox: excitatory and inhibitory effects of tendon vibration on single soleus muscle motor units in man. *J Physiol* **285**, 197–207.

Ekblom M & Thorstensson A (2011). Effects of prolonged vibration on H-reflexes, muscle activation, and dynamic strength. *Med Sci Sports Exerc* **43**, 1933–1939.

Enriquez-Denton M, Morita H, Christensen LO, Petersen N, Sinkjaer T & Nielsen JB (2002). Interaction between peripheral afferent activity and presynaptic inhibition of Ia afferents in the cat. *J Neurophysiol* **88**, 1664–1674.

Farabet A, Souron R, Millet GY & Lapole T (2016). Changes in tibialis anterior corticospinal properties after acute prolonged muscle vibration. *Eur J Appl Physiol* **116**, 1197–1205.

Fornal CA, Martin-Cora FJ & Jacobs BL (2006). "Fatigue" of medullary but not mesencephalic raphe serotonergic neurons during locomotion in cats. *Brain Res* **1072**, 55–61.

Fry A & Folland JP (2014). Prolonged infrapatellar tendon vibration does not influence quadriceps maximal or explosive isometric force production in man. *Eur J Appl Physiol* **114**, 1757–1766.

Giesebrecht S, Martin PG, Gandevia SC & Taylor JL (2010). Facilitation and inhibition of tibialis anterior responses to corticospinal stimulation after maximal voluntary contractions. *J Neurophysiol* **103**, 1350–1356.

Gillies JD, Lance JW, Neilson PD & Tassinari CA (1969). Presynaptic inhibition of the monosynaptic reflex by vibration. *J Physiol* **205**, 329–339.

Grospretre S, Lebon F, Papaxanthis C & Martin A (2018). Spinal plasticity with motor imagery practice. *J Physiol* **597**, 921–934.

Hayward LF, Nielsen RP, Heckman CJ & Hutton RS (1986). Tendon vibration-induced inhibition of human and cat triceps surae group I reflexes: evidence of selective Ib afferent fiber activation. *Exp Neurol* **94**, 333–347.

Heckmann CJ, Gorassini MA & Bennett DJ (2005). Persistent inward currents in motoneuron dendrites: implications for motor output. *Muscle Nerve* **31**, 135–156.

Heckman CJ, Mottram C, Quinlan K, Theiss R & Schuster J (2009). Motoneuron excitability: the importance of neuromodulatory inputs. *Clin Neurophysiol* **120**, 2040–2054.

Honig MG, Collins WF 3rd & Mendell LM (1983). Alpha-motoneuron EPSPs exhibit different frequency sensitivities to single Ia-afferent fiber stimulation. *J Neurophysiol* **49**, 886–901.

Hopkins WG (2000). Measures of reliability in sports medicine and science. *Sports Med* **30**, 1–15.

Hultborn H, Meunier S, Morin C & Pierrot-Deseilligny E (1987a). Assessing changes in presynaptic inhibition of I a fibres: a study in man and the cat. *J Physiol* **389**, 729–756.

Hultborn H, Meunier S, Pierrot-Deseilligny E & Shindo M (1987b). Changes in presynaptic inhibition of Ia fibres at the onset of voluntary contraction in man. *J Physiol* **389**, 757–772.

Iles JF (1996). Evidence for cutaneous and corticospinal modulation of presynaptic inhibition of Ia afferents from the human lower limb. *J Physiol* **491**, 197–207.

Jankowska E, McCrea D & Mackel R (1981). Pattern of 'non-reciprocal' inhibition of motoneurones by impulses in group Ia muscle spindle afferents in the cat. *J Physiol* **316**, 393–409.

Johannsson J, Duchateau J & Baudry S (2015). Presynaptic inhibition of soleus Ia afferents does not vary with center of pressure displacements during upright standing. *Neuroscience* **298**, 63–73.

Johnson KV, Edwards SC, van Tongeren C & Bawa P (2004). Properties of human motor units after prolonged activity at a constant firing rate. *Exp Brain Res* **154**, 479–487.

Johnson MD & Heckman CJ (2014). Gain control mechanisms in spinal motoneurons. *Front Neural Circuits* **8**, 81.

Lapole T, Canon F & Perot C (2012a). Acute postural modulation of the soleus H-reflex after Achilles tendon vibration. *Neurosci Lett* **523**, 154–157.

Lapole T, Deroussen F, Perot C & Petitjean M (2012b). Acute effects of Achilles tendon vibration on soleus and tibialis anterior spinal and cortical excitability. *Appl Physiol Nutr Metab* **37**, 657–663.

McNeil CJ, Butler JE, Taylor JL & Gandevia SC (2013). Testing the excitability of human motoneurons. *Front Hum Neurosci* **7**, 152.

McNeil CJ, Giesebrecht S, Gandevia SC & Taylor JL (2011). Behaviour of the motoneurone pool in a fatiguing submaximal contraction. *J Physiol* **589**, 3533–3544.

Martin PG, Butler JE, Gandevia SC & Taylor JL (2008). Noninvasive stimulation of human corticospinal axons innervating leg muscles. *J Neurophysiol* **100**, 1080–1086.

Mizuno Y, Tanaka R & Yanagisawa N (1971). Reciprocal group I inhibition on triceps surae motoneurons in man. *J Neurophysiol* **34**, 1010–1017.

Moolenaar GM, Holloway JA & Trouth CO (1976). Responses of caudal raphe neurons to peripheral somatic stimulation. *Exp Neurol* **53**, 304–313.

Munte TF, Jobges EM, Wieringa BM, Klein S, Schubert M, Johannes S & Dengler R (1996). Human evoked potentials to long duration vibratory stimuli: role of muscle afferents. *Neurosci Lett* **216**, 163–166.

Nardone A & Schieppati M (2005). Reflex contribution of spindle group Ia and II afferent input to leg muscle spasticity as revealed by tendon vibration in hemiparesis. *Clin Neurophysiol* **116**, 1370–1381.

Nielsen J & Petersen N (1994). Is presynaptic inhibition distributed to corticospinal fibres in man? *J Physiol* **477**, 47–58.

Pantaleo T, Duranti R & Bellini F (1986). Effects of vibratory stimulation on muscular pain threshold and blink response in human subjects. *Pain* **24**, 239–250.

Petersen NT, Taylor JL, Butler JE & Gandevia SC (2003). Depression of activity in the corticospinal pathway during human motor behavior after strong voluntary contractions. *J Neurosci* **23**, 7974–7980.

Regehr WG (2012). Short-term presynaptic plasticity. *Cold Spring Harb Perspect Biol* **4**, a005702.

Ritzmann R, Stark C & Krause A (2018). Vibration therapy in patients with cerebral palsy: a systematic review. *Neuropsychiatr Dis Treat* **14**, 1607–1625.

Roll JP & Vedel JP (1982). Kinaesthetic role of muscle afferents in man, studied by tendon vibration and microneurography. *Exp Brain Res* **47**, 177–190.

Roll JP, Vedel JP & Ribot E (1989). Alteration of proprioceptive messages induced by tendon vibration in man: a microneurographic study. *Exp Brain Res* **76**, 213–222.

Rothwell JC, Day BL, Berardelli A & Marsden CD (1986). Habituation and conditioning of the human long latency stretch reflex. *Exp Brain Res* **63**, 197–204.

Rudomin P & Schmidt RF (1999). Presynaptic inhibition in the vertebrate spinal cord revisited. *Exp Brain Res* **129**, 1–37.

Schieppati M (1987). The Hoffmann reflex: a means of assessing spinal reflex excitability and its descending control in man. *Prog Neurobiol* **28**, 345–376.

Souron R, Besson T, McNeil CJ, Lapole T & Millet GY (2017a). An acute exposure to muscle vibration decreases knee extensors force production and modulates associated central nervous system excitability. *Front Hum Neurosci* **11**, 519.

Souron R, Besson T, Millet GY & Lapole T (2017b). Acute and chronic neuromuscular adaptations to local vibration training. *Eur J Appl Physiol* **117**, 1939–1964.

Stein RB, Estabrooks KL, McGie S, Roth MJ & Jones KE (2007). Quantifying the effects of voluntary contraction and inter-stimulus interval on the human soleus H-reflex. *Exp Brain Res* **182**, 309–319.

Taylor JL, Amann M, Duchateau J, Meeusen R & Rice CL (2016). Neural contributions to muscle fatigue: from the brain to the muscle and back again. *Med Sci Sports Exerc* **48**, 2294–2306.

Ugawa Y, Genba-Shimizu K & Kanazawa I (1995). Electrical stimulation of the human descending motor tracts at several levels. *Can J Neurol Sci* **22**, 36–42.

Ugawa Y, Rothwell J, Day B, Thompson P & Marsden C (1991). Percutaneous electrical stimulation of corticospinal pathways at the level of the pyramidal decussation in humans. *Ann Neurol* **29**, 418–427.

Ushiyama J, Masani K, Kouzaki M, Kanehisa H & Fukunaga T (2005). Difference in aftereffects following prolonged Achilles tendon vibration on muscle activity during maximal voluntary contraction among plantar flexor synergists. *J Appl Physiol (1985)* **98**, 1427–1433.

Additional information

Competing interests

The authors declare no competing financial interests.

Author contributions

R.S., S.B., G.Y.M. and T.L. conceived and designed the research; R.S., S.B and T.L. performed experiments (experiments A and C were carried out at the Inter-university Laboratory of Human Movement Biology, Saint-Etienne; experiment B was carried out at the Laboratory of Applied Biology, Brussels); R.S., S.B. and T.L. analysed data; R.S., S.B., G.Y.M. and T.L. interpreted the results of experiments; R.S. prepared figures; R.S., S.B., G.Y.M. and T.L. drafted, edited and revised the manuscript. All authors approved the final version of the manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All persons designated as authors qualify for authorship, and all those who qualify for authorship are listed.

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