

Research article

Rhythmic wrist movements facilitate the soleus H-reflex and non-voluntary air-stepping in humans



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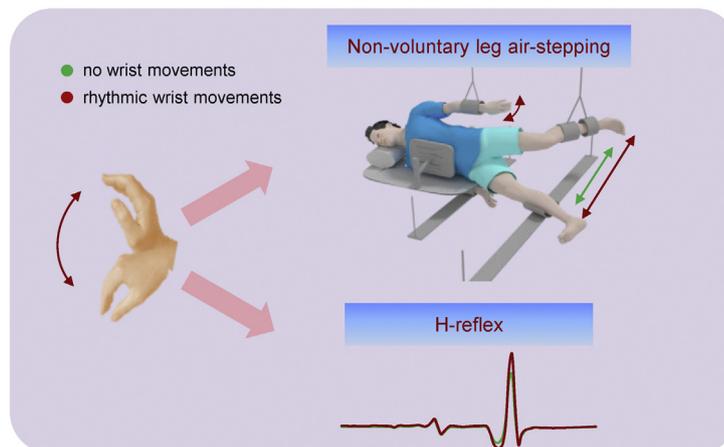
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HIGHLIGHTS

- Facilitatory effect of rhythmic wrist motion on leg rhythmogenesis was demonstrated.
- Wrist flexion-extension movements potentiated the soleus H-reflex.
- Rhythmicity of motion rather than tension in arm muscles underlay this effect.
- Physiologically relevant hand-foot neural coupling described.

GRAPHICAL ABSTRACT



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ABSTRACT

Neural coupling between the upper and lower limbs during human walking is supported by modulation of cross-limb reflexes and the presence of rhythmic activity in the proximal arm muscles. Nevertheless, the involvement of distal arm muscles in cyclic movements and sensorimotor neuromodulation is also suggested given their step-synchronized activation in many locomotor-related tasks (e.g., swimming, skiing, climbing, cycling, crawling, etc.). Here we investigated the effect of rhythmic wrist movements, separately and in conjunction with arm swinging, on the characteristics of non-voluntary cyclic leg movements evoked by muscle vibration in a gravity neutral position and on the soleus H-reflex of the stationary legs. For the H-reflex modulation, five conditions were compared: stationary arms, voluntary alternating upper limb swinging, combined upper limb and wrist motion, wrist movements only and motion of the upper limbs with addition of load. Rhythmic wrist movements significantly facilitated the amplitude of non-voluntary leg oscillations, including ankle joint oscillations, and the H-reflex. The latter effect was related to rhythmicity of wrist motion rather than to a simple extra tension in the upper limb

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muscles (a kind of the Jendrassik manoeuvre) since adding resistance to arm oscillations (without flexion-extension in the wrist joint) had an opposite inhibitory effect on the H-reflex. Our results further support the existence of connections between the distal parts of the upper and lower extremities at the neural level, suggesting that wrist joint movements can be an important component of motor neurorehabilitation.

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1. Introduction

Human locomotion shares many features with the forelimb and hindlimb coordination of quadrupeds even though the inter-limb coupling is weaker in humans [1,2]. Neural coupling between the upper and lower limbs is evidenced by modulation of cross-limb reflexes [2], the facilitatory effect of arm movements on rhythmic leg movements [3–5] and the presence of rhythmic activity in the proximal upper limb muscles during walking [6,7]. However, the involvement of distal arm segments (hands) in cyclic movements and sensorimotor neuromodulation may also be expected given their engagement in many locomotor-related tasks, e.g., swimming, skiing, climbing, rowing, cycling, crawling, etc. Therefore, it is of interest to explore neural coupling between the hand and the foot in the locomotor tasks.

Previous studies showed that both position of the upper limbs [8,9] and their movements [10–12] can affect spinal cord reflex excitability. Some interactions between the hands and feet have also been described. For instance, the combined movements of the hands and feet may influence each other [13], as well as inhibitory and excitatory relationships between the foot and hand motor cortices were documented [14,15]. In particular, the coordination of wrist and foot involves a distributed network, showing activation levels in the supplementary motor area, cingulate motor cortex, premotor cortex, primary sensorimotor cortex, and cerebellum that exceed the sum of the activations observed during the isolated limb movements [16]. As for the reflex interaction, cyclic movements of the foot modulate corticospinal reflex excitability in resting forearm muscles [17,18], whereas cutaneous inputs from the hand during walking modulate the soleus H-reflex [19]. Current data in animals suggest the presence of multiple flexor and extensor rhythm-generating modules for controlling different joints, which provides large flexibility to the network composition [20–23]. Even though cross-limb reflexes might not necessarily imply the existence of the putative cervical central pattern generator (CPG) in humans [3], it is reasonable to suggest that interactions between the foot and the hand exist also at the rhythm generation level. It is also worth noting that the work on humans suggests the CPG drive for rhythmic wrist motions [24]. The neuromechanical interactions between the limbs involve both propriospinal and supraspinal modulations [2].

The objective of the present study was to explore the influence of hand movements on the state of the lumbosacral circuitry. Specifically, we investigated the effect of rhythmic wrist movements, separately and in conjunction with arm swinging, on the characteristics of non-voluntary cyclic leg movements and on the soleus H-reflex, which are considered as important measures in evaluating spinal cord excitability. A gravity neutral position may be beneficial for CPG activation due to a facilitatory effect of simulated weightlessness on rhythmogenesis in upper and lower limbs in humans [3,25,26]. In particular, we tested the hypothesis that rhythmic movements of the distal parts of the upper limbs (hands) may potentiate rhythmogenesis of the lower limbs and reflex excitability.

2. Methods

2.1. Experimental setup and protocols

Participants were 22 healthy volunteers (17 men and 5 women, aged 32.9 ± 20.0 yrs). None of the subjects had any known neurological or motor disorder. The experiments were performed according to the procedures of the Ethics Committee of the Institute for Information Transmission Problems and in conformity with the declaration of Helsinki for experiments on humans. All subjects gave their written informed consent. The experimental setup was similar to that described in our previous study [3] (see Supplementary material, Fig. S1). To minimize the effects of gravity and external resistance, the subjects lay on their right side with the suspended arms and legs (Fig. 1, upper panel). The experiments consisted of three sessions conducted on different days.

In the first session (Exp. 1), we investigated the effect of rhythmic flexion-extension wrist joint movements on the characteristics of non-voluntary air-stepping evoked by continuous bilateral quadriceps muscle vibration. Vibration (40–60 Hz, ~1-mm amplitude, [3]) was applied for about 30–40 s. This tonic sensory stimulation elicits non-voluntary air-stepping in ~50% of subjects [27]. Eleven subjects who demonstrated non-voluntary leg air-stepping movements participated in this experiment. Subjects were instructed to relax and not to intervene with any leg movement that might be induced by vibratory stimulation. When the subject reached a relatively steady state of leg oscillations (typically after 5–15 s following stimulation), he/she was asked to start alternating wrist movements at a natural frequency and large amplitude (~90°, Fig. 1A).

In the second session (Exp. 2), we investigated the effect of wrist motion on the soleus H-reflex of the stationary legs. Four different conditions were studied: stationary arms, voluntary alternating upper limb swinging at a comfortable frequency (no wrist joint motion involved), upper limb + wrist motion (the frequency of movement in the wrist joint coincided with that in the shoulder joint) and wrist movements only. Angular movements for each condition are illustrated in Fig. 2A. Thirteen subjects participated in this experiment, the two of them also participated in Exp. 1. Hoffmann reflexes were elicited by delivering constant current square pulses (1 ms) to the posterior tibial nerve through bipolar surfaces electrodes, placed in the popliteal fossa of the left stationary leg [28]. The stimulus intensity (3.5–10 mA) was individually adjusted to obtain the M-wave of about 12–16% of the maximal M-response (M_{max}) (using supramaximal stimulus intensity) in the stationary suspended leg. A computer program was used to trigger the electric stimuli and to determine the timing of stimulation. The cycle was defined using shoulder or wrist movements (Fig. 2A, upper panels). Reflexes were evoked at four different points of the cycle, on average equally spaced throughout the cycle, using a feedback controlled on-line algorithm with the duration of the preceding cycle as a reference for calculating the relative time of stimulation. The stimuli were applied about once per cycle in a random order (though the minimal interval was set >2.5 s). The duration of each trial was 60 s. On average, 20–25 stimuli were delivered per trial. Six trials were recorded for each arm movement condition carried

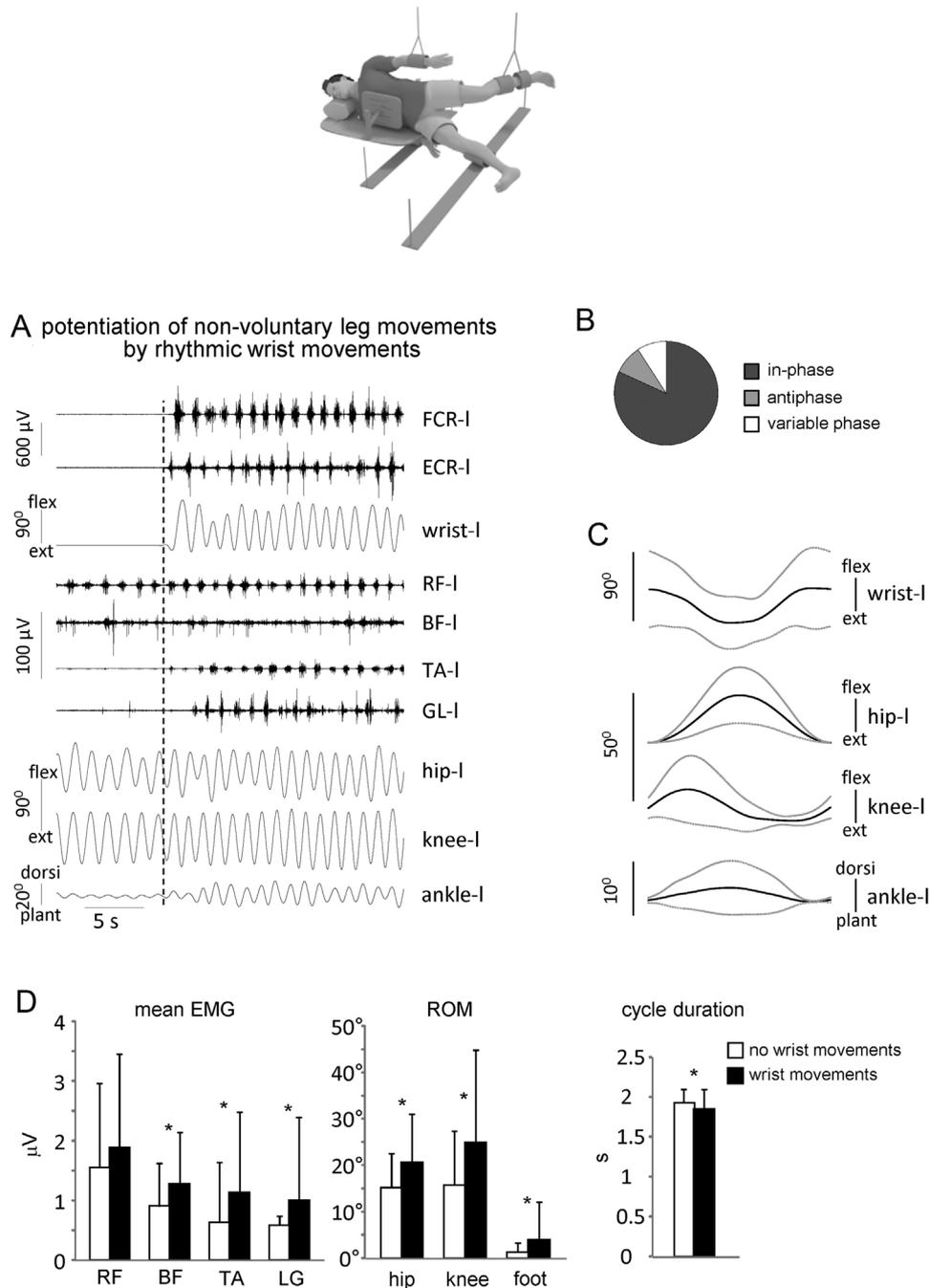


Fig. 1. Facilitatory effect of voluntary rhythmic wrist movements on non-voluntary leg air-stepping. A – an example of changes in leg kinematics and EMG activity. I – left. The subject lay on her/his right side on a couch with the arms and legs suspended (top panel). B – pie charts showing the percentage of subjects with different wrist-hip coupling (see Eq. (1)). C – ensemble averaged (\pm SD) angular movements in the wrist, hip, knee and ankle joints. Patterns are plotted vs the normalized cycle of leg oscillations (the onset of the cycle was defined as the maximum hip extension). D – mean EMG activity, range of motion (ROM) and cycle duration (mean + SD) of leg air-stepping movements with and without rhythmic wrist movements. Asterisks denote significant differences.

out in a random order. For the stationary arm condition, ten H-reflexes were recorded at the beginning, in the middle (two times) and at the end of the session (duration \sim 1.5–2 h).

In the third session (Exp. 3), we examined whether the facilitatory effect of wrist movements could be accounted for by an additional tension in the upper limb muscles (a kind of the Jendrassik manoeuvre, which may potentiate the soleus H-reflex [29]). To this end, we added resistance to arm oscillations. The subject was asked to perform voluntary rhythmic upper (left) arm oscillations at a natural frequency. The distal part of the arm was connected to the metal weight (2 kg) placed on the floor under the subject. The

subject moved the weight along a horizontal surface (via a cable and a system of two roller bearings, Fig. 3A upper panel), generating roughly a constant resistive load (friction \sim 6 N, estimated by the dynamometer). The right arm was held stationary. A similar protocol was used to investigate the soleus H-reflex during four phases of arm oscillations (the cycle was defined using shoulder movements) performed with and without load. Again, six trials were recorded for each arm movement condition. The same thirteen subjects, as in Exp. 2, participated in this study.

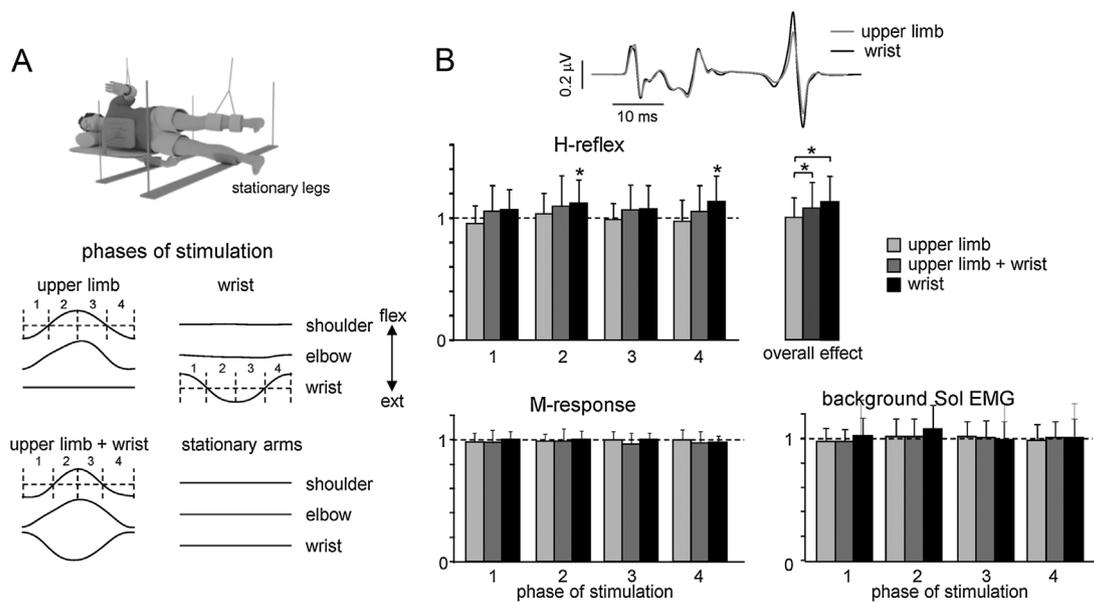


Fig. 2. Effect of rhythmic arm movements on the soleus H-reflex of the stationary legs. A – H-reflex during four different upper limb movement conditions: upper limb swinging, upper limb + wrist motion, wrist movements and stationary arms. From top to bottom: experimental setup and phases (1–4) of stimulation. Angular movements for each condition are shown for one representative subject. B – typical waveforms of the H-reflex ('upper limb' and 'wrist' conditions) and group means (\pm SD) of H-reflex amplitudes. For each subject, H-reflexes were normalized to the corresponding values during the stationary arm condition so that the amplitudes are expressed relative to 'stationary arms' base value (dashed horizontal line, corresponding to 1). Asterisks denote significant differences from the base value (left) and between the experimental conditions (right). Note a facilitatory effect of wrist movements on the H-reflex.

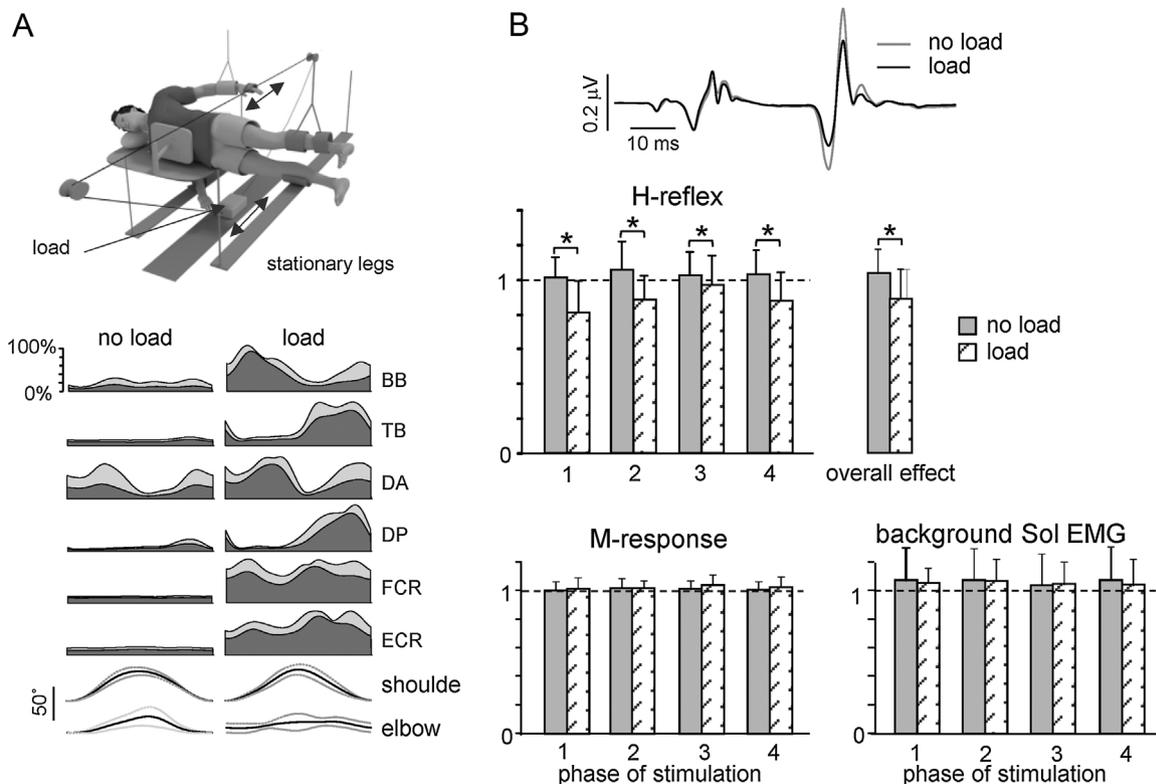


Fig. 3. Effect of loaded rhythmic upper (left) arm movements on the soleus H-reflex of the stationary legs. The right arm was hold stationary. A – experimental setup and ensemble averaged (\pm SD in light grey) EMG envelopes of arm muscles and angular joint motion (\pm SD) are shown for both loaded and unloaded conditions. B – H-reflex amplitudes (plotted in the same format as in Fig. 2B). Note an inhibitory effect of arm loading on the H-reflex.

2.2. Data recording and analysis

Recordings of EMG activity were obtained by means of surface bipolar electrodes with the wireless Delsys Trigno EMG system

(Delsys Inc., Boston, USA), bandwidth of 20–450 Hz, and overall gain of 1000. EMG activity was recorded on the left side of the body from the following muscles: soleus (SOL), rectus femoris (RF), biceps femoris (BF, long head), lateral gastrocnemius (LG), tibialis

anterior (TA), anterior (DA) and posterior (DP) deltoid muscles, biceps brachii (BB), triceps brachii (TB), flexor carpi radialis (FCR) and extensor carpi radialis (ECR). Angular movements in the three joints of both arms (shoulder, elbow, wrist) and both legs (hip, knee, ankle) were recorded using potentiometers attached laterally to each joint [3]. The kinematic and EMG data were sampled at 1000 Hz.

Cycle duration (T) and range of angular motion (ROM) were assessed as the movement parameters averaged across 10 cycles. Raw EMG data were numerically rectified, low-pass-filtered with a zero-lag Butterworth filter (10 Hz cut-off), time-interpolated over a time base with 100 points for individual step cycles and averaged. For group averaging of joint angular waveforms, data for each subject were time-interpolated over individual cycles to fit a normalized 100-point time base and averaged across strides. The onset of the cycle was defined as the maximum hip extension of the lower limbs and the maximum shoulder extension for the upper limbs. We also calculated the phase shift φ between wrist and leg movements in Exp. 1, defined as the interval between maxima of ipsilateral wrist and hip angles divided by the cycle duration:

$$\varphi = \frac{t_{\max_wrist} - t_{\max_hip}}{T} \times 100\% \quad (1)$$

If φ is close to 50% of cycle duration, wrist-hip movements are in-phase, if φ is close to 0%, movements are opposite (antiphased). Note that backward wrist and thigh movements in our setup correspond to wrist flexion and hip extension, respectively (Fig. 1A upper panel).

For the H-reflex analysis (Exp. 2 and 3), the peak-to-peak amplitudes of M-wave (over the 5–20 ms period after the stimulus) and H-reflex (25–60 ms after the stimulus) were calculated from the single unrectified sweeps of EMG. M-waves and H-reflexes were normalized to M_{\max} to reduce inter-subject variability. In our analysis, we accepted only probes with the M-wave in the range 12–16% of M_{\max} and the data with altered M-responses were discarded. The total number of H-reflexes we analysed in each subject was on average 75 ± 16 during each experimental condition (except for the stationary arm condition). For each subject, H-reflexes were normalized to the corresponding values during the stationary arm condition. The background SOL activity was calculated over 50 ms interval prior to the stimulus. For averaging arm muscle EMG envelopes in Exp. 3, EMG data for each subject were normalized to the largest value across conditions.

2.3. Statistics

Descriptive statistics included means and standard deviation of the mean. Paired t -tests and a repeated measures analysis of variance (RM ANOVA) were used to compare means between different conditions. If ANOVA resulted in a significant effect, a Tukey HSD post-hoc test was used to detect differences between conditions. The level of significance was set at 0.05.

3. Results

Fig. 1A illustrates an example of the effect of rhythmic wrist movements on non-voluntary leg air-stepping. Even though there was no special instruction for the frequency of voluntary hand oscillations, the subjects tended to coordinate upper and lower limb movements. Fig. 1C depicts ensemble averaged angular movements. The analysis of phase relationships showed that most ($n = 10$, 91%) subjects synchronized hand-leg oscillations: 82% – in-phase ($\varphi = 45 \div 50\%$) wrist-hip rotations, 9% – antiphase rotations ($\varphi = 0\%$) and one subject (9%) showed variable phase (Fig. 1B). Rhythmic wrist flexion-extension significantly increased the amplitude and frequency of air-stepping movements and EMG

activity of leg muscles (Fig. 1D). The range of motion in the distal (ankle) joint also significantly augmented (Fig. 1A and D). The latter effect was more noticeable in 6 out of the 11 subjects: these subjects tended to perform plantarflexion when the ipsilateral wrist was flexing.

In another experiment (Exp. 2), we investigated the effect of voluntary alternating (left-right) arm movements on the soleus H-reflex of the stationary legs (Fig. 2A). The period of arm movements was 1.85 ± 0.16 s in the ‘upper limb’ condition, and the ROM in the shoulder and elbow joints was $23 \pm 6^\circ$ and $26 \pm 17^\circ$, respectively. Adding rhythmic movements in the wrist joints (‘upper limb + wrist’, wrist joint angle oscillations were $87 \pm 19^\circ$) did not significantly change the amplitudes of movement in the other joints ($p = 0.38$ for shoulder and $p = 0.19$ for elbow, paired t -tests) nor the EMG activity of the shoulder muscles ($p > 0.1$ for each muscle). The M-response amplitudes were similar across arm movement conditions, phases of stimulation and during the stationary arm condition (RM ANOVA, $F_{12,144} = 0.845$, $p = 0.6$), the soleus background EMG activity was also similar (it was minute if any in the stationary legs, $F_{12,144} = 0.531$, $p = 0.9$). To test our hypothesis, we compared the H-reflex between three arm movement conditions: ‘upper limb’, ‘upper limb + wrist’, ‘wrist’. RM ANOVA (3 conditions \times 4 phases of stimulation) revealed a significant effect of condition ($F_{2,24} = 6.643$, $p = 0.005$). In particular, post hoc analysis showed that the H-reflex increased with respect to the ‘upper limb’ condition when rhythmic wrist movements were performed either in conjunction with arm swinging or separately ($p = 0.05$ for ‘upper limb + wrist’ and $p = 0.004$ for ‘wrist’, Fig. 2B). There was also an effect of phase ($F_{3,36} = 4.236$, $p = 0.012$): the H-reflex was enhanced during phase 2 with respect to phase 1 ($p = 0.007$, Tukey test). We also compared the H-reflex during each phase of stimulation with that during the ‘stationary arms’ condition: it was significantly augmented in phase 2 ($p < 0.02$) and 4 ($p < 0.01$) for the ‘wrist’ condition (Fig. 2B).

In the control experiment (Exp. 3), we examined whether the facilitatory effect of wrist movements on the H-reflex (Fig. 3A) could be accounted for by a simple effect of extra tension in the upper limb muscles rather than by rhythmic movements per se. To this end, we added resistance to arm oscillations. Fig. 3B illustrates the results of this experiment. Under the loaded condition, EMG activity of all recorded upper limb muscles substantially increased (paired t -tests, $p < 0.001$ for each muscle) (Fig. 3A lower panels). The amplitudes in the elbow ($p = 0.25$) and shoulder ($p = 0.13$) joints and the frequency of movements were similar in these two conditions. As in Exp. 2, the amplitude of M-responses and the background soleus EMG activity were similar across conditions. As to the H-reflex, RM ANOVA (2 conditions \times 4 phases) revealed a significant effect of condition ($F_{1,12} = 48.2$, $p = 0.00007$), phase ($F_{3,36} = 6.57$, $p = 0.001$) and interaction ($F_{3,36} = 11.5$, $p = 0.00001$). Post hoc analysis showed significantly reduced reflex responses for the loaded arm condition during all phases of stimulation ($p < 0.001$ for phases 1, 2 and 4, and $p < 0.03$ for phase 3) (Fig. 3B). Besides, the H-reflex during arm loading was reduced more significantly in phase 1.

4. Discussion

The present findings showed that both lower limb rhythmic movement generation (Fig. 1) and the soleus H-reflex (Fig. 2) were potentiated by rhythmic wrist movements. The current results extend the existing findings demonstrating the conditioning effects of upper limb movements on the lumbosacral motor pool's excitation [2,3]. Yet, the extent to which rhythmic hand movements per se can influence spinal excitability has not previously been reported.

Our findings demonstrated that not only arm movements [3,4] but also hand movements can elicit significant facilitation of the leg motor output and reflex excitability (Figs. 1 and 2). Interest-

ingly, flexion–extension wrist motion facilitated movement of the legs and also involved the foot (Fig. 1), suggesting neural interaction between the distal segments of the upper and lower limbs. This is remarkable because during air-stepping the ankle joint angle is typically non-involved, unless minimal loading forces are applied to the foot [27], consistent with significant contribution of load-related sensory input to the pre-programmed motoneuronal drive of the distal muscles during walking [30]. Identification of pathways capable of influencing excitability of rhythm-generating modules controlling different joints [20] allows physiologically relevant assessments and can reveal potential therapeutic targets [31,32].

The H-reflex constitutes one of the major available probes to assess excitability and plasticity of interneuronal networks even though it characterises only a part of neuronal pathways [10,33,34]. The influence of cyclic wrist movements on the soleus H-reflex (Fig. 2) may contribute to our understanding of sensorimotor integration underlying the spinal inhibitory pathways and interactions between cervical and lumbosacral circuitries. In our study, we did not observe the H-reflex inhibition during arm movements, as opposed to other studies [10,35]. In those works, however, assessment of H-reflex excitability was performed in the presence of foot contact with the support that may change the state of the motoneurons given also the dependence of the H-reflex on the spatial position of the body [35,36]. For instance, it has been shown that, both in sitting [37] and lying [38] position, mechanical loading of the sole of the foot inhibited the soleus H-reflex. Second, it has been shown that the degree of H-reflex suppression during ipsilateral or contralateral arm movements depends on the stature [35]: the suppression is greater in the sitting position as compared to the standing position. The third reason may be related to the frequency of arm movements in a gravity neutral position (<0.55 Hz, see Section 3), which was significantly lower than the effective frequency for H-reflex suppression reported in other studies [11]. Whatever the reason for the lack of changes during upper limb movements with respect to the stationary arms, a particularly interesting result of our study is a substantial potentiation of the H-reflex during hand movements (Fig. 2B). It is also worth noting that the greatest effect was observed in phase 2 and 4 during the ‘wrist’ condition, while such modulation was lacking during the ‘upper limb’ condition (Fig. 2B). Moreover, it is unlikely that this phenomenon was simply related to an extra tension in arm muscles since adding resistance to arm oscillations had an opposite inhibitory effect on the H-reflex (Fig. 3B). Rather, generation of rhythmic hand movements contributed to the observed increment of the lumbosacral motor pool’s excitability state.

The current data do not allow differentiating the contribution of descending supraspinal versus propriospinal influences from rhythmic hand movements on the lumbosacral motor circuitry. Likely, both pathways are important considering neural coupling between cervical and lumbosacral pattern generation circuitries [2,3,39] and an essential and more important role of the supraspinal motor areas in human walking than in animals [40]. The coordination between wrist and foot may involve a distributed network [16]. Whatever their relative impact on the observed increase of excitability of the lumbosacral motor pools (Figs. 1 and 2), the current results support the idea of active engagement of upper limb movements in developing CPG-modulating therapies [39]. For instance, arm movements may increase muscle activity in both paretic and nonparetic legs in stroke patients [41] or in individuals with incomplete spinal cord injury [42]. As compared with previous studies, our findings highlight the existence of neural connections between the distal parts of the upper and lower extremities, suggesting that wrist joint movements can be an important component of motor neurorehabilitation.

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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.neulet.2016.12.007>.

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