

Intramuscular Coherence of the Lower Flexor Muscles During Robotic Ankle-assisted Gait

Kei Nakagawa

Hiroshima University

Naoto Kadono

Hiroshima University

Takafumi Mitsuhashi

Hiroshima University

Eiichiro Tanaka

Waseda University

Louis Yuge (✉ ryuge@hiroshima-u.ac.jp)

Division of Bio-Environmental Adaptation Sciences, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan

Research

Keywords: walking assistive robot, ankle, tibialis anterior muscle, intramuscular coherence, learning of gait

Posted Date: December 18th, 2020

DOI: <https://doi.org/10.21203/rs.3.rs-128352/v1>

License:  This work is licensed under a Creative Commons Attribution 4.0 International License.

[Read Full License](#)

Version of Record: A version of this preprint was published at Journal of Motor Behavior on September 24th, 2021. See the published version at <https://doi.org/10.1080/00222895.2021.1965527>.

1 **Intramuscular coherence of the lower flexor muscles during robotic ankle-assisted gait**

2 Kei Nakagawa¹, Naoto Kadono¹, Takafumi Mitsuhashi², Eiichiro Tanaka³, Louis Yuge¹

3

4 1. Division of Bio-Environmental Adaptation Sciences, Graduate School of Biomedical and
5 Health Sciences, Hiroshima University, Hiroshima, Japan

6 2. Department of Neurosurgery, Graduate School of Biomedical and Health Sciences, Hiroshima
7 University, Hiroshima, Japan

8 3. Graduate School of Information, Production and Systems, Faculty of Science and Engineering,
9 Waseda University, Kita-Kyushu, Japan

10

11

12 **Corresponding Author**

13 Dr. Louis Yuge, Ph.D.

14 Division of Bio-Environmental Adaptation Sciences, Graduate School of Biomedical and Health
15 Sciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima 734-8551, Japan.

16 Email: ryuge@hiroshima-u.ac.jp, Tel: 81-82-257-5425, Fax: 81-82-257-5344

17

18

19

1 **Abstract**

2 **Background:** A close-fitting assisted walking device (RE-Gait) designed to assist ankle
3 movements might be a novel approach for acquiring the forefoot rocker function in the gait cycle.
4 The purpose of the present study was to investigate the effects of using RE-Gait by evaluating the
5 intramuscular coherence (IMC) of the two parts of the tibialis anterior muscles (TA) in the initial,
6 mid, and terminal swing phase, which could indicate whether the common synaptic drive of motor
7 neurons was populated.

8 **Methods:** Seventeen healthy volunteers walked on a treadmill at a comfortable speed before,
9 during, and immediately after 15-minute RE-Gait intervention (pre / RG / post). RE-Gait
10 supported plantar flexion at toe lift-off in the terminal stance phase and dorsiflexion in the initial
11 swing phase. Electromyograms of the right lower leg and gait parameters were analyzed for each
12 session.

13 **Results:** After RE-Gait intervention, the step length was significantly increased. IMC of the two
14 parts of the TA muscles in the beta frequency band in the initial swing phase was significantly
15 enhanced during RE-Gait intervention compared with pre session. In addition, IMCs in the beta
16 and low-gamma frequency bands were significantly correlated with the enhancement ratio of the
17 step length.

18 **Conclusions:** These results suggest that robotic ankle planter flexion and dorsiflexion assistance

1 in the pre- and initial swing phase would be effective for learning adaptively modified walking
2 by activating corticospinal tracts. RE-Gait will be a useful tool for re-learning of gait with smooth
3 switching with appropriate forefoot rocker function.

4

5 **Key words:** walking assistive robot; ankle; tibialis anterior muscle; intramuscular coherence;
6 learning of gait

7

8

9

1 **Introduction**

2 Walking in humans depends on the integrated hierarchical activities of supraspinal and spinal
3 neural controls, including the primary motor cortex and corticospinal tract [1-6]. The corticospinal
4 inputs are critical for foot flexor muscle activities in the initial swing phase of the gait cycle, while
5 they have little effect on the extensor muscles [1, 3, 4]. A recent study demonstrated that gait-
6 combined rhythmic brain stimulation over the primary motor cortex in the swing phase could alter
7 neuroplasticity in the corticospinal pathways and enhance gait performance [7]. The required
8 corticospinal inputs are, however, impaired in patients with central nervous system disorders [8,
9 9].

10 From the pre-swing to the initial swing phase of the gait, the forefoot rocker function plays a
11 crucial role in smooth energy utilization, generating plantar flexion torque in the pre-swing phase
12 and switching dorsiflexion movement. Smooth switching is essential for efficient walking;
13 however, we cannot provide enough assistance for the forefoot rocker function using manual
14 support alone. To address this, robotic walking rehabilitation devices have been developed. A
15 close-fitting assisted walking device (RE-Gait; Space Bio-Laboratories Co., Ltd, Hiroshima,
16 Japan) designed to assist ankle dorsiflexion and plantar flexion movements [10] might be an
17 effective approach for supporting the forefoot rocker function. Our previous studies revealed that
18 short-term use of RE-Gait enhanced step length [10, 11] and modulated spinal cord excitability

1 [11]. Continuous use of RE-Gait might be effective for re-learning of gait with smooth switching.

2 However, there is currently insufficient neurophysiological evidence to support this effect.

3 In addition to background electromyographic (EMG) recordings of the lower legs, intramuscular

4 coherence (IMC) analysis of the paired electromyographic recordings has previously been utilized

5 to evaluate corticospinal function during walking [1, 12-17]. IMC in the alpha, beta, and low-

6 gamma frequency bands are thought to reflect coupling of motor unit activities that originate from

7 common cortical sources. Therefore, IMC from the two parts of the tibialis anterior (TA) muscles

8 can indicate whether the common synaptic drive of TA motor neurons is populated in the swing

9 phase of the gait cycle.

10 In clinical studies, coupling of motor unit activities in the 10- to 20-Hz frequency band of the

11 two parts of the TA muscles was severely reduced in patients with spinal cord injuries (SCI),

12 suggesting that motor unit synchrony during walking depends on an intact supraspinal drive to

13 the spinal cord [18]. Similar findings were reported in the paralyzed lower legs of hemiplegic

14 patients [16]. Children with cerebral palsy showed reductions in beta and low-gamma band

15 coherence [19, 20], but this improved after four weeks of gait training [20] and also reflected

16 improved maturation of ankle control [21]. These findings support the view that a loss of IMC

17 during walking is associated with a deficit in motor drive from the corticospinal tract.

18 The aim of the present study was to investigate the effects of RE-Gait by evaluating

- 1 corticospinal function in the swing phase of the gait using background EMG and IMC analysis of
- 2 the two parts of the TA muscles.

1 **Methods**

2 **Participants**

3 Seventeen healthy volunteers (age 25.7 ± 6.3 years, 8 women) participated in the present study.
4 None of the participants had a history of neurological or orthopedic disorders. This study was
5 approved in advance by the Ethical Committee for Epidemiology of Hiroshima University in
6 accordance with the Declaration of Helsinki, and written consent was obtained from all
7 participants.

8
9 **RE-Gait**

10 RE-Gait is a close-fitting assisted walking device shaped like an ankle-foot orthosis. It weighs 1
11 kg, and is easy to wear (Fig. 1A). It decodes the gait cycle by using two pressure sensors located
12 at the toe and heel, and a geared motor assists ankle movement, which can control angular velocity
13 in each gait cycle at the preferred timing. In the present study, the participants wore RE-Gait on
14 their right leg, and the parameter of the assist was set to aid their forefoot rocker function; plantar
15 flexion torque was applied at toe lift-off in the pre-swing phase (50-60% of the gait cycle), and
16 dorsiflexion torque was applied in the initial swing phase (60-80% of the gait cycle) (Fig. 1B).
17 The length of the gait cycle was measured before the experiment, and was set individually.

18

1

2 **Experimental protocols**

3 EMG of the right lower leg was recorded before, during, and immediately after a 15-minute
4 RE-Gait intervention (pre / RG / post). For each session, participants were asked to walk on a
5 treadmill at their comfortable speed (2.0-3.3 km/h), which was measured before the experiment.
6 The speed was constant across the three sessions. The pre and post sessions lasted five minutes,
7 with the first two minutes serving as a warm-up. The last three minutes of each session were used
8 for analysis.

9 EMG was recorded by single differential surface electrodes (FAD-SEMG1: 4Assist, Inc, Tokyo,
10 Japan) during walking. The electrodes were placed on the proximal and distal ends of the tibialis
11 anterior muscles (TAp, TAd; 8-10 cm distance between the two sets of electrodes). The EMG
12 signals were amplified (x100) with an EMG amplifier system (FAD-ABOX8, 4Assist, Inc), and
13 digitized at 1000 Hz using a Power Lab system (PowerLab8/35, AD Instruments, Australia). To
14 identify the gait cycle, foot sensors (FA-DL-250: 4Assist, Inc) were located on the heel and
15 forefoot of the right foot.

16 The movement of the right leg was also recorded from the sagittal plane using a digital video
17 camera during each session (frame rate=30 fps).

18

1 Analysis

2 The EMG data were band-pass filtered at 10-200 Hz and rectified for off-line analysis with
3 LabChart v.8.1.12 (AD Instruments). We defined the gait cycle by identifying two consecutive
4 heel contacts, and time-normalized and rectified the EMG signals into 100 data points for each
5 gait cycle. The EMG signals were averaged over the gait cycle for each muscle and each
6 participant. Epochs with motion artifacts were excluded from averaging. The averaged EMG data
7 were divided into seven phases as follows: initial loading (0-12% of the gait cycle), mid stance
8 (12-30%), terminal stance (30-50%), pre swing (50-62%), initial swing (62-75%), mid swing (75-
9 87%), and terminal swing phase (87-100%), in accordance with some previous studies [22, 23].

10 The correlations between the EMG signals were assessed with IMC functions [14]. As rectified
11 EMG signals have been shown to enhance test-retest reliability[17], we used the rectified EMG
12 signals of the TAp and TAd muscles. Because remarkable IMC was previously detected in the
13 initial and terminal swing phase [13], we analyzed IMC by dividing the swing phase into initial,
14 mid, and terminal parts. The frequency-domain analyses were performed based on previous
15 studies [6, 12-18, 20, 21]. The IMC between the two rectified EMG signals (x and y) at frequency
16 (λ) was defined as:

$$17 \quad |R_{xy}(\lambda)|^2 = |f_{xy}(\lambda)|^2 / f_{xx}(\lambda) f_{yy}(\lambda)$$

18 where $f_{xx}(\lambda)$ and $f_{yy}(\lambda)$ represent values of auto spectra, and $f_{xy}(\lambda)$ represents values of cross

1 spectra, calculated with a discrete Fourier transformation. The IMC function ($|R_{xy}(\lambda)|^2$) provides
2 normative measures of linear association on a scale from 0 to 1 in the frequency domain, where
3 1 indicates a perfect linear correlation. Meaningful coherence was defined when the values
4 exceeded a confidence limit (CL) with a probability of 95% ($\alpha=0.05$). CL was calculated as
5 follows:

$$6 \quad CL=1-\alpha^{1/(N-1)}$$

7 where N represents the number of analyzed segments.

8 In the time domain analysis, estimates of cumulant density function were used to characterize
9 the correlation as follows:

$$10 \quad q_{xy}(u)=\int f_{xy}(\lambda) e^{i\lambda u} d\lambda$$

11 where $q_{xy}(u)$ is the cumulant density function defined as the inverse Fourier transform of the cross
12 spectrum. The dominant feature is that the cumulant density reflects the presence of common
13 synaptic input.

14 To evaluate the coherence variables, the areas between the coherence spectrum and the CLs of
15 the alpha (10-15 Hz), beta (15-30 Hz), and low-gamma (30-45 Hz) frequency bands in the initial,
16 mid, and terminal swing phase were examined. The IMC analyses were performed using
17 Neurospec 2.0 (<http://www.neurospec.org/>) and MATLAB R2019b (MathWorks, Inc) software.

18 The gait parameters were assessed from the step length and trailing limb angle (TLA). The

1 right and left step lengths were obtained from as the anterior-posterior distance between both
2 heels at the moment of initial contact phase. TLA was defined as the angle between the vertical
3 axis and the vector joining the greater trochanter with the fifth metatarsal head at the moment of
4 toe-off phase. They were analyzed from 10 gait cycles in each session by using Image J software
5 (<https://imagej.nih.gov/ij/>).

6 In addition, the enhancement of step length on the right leg after RE-Gait intervention (Δ step)
7 was calculated respectively as follows:

$$8 \quad \Delta\text{step} = \frac{\text{step length (post)} - \text{step length (pre)}}{\text{step length (post)} + \text{step length (pre)}}$$

9

10 The step length was compared using a two-way repeated ANOVA (3 sessions \times right and left
11 legs), and TLA was compared using a one-way repeated ANOVA. Each EMG activity and the
12 areas of IMC in the alpha, beta, and low-gamma frequency bands were compared using one-way
13 repeated ANOVA among the three sessions (pre, RG, and post). Post-hoc analyses were carried
14 out where appropriate to compare differences in the sessions using paired *t*-tests with
15 Bonferroni's correction. To determine the association between the behavioral and
16 neurophysiological data, the correlation between Δ step and the area of IMC in each frequency
17 band in RG session was also calculated. The level of significance was set at $p < 0.05$ for each

1 analysis. All statistical analyses were carried out using the JMP software (version 15, IBM, New
2 York, U.S.A.).

3 **Results**

4 All participants could perform the intervention without stumbling or feeling strong fatigue.

5 A two-way repeated ANOVA (3 sessions (pre, RG, post) \times 2 legs (right and left)) revealed a
6 significant difference in the step length among the sessions ($F(2, 80)=16.56, p<0.001$), whereas
7 no significant differences were found between legs ($F(1, 80)=2.93, p=0.09$) or in the interaction
8 between the two factors ($F(2, 80)=0.85, p=0.43$). Post-hoc tests revealed that the step length of
9 the RG session was significantly longer than that of the pre session for both legs ($p<0.01$), and
10 that of the post session was significantly longer than that of the pre session for the right leg
11 ($p<0.05$) (Fig. 2A). This tendency was in agreement with our previous study, in which RG
12 intervention was effective for the enhancement of step length [10, 11].

13 Significant difference was also revealed in TLA ($F(2, 32)=13.62, p<0.001$). Post-hoc test showed
14 that of the RG session was significantly increased compared to the pre ($p<0.01$) and post ($p<0.05$)
15 session, and that of the post session was increased than the pre session ($p<0.05$) (Fig. 2B).

16 The pooled EMG activities of the right TA muscles are shown in Fig. 3. The EMG patterns
17 were not different among the three sessions, but the RG session showed unique features during
18 the swing phase. TA activities tended to be higher in the initial swing phase, but lower in the

1 terminal swing phase and initial loading phases. The TAd activities were significantly increased
2 compared with the post session ($p<0.05$). In contrast, the pre and post session EMG activities
3 were not different.

4 IMC between the two parts of the TA muscles were analyzed to investigate the effects of the
5 cortico-spinal function in the swing phase. The averaged IMC from all participants in the initial,
6 mid, and terminal swing phase are shown in Fig. 4. Each IMC was obtained from restricted
7 frequency bands in all participants without high coherence across the frequency bands, which
8 means that crosstalk did not affect the data [18, 24]. IMC for frequency ranges of 10-40 Hz were
9 enhanced in the initial swing phase in the RG session. The areas of IMC in the beta frequency
10 band were significantly different in the initial swing phase (alpha: $F(2,32)=2.22$, $p=0.12$, beta:
11 $F(2,32)=3.40$, $p<0.05$, low-gamma: $F(2,32)=0.45$, $p=0.64$). Post hoc test revealed that the RG
12 session significantly enhanced the IMC in the beta band compared with the pre session ($p<0.05$).
13 In contrast, there were no significant differences in the mid (alpha: $F(2,32)=1.12$, $p=0.34$, beta:
14 $F(2,32)=1.41$, $p=0.26$, low-gamma: $F(2,32)=1.37$, $p=0.27$) and terminal swing phase (alpha:
15 $F(2,32)=2.30$, $p=0.12$, beta: $F(2,32)=0.09$, $p=0.91$, low-gamma: $F(2,32)=0.06$, $p=0.94$) in each
16 frequency band.

17 Comparing the behavioral and neurophysiological data, a significant correlation was found
18 between the enhancement ratio of the right step length after RE-Gait intervention (Δ step) and

- 1 IMC in the beta and low-gamma frequency bands in the RG session (alpha: $r=0.41$, $p=0.11$, beta:
- 2 $r=0.56$, $p=0.018$, low-gamma: $r=0.54$, $p=0.025$) (Fig. 5)..

1 **Discussion**

2 This is the first study to assess EMG activities and IMC of the two parts of the TA muscles
3 during a robot-supported gait using an ankle assistive device, RE-Gait. We revealed that IMC in
4 the beta frequency band of the two parts of the TA muscles in the initial swing phase was
5 significantly enhanced by using RE-Gait. In addition, the amplitudes of IMC in the beta and low-
6 gamma frequency bands during RE-Gait intervention were correlated with the enhancement ratio
7 of the step length. These results suggest that robotic ankle planter flexion and dorsiflexion
8 assistance in the pre- and initial swing phase would be effective for learning an adaptively
9 modified gait by activating the corticospinal tracts.

10 After 15-minute RE-Gait intervention, step lengths on both sides were significantly extended.
11 This finding was consistent with our previous studies [10, 11]. We consider this might be due to
12 better toe clearance after the intervention resulting from smooth energy utilization by generating
13 plantar-flexion and dorsiflexion torque. It was supported by the enhancement of TLA during and
14 after the intervention. TLA was mainly contributed to the increase in propulsion force [25], and
15 correlated with step length and walking speed [26]. A previous study suggested that gait retraining
16 in the chronic phase of stroke recovery were related to the propulsive force on paretic limb in the
17 neuromotor recovery [27]. By inducing the plantar flexion torque in the pre-swing phase, the
18 potential energy for lifting the heel was generated, and subsequent dorsiflexion torque in the initial

1 swing phase might support smooth replacement with the kinetic energy.

2 A characteristic EMG pattern was observed during RE-Gait intervention. TA activation tended
3 be smaller in the terminal swing and initial loading phases, but was obviously enhanced in the
4 initial swing phase. Several previous studies have suggested that robot-assisted walking is
5 associated with lower levels of muscle activities [22, 28], and increasing body weight support and
6 guidance force decreased the activity of specific muscles during robot assisted walking [29],
7 which means that the robotic devices could facilitate movement control of the legs by reducing
8 muscle loads. The decrement in the TA activities related to initial heel strike in the present study
9 could reflect a similar effect of robotic support. That is, the ankle dorsiflexion support and heel
10 rocker support from the exoskeleton could produce a clear heel strike with a small TA muscle load
11 from eccentric contraction.

12 In contrast, TA activity in the initial swing phase was enhanced in the RG session. Notably,
13 IMC in the beta frequency band of the two parts of the TA muscles was significantly increased
14 compared with the pre session.

15 IMC analysis is a helpful tool to evaluate the corticospinal pathway in walking [6, 12-18, 20,
16 21]. The test-retest reliability was recently confirmed, indicating that beta-band IMC is a reliable
17 method to assess corticospinal control of gait in young subjects [30]. In addition, IMC was higher
18 in young subjects than older subjects [31]. Therefore, the frequency-dependent IMC changes of

1 young participants in the present study would be reliable.

2 Some previous studies have reported a linkage between the IMC and behavioral deficits. One
3 study demonstrated a positive correlation between the IMC of the two parts of the TA muscles
4 and highest toe elevation in SCI patients [12]. Another showed a significant correlation between
5 gait speed and IMC on the paretic side in hemiplegic patients [15]. Lower step-to-step variability
6 in the swing phase was positively correlated with IMC in healthy children [32]. These studies
7 suggest that IMC would reflect the corticospinal control of ankle movement and ambulatory
8 function.

9 During visual guided walking with visual feedback, IMC was significantly enhanced compared
10 with normal treadmill walking [31, 33]. In split-belt treadmill training, IMC was increased during
11 the initial adaptation stage. Interestingly, a significant correlation was found between IMC in the
12 initial adaptation stage and the double support symmetry ratio, implying that IMC might be a
13 predictor for locomotor adaptation [34]. In the present study, we also observed an IMC increment
14 in the initial swing phase during RE-Gait intervention, which indicates that the participants
15 required corticospinal activity to control ankle lifting even with the assistance of RE-Gait. In other
16 words, the aid can be a useful intervention for learning adaptively modified walking. This
17 possibility was supported by the significant correlation between the area IMC in the beta and low-
18 gamma frequency band and the enhancement ratio of the step length after the intervention. In

1 addition, significant changes of IMC were observed in the initial swing phase but not in the mid
2 and terminal phases, which matched the timing of the assistance.

3 A significant IMC increment during RE-Gait intervention was found in the beta frequency band,
4 and a significant correlation between the behavioral and neurophysiological results was found in
5 the beta and low-gamma frequency bands. These frequency-dependent IMC changes might be
6 explained by the neural origin of the IMC. Beta band oscillatory activation of the sensorimotor
7 cortex (SMC) plays a key role in motor control [35], and beta band IMC is thought to originate
8 from the SMC [36, 37]. The low-gamma band also indicates corticospinal activity, which is
9 clearly observed during voluntary muscle contractions [38]. On the other hand, the neural origin
10 of the alpha band oscillatory activity is debated; it is considered to reflect a different mechanism
11 from the beta and low-gamma bands, because cortico-muscular coherence is absent in the alpha
12 band[32, 39, 40]. IMC was found in the restricted lower-frequency band in patients after complete
13 SCI, suggesting that the origin is likely to be spinal [41]. Subcortical activities including the
14 cerebellum may contribute to alpha oscillatory coherence [37].

15 The present study had several limitations. First, the study was conducted on healthy participants.
16 Compared with healthy participants, patients with central nervous system disorders have lower
17 IMCs associated with deficits in motor drive during their gait [12, 15, 16]. Although only a small
18 number of studies have been reported, gait training increased the IMC in children with cerebral

1 palsy[20]. Further studies are needed to investigate the effects of RE-Gait intervention for patients.
2 Second, our study did not directly measure corticospinal function (e.g., magnetic evoked
3 potentials, cortico-muscular coherence) in parallel with IMC. IMC indicates not only the
4 corticospinal drive, but also signals from other cortical areas including inhibitory signals [42].
5 Because not only the cortico-spinal tracts are involved in gait control [43], but the effects on other
6 signals should also be considered in future studies.

7

8

9 **Conclusion**

10 Robotic ankle planter flexion and dorsiflexion assistance in the pre- and initial swing phase
11 would be effective for learning adaptively modified walking by activating corticospinal tracts.
12 RE-Gait will be a useful tool for re-learning of gait with smooth switching with appropriate
13 forefoot rocker function.

14

15

1 **List of abbreviations**

2 ANOVA, analysis of variance

3 CL, confidence limit

4 EMG, electromyogram

5 IMC, intramuscular coherence

6 SCI, spinal cord injuries

7 TA, tibialis anterior muscle

8 TAd, distal part of tibialis anterior muscle

9 TAp, proximal part of tibialis anterior muscle

10 TLA, trailing limb angle

11 RG, RE-Gait

12

13 **Ethics approval and consent to participate**

14 This study was approved in advance by the Ethical Committee for Epidemiology of Hiroshima

15 University (E-2096) in accordance with the Declaration of Helsinki, and written consent was

16 obtained from all participants.

17

18 **Consent for publication**

1 Written informed consent for publication was obtained from all the participants.

2

3 **Availability of data and materials**

4 The datasets used and/or analyzed during the current study are available from the corresponding
5 author on reasonable request.

6

7 **Competing interests**

8 LY is a director of Space Bio-Laboratories Co., Ltd, but did not contribute to measurement and
9 analysis of the data. The potential conflicts of interest associated with this study have been
10 approved by the Conflict of Interest Management Committee of Hiroshima University. By
11 regularly reporting research progress to the Conflicts of Interest Management Committee, we
12 will maintain fairness regarding the interests of this study.

13

14 **Funding**

15 Not applicable.

16

17 **Authors' contributions**

1 KN and NK made substantial contributions to experimental design, data collection, data
2 analysis and drafting the manuscript. TM, ET and LY critically reviewed the manuscript. All
3 authors have read and approved the final manuscript.

4

5 **Acknowledgements**

6 We thank all of the subjects for their voluntary participation in the present study.

7

8

9

10

11

1 **Figure Captions**

2 **Fig.1** RE-Gait. (A) RE-Gait close-fitting type assisted walking device resembling an ankle-foot
3 orthosis. Dimensions: 300 mm (W) ×140 mm (D) ×365 mm (H)/ aluminum base alloy/ 1,000 g,
4 control box: 900 g. (B) Schema of RE-Gait assistance. The graph shows the setting of the ankle
5 movement assisted by RE-Gait. Timing and angular velocity are controlled to assist forefoot
6 rocker function.

7
8 **Fig.2** Gait parameters. (A) The averaged data of the step length of the right leg (filled circles) and
9 left leg (open circles). (B) The averaged data of TLA. Data represent the mean ± standard error.
10 * p<0.05, ** p<0.01.

11

12 **Fig.3** EMG activities. (A) Pooled EMG activities of the right leg during the gait cycle. The black
13 and grey areas represent mean EMG amplitude and standard deviations. (B) Averaged EMG
14 activities of the seven gait phases. The blue, red, and yellow bars indicate the pre, RG, and post
15 sessions, respectively. Each bar represents the mean values averaged over all participants, and the
16 standard errors are represented by error bars. IL: initial loading, MSt: mid-stance, TSt: terminal
17 stance, PSw: pre swing, ISw: initial swing, MSw: mid-swing, TSw: terminal swing phase. TAp:
18 proximal part of tibialis anterior muscles, TAd: distal part of tibialis anterior muscles. * p<0.05

1

2 **Fig.4** IMC of the paired TA muscles. (A-C) Pooled IMC of the paired TA muscles in frequency
3 domain during each swing phase of the pre (blue), RG (red), and post (yellow) sessions. The
4 horizontal dashed lines indicate the pooled 95% confidence limit of coherence in each walking
5 condition. Data are shown as mean±standard error. (D-F) Pooled cumulant density function in
6 time domain of the pre (blue), RG (red), and post (yellow) sessions. (G-I) Comparisons of the
7 IMC area under the coherence curve in each frequency band. The blue, red, and yellow bars
8 indicate pre, RG, and post respectively. Data are the mean values averaged over all participants,
9 and the standard errors are represented by error bars. * p<0.05

10

11 **Fig.5** Correlation between the step length and IMC. The graph shows the correlation between the
12 enhancement ratio of the right step length after the RG intervention (Δ step) and IMC in each
13 frequency band in the RG session.

14

15

References

1. Capaday C, Lavoie BA, Barbeau H, Schneider C, Bonnard M: **Studies on the corticospinal control of human walking. I. Responses to focal transcranial magnetic stimulation of the motor cortex.** *Journal of neurophysiology* 1999, **81**(1):129-139.
2. la Fougère C, Zwergal A, Rominger A, Förster S, Fesl G, Dieterich M, Brandt T, Strupp M, Bartenstein P, Jahn K: **Real versus imagined locomotion: a [18F]-FDG PET-fMRI comparison.** *NeuroImage* 2010, **50**(4):1589-1598.
3. Petersen NT, Butler JE, Marchand-Pauvert V, Fisher R, Ledebt A, Pyndt HS, Hansen NL, Nielsen JB: **Suppression of EMG activity by transcranial magnetic stimulation in human subjects during walking.** *The Journal of physiology* 2001, **537**(Pt 2):651-656.
4. Schubert M, Curt A, Jensen L, Dietz V: **Corticospinal input in human gait: modulation of magnetically evoked motor responses.** *Experimental brain research* 1997, **115**(2):234-246.
5. Barthélemy D, Grey MJ, Nielsen JB, Bouyer L: **Involvement of the corticospinal tract in the control of human gait.** *Progress in brain research* 2011, **192**:181-197.
6. Nielsen JB: **How we walk: central control of muscle activity during human walking.** *The Neuroscientist : a review journal bringing neurobiology, neurology and psychiatry* 2003, **9**(3):195-204.
7. Koganemaru S, Mikami Y, Maezawa H, Matsushashi M, Ikeda S, Ikoma K, Mima T: **Anodal transcranial patterned stimulation of the motor cortex during gait can induce activity-dependent corticospinal plasticity to alter human gait.** *PloS one* 2018, **13**(12):e0208691.
8. Cacchio A, Paoloni M, Cimini N, Mangone M, Liris G, Aloisi P, Santilli V, Marrelli A: **Reliability of TMS-related measures of tibialis anterior muscle in patients with chronic stroke and healthy subjects.** *Journal of the neurological sciences* 2011, **303**(1-2):90-94.
9. Miyai I, Yagura H, Oda I, Konishi I, Eda H, Suzuki T, Kubota K: **Premotor cortex is involved in restoration of gait in stroke.** *Annals of neurology* 2002, **52**(2):188-194.
10. Tanaka E, Watanuki K, Saegusa S, Yuge L: **Walking assistance apparatus enabled for neurorehabilitation of patients and its effectiveness.** *Mechanical Engineering Letters* 2015, **1**:1-7.
11. Nakagawa K, Tomoi M, Higashi K, Utsumi S, Kawano R, Tanaka E, Kurisu K, Yuge L: **Short-term effect of a close-fitting type of walking assistive device on spinal cord reciprocal inhibition.** *Journal of clinical neuroscience : official journal of the Neurosurgical Society of Australasia* 2020, **77**:142-147.
12. Barthélemy D, Willerslev-Olsen M, Lundell H, Conway BA, Knudsen H, Biering-Sorensen F, Nielsen JB: **Impaired transmission in the corticospinal tract and gait disability in spinal cord injured persons.** *Journal of neurophysiology* 2010, **104**(2):1167-1176.

- 1 13. Halliday DM, Conway BA, Christensen LO, Hansen NL, Petersen NP, Nielsen JB: **Functional**
2 **coupling of motor units is modulated during walking in human subjects.** *Journal of*
3 *neurophysiology* 2003, **89**(2):960-968.
- 4 14. Halliday DM, Rosenberg JR, Amjad AM, Breeze P, Conway BA, Farmer SF: **A framework for**
5 **the analysis of mixed time series/point process data--theory and application to the**
6 **study of physiological tremor, single motor unit discharges and electromyograms.** *Prog*
7 *Biophys Mol Biol* 1995, **64**(2-3):237-278.
- 8 15. Kitatani R, Ohata K, Aga Y, Mashima Y, Hashiguchi Y, Wakida M, Maeda A, Yamada S:
9 **Descending neural drives to ankle muscles during gait and their relationships with**
10 **clinical functions in patients after stroke.** *Clinical neurophysiology : official journal of the*
11 *International Federation of Clinical Neurophysiology* 2016, **127**(2):1512-1520.
- 12 16. Nielsen JB, Brittain JS, Halliday DM, Marchand-Pauvert V, Mazevet D, Conway BA:
13 **Reduction of common motoneuronal drive on the affected side during walking in**
14 **hemiplegic stroke patients.** *Clinical neurophysiology : official journal of the International*
15 *Federation of Clinical Neurophysiology* 2008, **119**(12):2813-2818.
- 16 17. van Asseldonk EH, Campfens SF, Verwer SJ, van Putten MJ, Stegeman DF: **Reliability and**
17 **agreement of intramuscular coherence in tibialis anterior muscle.** *PloS one* 2014,
18 **9**(2):e88428.
- 19 18. Hansen NL, Conway BA, Halliday DM, Hansen S, Pyndt HS, Biering-Sørensen F, Nielsen JB:
20 **Reduction of common synaptic drive to ankle dorsiflexor motoneurons during walking**
21 **in patients with spinal cord lesion.** *Journal of neurophysiology* 2005, **94**(2):934-942.
- 22 19. Petersen TH, Farmer SF, Kliim-Due M, Nielsen JB: **Failure of normal development of**
23 **central drive to ankle dorsiflexors relates to gait deficits in children with cerebral palsy.**
24 *Journal of neurophysiology* 2013, **109**(3):625-639.
- 25 20. Willerslev-Olsen M, Petersen TH, Farmer SF, Nielsen JB: **Gait training facilitates central**
26 **drive to ankle dorsiflexors in children with cerebral palsy.** *Brain : a journal of neurology*
27 2015, **138**(Pt 3):589-603.
- 28 21. Petersen TH, Kliim-Due M, Farmer SF, Nielsen JB: **Childhood development of common**
29 **drive to a human leg muscle during ankle dorsiflexion and gait.** *The Journal of*
30 *physiology* 2010, **588**(Pt 22):4387-4400.
- 31 22. Coenen P, van Werven G, van Nunen MP, Van Dieën JH, Gerrits KH, Janssen TW: **Robot-**
32 **assisted walking vs overground walking in stroke patients: an evaluation of muscle**
33 **activity.** *Journal of rehabilitation medicine* 2012, **44**(4):331-337.
- 34 23. Hidler JM, Wall AE: **Alterations in muscle activation patterns during robotic-assisted**
35 **walking.** *Clinical biomechanics (Bristol, Avon)* 2005, **20**(2):184-193.
- 36 24. Farmer SF, Bremner FD, Halliday DM, Rosenberg JR, Stephens JA: **The frequency content**

- 1 of common synaptic inputs to motoneurons studied during voluntary isometric
2 contraction in man. *The Journal of physiology* 1993, **470**:127-155.
- 3 25. Hsiao H, Knarr BA, Higginson JS, Binder-Macleod SA: **Mechanisms to increase propulsive**
4 **force for individuals poststroke.** *Journal of neuroengineering and rehabilitation* 2015,
5 **12**:40.
- 6 26. Tyrell CM, Roos MA, Rudolph KS, Reisman DS: **Influence of systematic increases in**
7 **treadmill walking speed on gait kinematics after stroke.** *Physical therapy* 2011,
8 **91**(3):392-403.
- 9 27. Hsiao H, Awad LN, Palmer JA, Higginson JS, Binder-Macleod SA: **Contribution of Paretic**
10 **and Nonparetic Limb Peak Propulsive Forces to Changes in Walking Speed in**
11 **Individuals Poststroke.** *Neurorehabilitation and neural repair* 2016, **30**(8):743-752.
- 12 28. van Kammen K, Boonstra AM, van der Woude LHV, Reinders-Messelink HA, den Otter R:
13 **Differences in muscle activity and temporal step parameters between Lokomat guided**
14 **walking and treadmill walking in post-stroke hemiparetic patients and healthy walkers.**
15 *Journal of neuroengineering and rehabilitation* 2017, **14**(1):32.
- 16 29. Lin J, Hu G, Ran J, Chen L, Zhang X, Zhang Y: **Effects of bodyweight support and guidance**
17 **force on muscle activation during Locomat walking in people with stroke: a cross-**
18 **sectional study.** *Journal of neuroengineering and rehabilitation* 2020, **17**(1):5.
- 19 30. Gennaro F, de Bruin ED: **A pilot study assessing reliability and age-related differences in**
20 **corticomuscular and intramuscular coherence in ankle dorsiflexors during walking.**
21 *Physiological reports* 2020, **8**(4):e14378.
- 22 31. Spedden ME, Choi JT, Nielsen JB, Geertsen SS: **Corticospinal control of normal and**
23 **visually guided gait in healthy older and younger adults.** *Neurobiology of aging* 2019,
24 **78**:29-41.
- 25 32. Petersen TH, Willerslev-Olsen M, Conway BA, Nielsen JB: **The motor cortex drives the**
26 **muscles during walking in human subjects.** *The Journal of physiology* 2012,
27 **590**(10):2443-2452.
- 28 33. Jensen P, Jensen NJ, Terkildsen CU, Choi JT, Nielsen JB, Geertsen SS: **Increased central**
29 **common drive to ankle plantar flexor and dorsiflexor muscles during visually guided**
30 **gait.** *Physiological reports* 2018, **6**(3).
- 31 34. Sato S, Choi JT: **Increased intramuscular coherence is associated with temporal gait**
32 **symmetry during split-belt locomotor adaptation.** *Journal of neurophysiology* 2019,
33 **122**(3):1097-1109.
- 34 35. van Wijk BC, Beek PJ, Daffertshofer A: **Neural synchrony within the motor system: what**
35 **have we learned so far?** *Frontiers in human neuroscience* 2012, **6**:252.
- 36 36. Fisher KM, Zaaimi B, Williams TL, Baker SN, Baker MR: **Beta-band intermuscular**

- 1 coherence: a novel biomarker of upper motor neuron dysfunction in motor neuron
2 disease. *Brain : a journal of neurology* 2012, 135(Pt 9):2849-2864.
- 3 37. Grosse P, Cassidy MJ, Brown P: **EEG-EMG, MEG-EMG and EMG-EMG frequency analysis:**
4 **physiological principles and clinical applications.** *Clinical neurophysiology : official*
5 *journal of the International Federation of Clinical Neurophysiology* 2002, 113(10):1523-
6 1531.
- 7 38. Kattla S, Lowery MM: **Fatigue related changes in electromyographic coherence between**
8 **synergistic hand muscles.** *Experimental brain research* 2010, 202(1):89-99.
- 9 39. Gwin JT, Ferris DP: **Beta- and gamma-range human lower limb corticomuscular**
10 **coherence.** *Frontiers in human neuroscience* 2012, 6:258.
- 11 40. Mima T, Hallett M: **Electroencephalographic analysis of cortico-muscular coherence:**
12 **reference effect, volume conduction and generator mechanism.** *Clinical*
13 *neurophysiology : official journal of the International Federation of Clinical*
14 *Neurophysiology* 1999, 110(11):1892-1899.
- 15 41. Norton JA, Wood DE, Marsden JF, Day BL: **Spinally generated electromyographic**
16 **oscillations and spasms in a low-thoracic complete paraplegic.** *Movement disorders :*
17 *official journal of the Movement Disorder Society* 2003, 18(1):101-106.
- 18 42. Nojima I, Watanabe T, Saito K, Tanabe S, Kanazawa H: **Modulation of EMG-EMG**
19 **Coherence in a Choice Stepping Task.** *Frontiers in human neuroscience* 2018, 12:50.
- 20 43. Sivaramakrishnan A, Madhavan S: **Absence of a Transcranial Magnetic Stimulation-**
21 **Induced Lower Limb Corticomotor Response Does Not Affect Walking Speed in Chronic**
22 **Stroke Survivors.** *Stroke* 2018, 49(8):2004-2007.

23
24
25
26
27
28
29
30
31
32
33
34
35

Figures

(A)



(B)

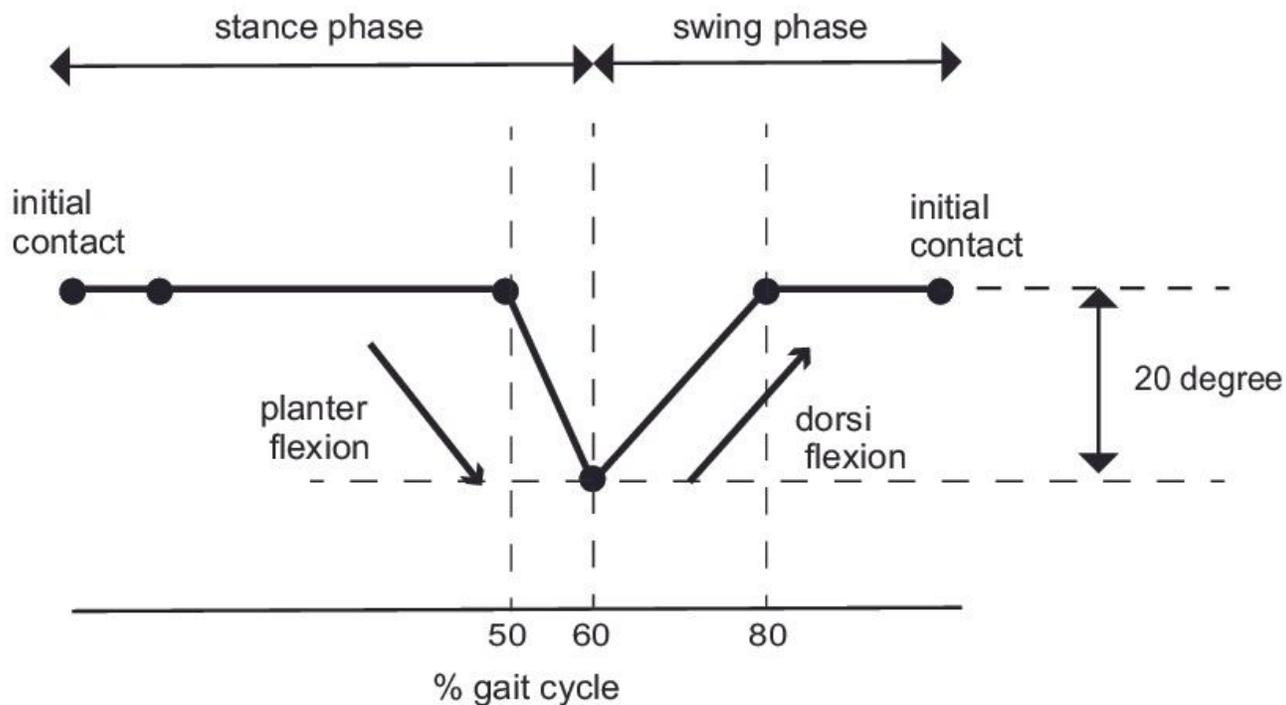


Figure 1

RE-Gait. (A) RE-Gait close-fitting type assisted walking device resembling an ankle-foot orthosis. Dimensions: 300 mm (W) × 140 mm (D) × 365 mm (H)/ aluminum base alloy/ 1,000 g, control box: 900 g. (B) Schema of RE-Gait assistance. The graph shows the setting of the ankle movement assisted by RE-Gait. Timing and angular velocity are controlled to assist forefoot rocker function.

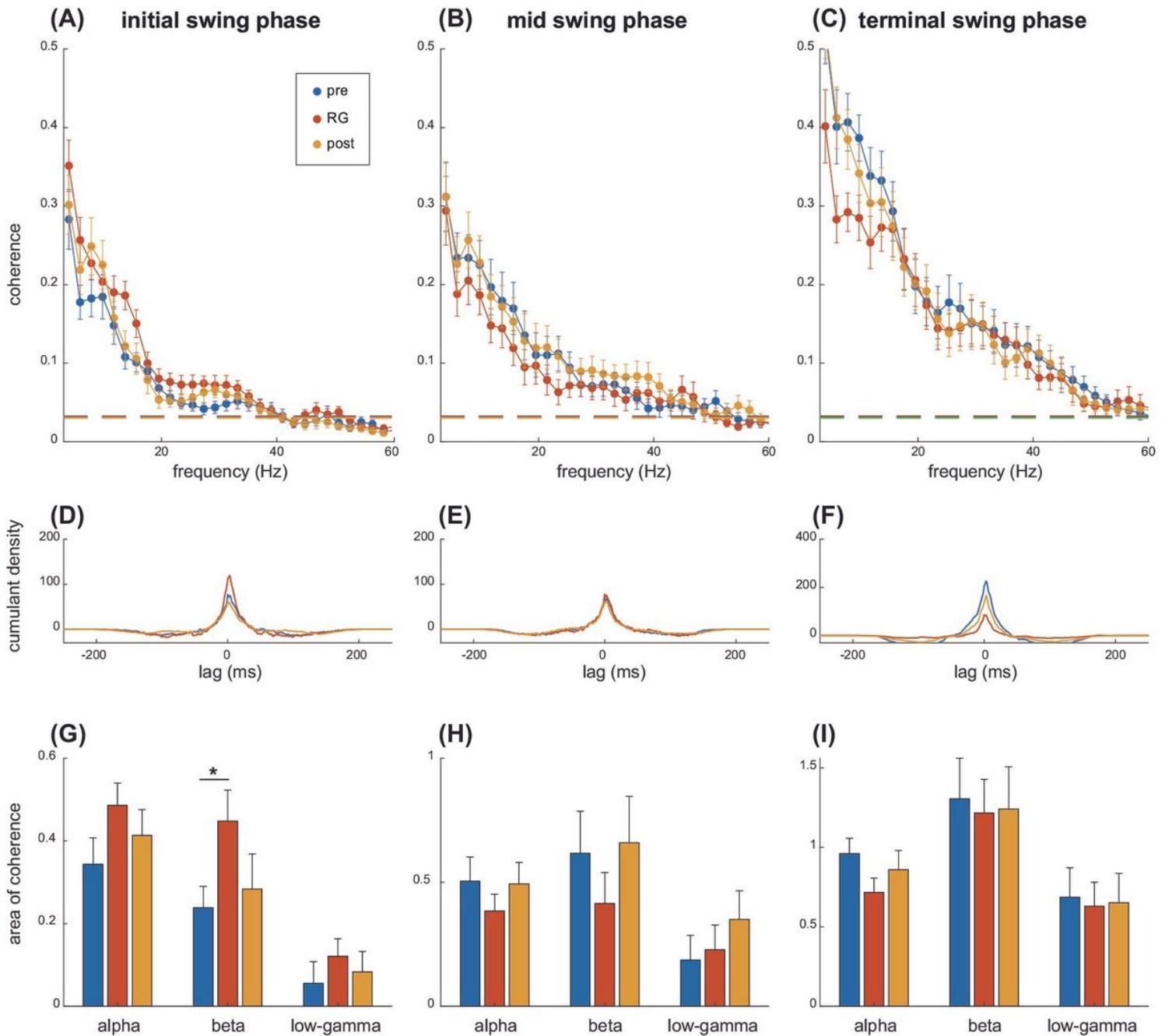


Figure 1

IMC of the paired TA muscles. (A-C) Pooled IMC of the paired TA muscles in frequency domain during each swing phase of the pre (blue), RG (red), and post (yellow) sessions. The horizontal dashed lines indicate the pooled 95% confidence limit of coherence in each walking condition. Data are shown as mean \pm standard error. (D-F) Pooled cumulant density function in time domain of the pre (blue), RG (red), and post (yellow) sessions. (G-I) Comparisons of the IMC area under the coherence curve in each frequency band. The blue, red, and yellow bars indicate pre, RG, and post respectively. Data are the mean values averaged over all participants, and the standard errors are represented by error bars. * $p < 0.05$

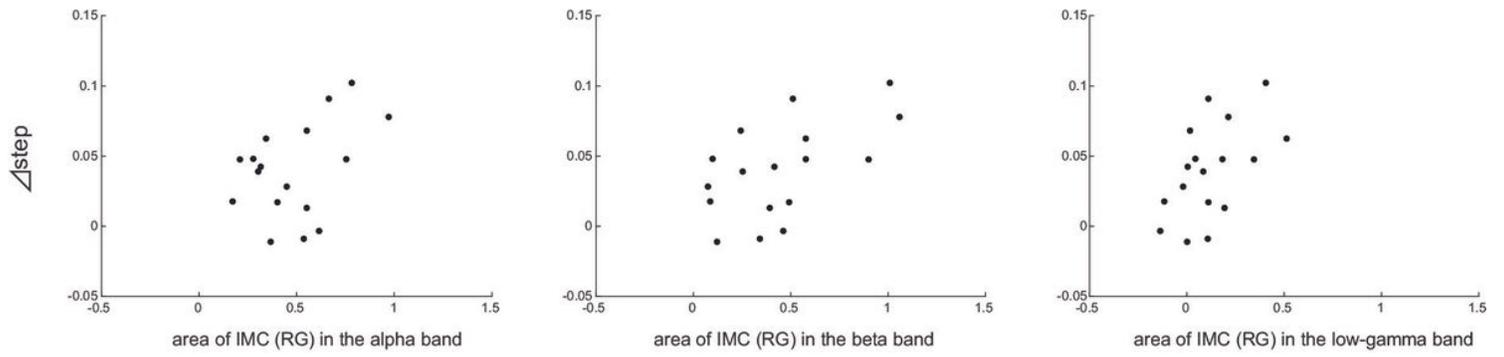
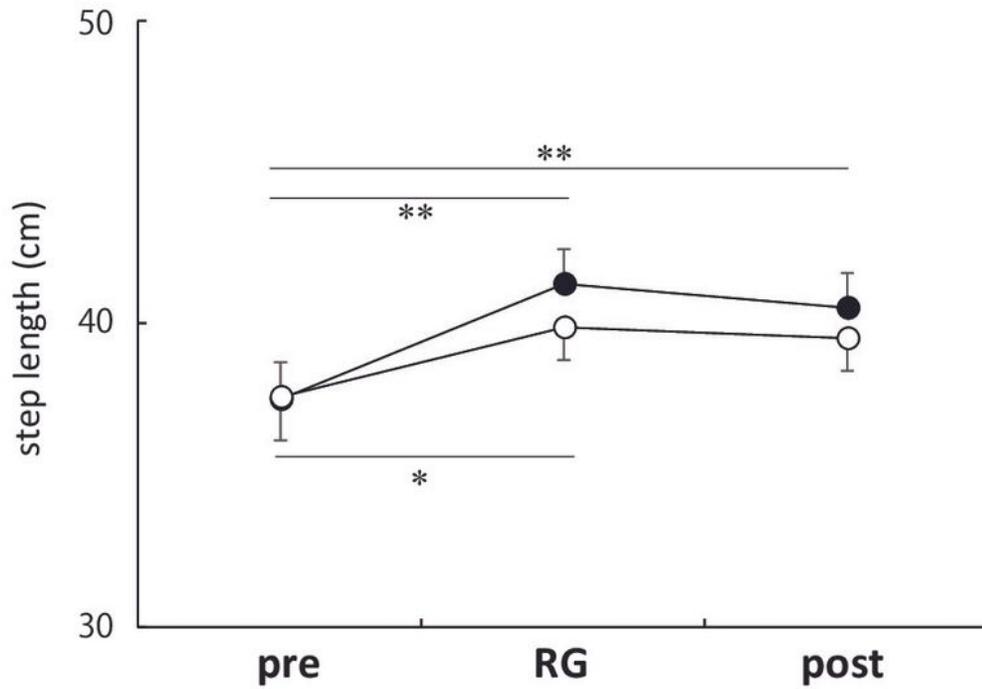


Figure 1

Correlation between the step length and IMC. The graph shows the correlation between the enhancement ratio of the right step length after the RG intervention (Δstep) and IMC in each frequency band in the RG session.

(A)



(B)

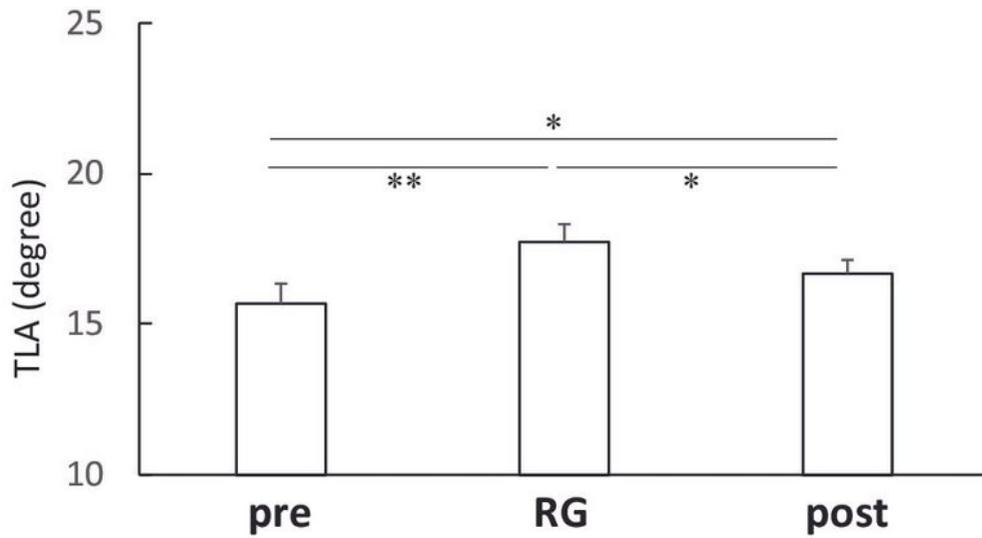


Figure 1

Gait parameters. (A) The averaged data of the step length of the right leg (filled circles) and left leg (open circles). (B) The averaged data of TLA. Data represent the mean \pm standard error. * $p < 0.05$, ** $p < 0.01$.

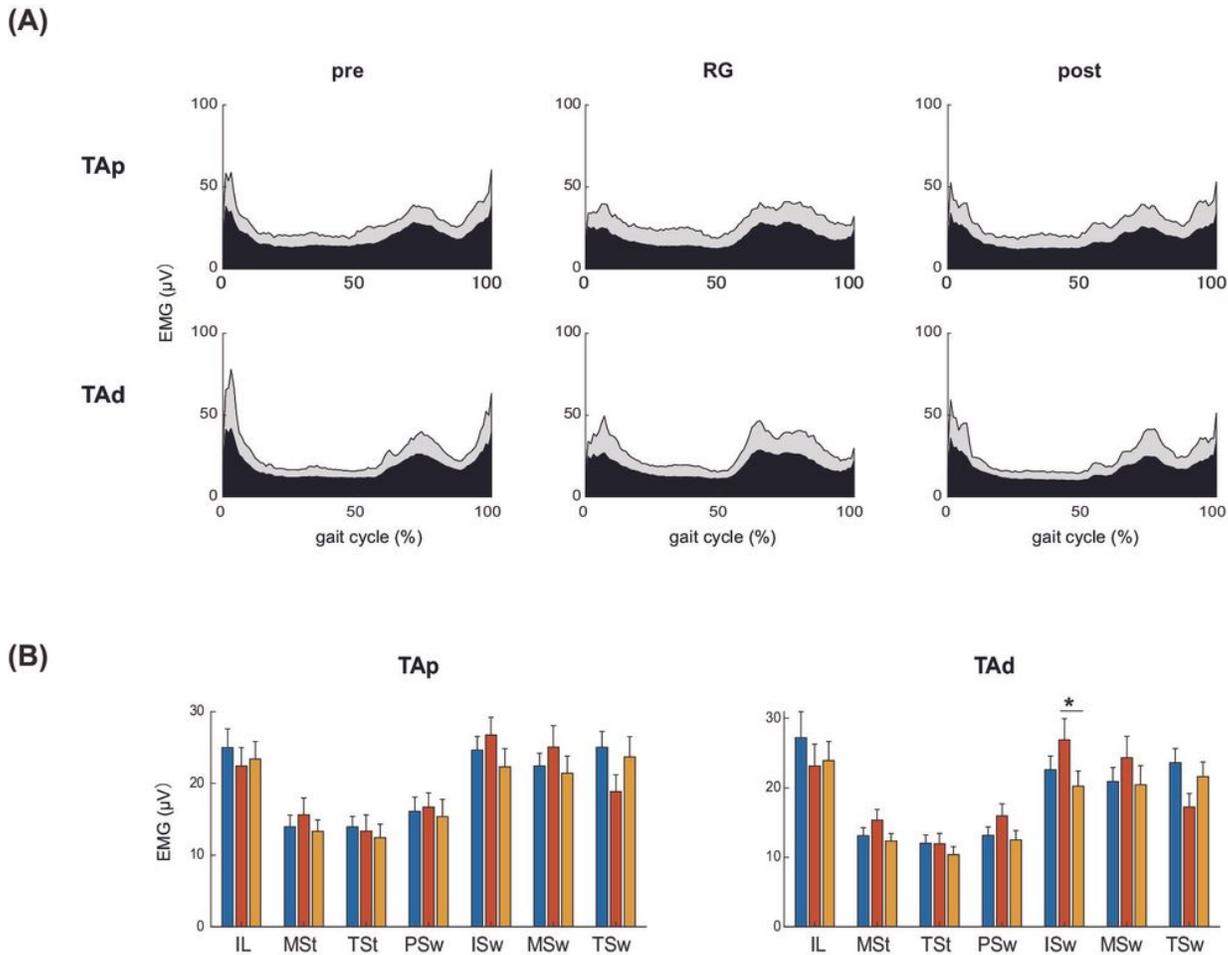


Figure 1

EMG activities. (A) Pooled EMG activities of the right leg during the gait cycle. The black and grey areas represent mean EMG amplitude and standard deviations. (B) Averaged EMG activities of the seven gait phases. The blue, red, and yellow bars indicate the pre, RG, and post sessions, respectively. Each bar represents the mean values averaged over all participants, and the standard errors are represented by error bars. IL: initial loading, MSt: mid-stance, TSt: terminal stance, PSw: pre swing, ISw: initial swing, MSw: mid-swing, TSw: terminal swing phase. TAp: proximal part of tibialis anterior muscles, TAd: distal part of tibialis anterior muscles. * $p < 0.05$