Descending neural drives to ankle muscles during gait and their relationships with clinical functions in patients after stroke
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Descending neural drives to ankle muscles during gait and their relationships with clinical functions in patients after stroke

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Highlights

- Descending neural drive to each muscle was reduced on the paretic side during gait.
- Neural drive to antagonist muscles was increased during gait in stroke patients.
- Increased drive to antagonist muscles was related to paretic ankle muscle weakness.

Abstract

Objective: The objective of this study was to investigate the descending neural drive to ankle muscles during gait in stroke patients using a coherence analysis of surface electromyographic (EMG) recordings and the relationships of the drive with clinical functions.

Methods: EMG recordings of the paired tibialis anterior (TA), medial and lateral gastrocnemius (MG and LG), and TA-LG muscles were used to calculate intramuscular, synergistic, and agonist-antagonist muscle coherence, respectively, in 11 stroke patients and 9 healthy controls. Paretic motor function, sensory function, spasticity, ankle muscle strength, and gait performance were evaluated.

Results: Paretic TA-TA and MG-LG beta band (15-30 Hz) coherences were significantly lower compared with the non-paretic side and controls. TA- LG beta band coherence was significantly higher on both sides compared with controls. Paretic TA-TA beta band coherence positively correlated with gait speed, and paretic TA-LG beta band coherence negatively correlated with paretic ankle plantar flexor muscle strength.

Conclusions: The intramuscular and synergistic muscle neural drives were reduced during gait on the paretic side in stroke patients. The agonist-antagonist muscle neural drive was increased to compensate for paretic ankle muscle weakness.

Significance: Descending neural drive reorganization to agonist-antagonist muscles is important for patients with paretic ankle muscle weakness.

Keywords: Coherence; Electromyography; Gait; Stroke; Muscle coactivation

1. Introduction

Gait is a fundamental component of human daily life. Patients who have suffered central nervous system (CNS) lesions that impair descending motor pathways have difficulty walking independently (Dietz et al., 1995; Jørgensen et al., 1995; Rossignol, 2000). Thus, walking in humans depends on the integrated action of hierarchical levels of supraspinal and spinal neural control (Nielsen, 2003; Yang and Gorassini, 2006), within which the contributions of the primary motor cortex and corticospinal tract are particularly important (Barthélemy et al., 2011; Petersen et al., 2012). Significant activation has been observed in the primary sensorimotor cortex (SMC) during gait in healthy human subjects using neuroimaging techniques (Fukuyama et al., 1997; Miyai et al., 2001; la Fougere et al., 2010). Previous transcranial magnetic stimulation studies have demonstrated that the corticospinal tract is rhythmically excited throughout the gait cycle (Schubert et al., 1997; Capaday et al., 1999; Petersen et al., 2001).

After stroke, patients exhibit asymmetrical SMC activation during gait due to the reduced SMC activation in the affected hemisphere (Miyai et al., 2002). More symmetric SMC activation and increased corticospinal excitability correlate with improvements in gait parameters after stroke rehabilitation (Miyai et al., 2003; Yen et al., 2008). These results suggest that increased SMC activation and corticospinal excitability in the affected hemisphere may play an important role in locomotor recovery after stroke. Therefore, a new clinically convenient technique that can assess the functional contribution of the SMC and that can be used as a surrogate marker of corticospinal control during gait in patients after stroke is needed.

Recent studies have suggested that coherence analyses of paired surface

electromyographic (EMG) recordings can quantitatively evaluate the descending neural drive from the SMC during gait (Halliday et al., 2003; Hansen et al., 2005; Norton and Gorassini, 2006; Nielsen et al., 2008; Barthélemy et al., 2010, 2015; Petersen et al., 2010, 2013; Willerslev-Olsen et al., 2015). Coherence analyses measure the linear correlation between a pair of signals in the frequency domain (Halliday et al., 1995), and the beta to gamma frequency bands are strongly related to the corticospinal drive (Conway et al., 1995; Mima and Hallett, 1999; Grosse et al., 2002; Petersen et al., 2012). EMG-EMG intramuscular and synergistic muscle coherences are observed in these frequency bands in healthy subjects (Farmer et al., 1993; Halliday et al., 2003), and they are reduced in patients with CNS disorders during static muscle contraction (Farmer et al., 1993; Fisher et al., 2012) and gait (Hansen et al., 2005; Nielsen et al., 2008; Barthélemy et al., 2010, 2015; Petersen et al., 2013). Furthermore, EMG-EMG beta band coherence can detect cortical excitability changes following transcranial direct current stimulation over the SMC (Power et al., 2006). Therefore, an EMG-EMG coherence analysis might be a promising candidate marker of the corticospinal control of walking.

Several previous studies have investigated intramuscular coherence during gait in patients with CNS disorders, such as spinal cord injury (SCI) (Hansen et al., 2005; Barthélemy et al., 2010, 2015), stroke (Nielsen et al., 2008), and cerebral palsy (Petersen et al., 2013; Willerslev-Olsen et al., 2015). Intramuscular coherence recorded at the tibialis anterior (TA) muscle during gait correlated with the gait parameters in patients after SCI (Barthélemy et al., 2010, 2015) and children with cerebral palsy (Petersen et al., 2013; Willerslev-Olsen et al., 2015). Although several physical

functions such as lower limb muscle strength are strongly correlated with gait function in patients after stroke (Nadeau et al., 1999b), it is unclear whether these clinical functions also correlate with EMG-EMG intramuscular and synergistic muscle coherence during gait in patients after stroke.

EMG-EMG coherence between agonist and antagonist muscles has not generally been observed during gait in healthy subjects (Halliday et al., 2003; Norton and Gorassini, 2006). However, the beta to low-gamma (24–40 Hz) band coherence between agonist-antagonist muscles during gait is only present in patients who responded to treadmill training compared with non-responding patients after SCI (Norton and Gorassini, 2006). These results imply that increases in the descending neural drive to agonist-antagonist muscles might contribute to the generation of functional, but not necessarily normal, walking (Norton and Gorassini, 2006). Although increased agonist-antagonist muscle coactivation has frequently been observed during gait in patients after stroke (Rosa et al., 2014), no previous studies have investigated the EMG-EMG coherence between agonist-antagonist muscles during gait in patients after stroke.

Clarifying the relationship between clinical functions and EMG-EMG coherence during gait would be helpful in understanding the mechanisms by which corticospinal control of walking contributes to functional recovery in patients after stroke. The aim of the present study was to investigate the EMG-EMG intramuscular, synergistic muscle, and agonist-antagonist muscle coherences during gait and their relationships with clinical functions in patients after stroke.

2. Methods

2.1. Subjects

Eleven patients who suffered from a stroke and age- and sex-matched nine healthy control subjects participated in the present study (Table 1). The inclusion criteria of the patients were the following: (1) a single stroke that occurred more than 6 months prior to the present study, (2) no history of other neurological diseases (e.g., parkinsonism and ataxia) or rheumatic or orthopedic conditions that could interfere with gait, (3) the ability to walk independently without an ankle-foot orthosis for 10 m several times (Functional Ambulation Category score of at least 4) (Holden et al., 1984), and (4) no difficulty understanding the experimental tasks because of cognitive problems. None of the healthy controls had a neurological or orthopedic disorder or apparent gait abnormality. All subjects provided informed consents prior to beginning the study. All procedures were approved by the ethics committee of Kyoto University Graduate School and Faculty of Medicine, and were consistent with the Declaration of Helsinki.

2.2. Measurements of clinical functions

The Brunnstrom recovery stage descriptions (Brunnstrom, 1966) were used to evaluate the motor functions of the paretic lower limbs in the patients after stroke. Plantar cutaneous sensation was assessed on the paretic side with light touch (Fugl-Meyer et al., 1975), and the patients rated their perceived sensation on a 0–10 point scale. The position sense of the great toe on the paretic side was assessed 10 times with up or down passive movements of the great toe (Fugl-Meyer et al., 1975), and the number of correct answers in the direction of the passive movement was

counted. Muscle hypertonia of the plantar flexors (PFs) on the paretic side was estimated with the modified Ashworth scale (Bohannon and Smith, 1987), which was scored from 0–4 for 6 levels. The maximum strengths of the isometric ankle dorsiflexor (DF) and PF muscles on the paretic side were measured using a hand-held dynamometer (μ-tas F-1; ANIMA Corp., Tokyo, Japan) with the patients in seated and prone positions. The ankle muscle strength torques (Nm) were normalized by dividing by body weight (kg), and the muscle strengths were expressed as Nm/kg.

Gait measurements were recorded without an ankle-foot orthosis to avoid motion artifacts introduced by contact between the EMG electrodes and the orthosis. For the assessment of gait performance, all patients after stroke were asked to walk on a 10-m walkway with a 2-m distance for acceleration and deceleration at a comfortable speed. All healthy controls were asked to walk slowly on the walkway to match the gait speed of patients after familiarization with walking slowly. About 8 to 12 walking tests with resting intervals were conducted to simultaneously collect EMG recordings of all subjects. Gait speed (m/s) was calculated by averaging the outcomes of all walking tests in each subject. Two triaxial accelerometers (TeleMyo system; Noraxon U.S.A. Inc., Scottsdale, AZ, USA) that were positioned at the heels of both sides in patients after stroke and healthy controls were used to detect foot strikes and foot-off events in each walking test. The accelerometric data analysis was performed using a MyoResearch XP Master Edition (Noraxon U.S.A. Inc.), based on the method developed by Rueterbories et al. (2010). The swing time symmetry ratio (swing time on the paretic side/swing time on the non-paretic side) was calculated from the data from all walking tests in each patient after stroke (Patterson et al., 2010). Stride time

was calculated as the time from a foot strike to the next foot strike on the paretic side in patients after stroke. To determine gait variability, we calculated the stride time coefficient of variation by dividing the stride time standard deviation by the mean stride time that was determined from all walking tests in each patient after stroke (Hausdorff et al., 1997; Hausdorff, 2005). All measurements were conducted by experienced physical therapists. All clinical assessments have been reported to show high reliability (Shah, 1984; Gregson et al., 2000; Lin et al., 2004; Bohannon, 2007; Lau and Tong, 2008).

2.3. EMG recordings and coherence analysis

During the walking tests, EMG signals were recorded using the TeleMyo system at a sampling rate of 1500 Hz. The EMG signals were amplified (gain 500), filtered (band-pass at 10–500 Hz), and stored on a MyoResearch XP Master Edition. Each subject's skin was cleaned with alcohol to reduce impedance. Bipolar Ag-AgCl surface electrodes (BlueSensor M, Ambu A/S, Ballerup, Denmark) were then placed on the skin with 2.0-cm inter-electrode distances (center-to-center) over the proximal and distal ends of the TA muscle and the muscle bellies of the medial and lateral gastrocnemius (MG and LG) muscles on the paretic and non-paretic sides in patients after stroke and on the right side in healthy controls. Because other adjacent muscles, such as the extensor hallucis muscles are likely to influence the EMG recording of the distal end of the TA muscle, we attempted to minimize the cross talk by testing simple voluntary movements associated with the TA and extensor hallucis muscles in healthy controls and on the non-paretic side in patients after stroke. On the paretic side, we

first placed the electrodes at the proximal end of the TA muscle, and then selected the distal electrode site so that the electrode distance of the TA muscle on the paretic side was shorter than or at least similar to that on the non-paretic side. To minimize the risk of cross talk between the pairs of EMG electrodes due to the activity detected from overlapping motor unit territories or from the passive electronic conduction of activity from nearby muscle tissue, the recording sites of the 2 electrode pairs on the proximal and distal ends of the TA muscle were separated by a minimum distance of 10 cm (Hansen et al., 2005). The electrode placements on the MG and LG muscles were based on the SENIAM recommendations (http://www.seniam.org). The foot strike data that were detected by the accelerometers were used as triggers for the EMG epochs that were used in the frequency-domain analysis (Halliday et al., 2003).

All frequency-domain analyses of the data were performed based on the methods of Halliday et al. (1995) using MATLAB software (The MathWorks, Inc., Natick, MA, USA). Surface EMG signals were full-wave rectified. This approach has been shown to enhance the test-retest reliability and agreement of variables that were derived from the intramuscular coherence during gait (van Asseldonk et al., 2014). For the coherence analysis, the rectified EMG signals were segmented into epochs of 300-ms data segments that corresponded to the fixed periods of the paired EMG recordings following muscle activities (Figure 1). The EMG activities of the paired TA muscle during the initial swing phase and the MG and LG muscle activities during the mid-to-terminal stance phase were used in the intramuscular (TA-TA) and synergistic muscle (MG-LG) coherence analyses, respectively. These segments were similar to those that were used in healthy subjects by Halliday et al. (2003). Because ankle

muscle coactivation mostly increases in the weight acceptance phase during gait (Falconer and Winter, 1985), the overlapping co-activities of the proximal end of the TA muscle and the LG muscle during the initial-to-mid stance phase were used in the agonist-antagonist muscle (TA-LG) coherence analysis. We confirmed that the average EMG amplitudes during these periods were at least 3 standard deviations greater than those during the baseline resting period. We did not examine any EMG data at the time point of a foot strike and excluded any foot strike artifacts and visible motion artifacts from the analysis. We used 70 stable steps on each side in each subject as Norton and Gorassini (2006) used a similar number of steps. The segmented EMG signals were windowed with a Hanning window to reduce spectral leakage (Farmer et al., 1993).

The correlations between the EMG signals were assessed with coherence functions (Halliday et al., 1995). The coherence between the two rectified EMG signals (x and y) was defined as the square of the cross-spectra normalized with auto-spectra according to the following equation:

$$|R_{xy}(i)|^2 = \frac{|f_{xy}(i)|^2}{f_{xx}(i) f_{yy}(i)}$$

where fxx(i), fyy (i), and fxy (i) were the values of the auto- and cross-spectra throughout the segments for a given frequency i, which were calculated with a discrete Fourier transformation. The coherence functions, which provided normative measures of the linear correlations in the frequency domain, ranged from 0 to 1, with 1 indicating a perfect linear correlation. The EMG-EMG coherence estimates provided measures of the fractions of activity in one surface EMG signal at a given frequency that could be predicted by the activity in the other surface EMG signal, and quantified

the strengths and ranges of the frequencies of the common synaptic inputs that were distributed across the spinal motoneuron pool (Farmer et al., 1993). We confirmed that high coherence across all frequency bands, which may result from cross talk between pairs of EMG electrodes (Hansen et al., 2005), was not observed. We took care to avoid the influences of motion artifacts and cross talk in the coherence analysis.

The distribution of coherence was normalized with an arc hyperbolic tangent transformation (Halliday et al., 1995). Coherence was considered significant when it was higher than the 95% confidence limit under the hypothesis of independence, and the 95% confidence limit of coherence for significant difference from zero was 0.042 for 70 epochs in the present study (Halliday et al., 1995). We first determined the number of subjects that showed significant coherences in each paired EMG signals. To quantitatively evaluate the magnitudes of the coherence and the relationships of coherence with clinical functions, we calculated the area under the coherence curve within the 15- to 30-Hz band (beta) and 30- to 45-Hz band (low-gamma) frequency ranges because coherence in these frequency bands is strongly related to corticospinal drive (Grosse et al., 2002; Petersen et al., 2012). In addition, we calculated the pooled EMG-EMG coherences for all patients after stroke and all healthy controls (Amjad et al., 1997). This enabled the visual comparison of the average tendency of EMG-EMG coherence between patients after stroke and healthy controls.

2.4. Statistical analysis

SPSS version 20.0 for Windows (IBM Japan Ltd, Tokyo, Japan) was used for the statistical data analysis. We compared the area under the coherence curve of each

paired EMG signal for the beta band between the patients after stroke (paretic and non-paretic sides) and healthy controls and between the paretic and non-paretic sides in patients after stroke using unpaired *t*-tests and paired *t*-tests, respectively, with Holm adjustments. The same analysis was also performed for the low-gamma band. We then investigated the relationships of the areas under the coherence curves of all paired EMG signals with paretic motor function, sensory function, spasticity, ankle muscle strengths, and gait performances using Pearson's product-moment correlation coefficients and/or Spearman's rank correlation coefficients, depending on the normality of each variable. Statistical significance was set at $p < 0.05$.

3. Results

Table 1 lists the characteristics of the patients after stroke and healthy controls that were examined in the present study. Most of the patients were categorized as limited community ambulators (Perry et al., 1995) as their gait speed was 0.58 ± 0.21 m/s. The swing time symmetry ratio of the patients was 1.53 ± 0.34, and most of the patients had longer swing times on the paretic side than those on the non-paretic side. The stride time coefficient of variation of the patients was 4.80 ± 1.18. These gait performances indicated that most of the patients had a mild to moderate gait abnormality.

3.1. Significant EMG-EMG coherence of all paired EMG signals during gait

There were no subjects with high coherence across all frequency bands, which might have been attributable to cross talk between the pairs of EMG electrodes (Hansen et al., 2005). Therefore, all EMG recordings that were used in the analysis showed coherence

of all paired EMG signals only for the restricted frequency bands, and this cannot be explained by cross talk.

Figure 2 depicts the typical patterns of EMG-EMG coherence in healthy controls and patients after stroke. A very high coherence of all paired EMG signals was observed at frequencies less than 10 Hz, which might reflect the envelope of the EMG activity during the gait cycle (Halliday et al., 2003). The TA-TA and MG-LG coherences were typically observed at frequencies around 15 Hz up to about 45 Hz in healthy controls and on the non-paretic side, and were lower on the paretic side than those in healthy controls and on the non-paretic side. All healthy controls showed significant TA-TA and MG-LG coherences in the beta to low-gamma bands (ranges of peak coherence: 0.065–0.314 and 0.066–0.338, respectively). All patients after stroke showed significant TA-TA and MG-LG coherences in the beta to low-gamma bands on the non-paretic side (ranges of peak coherence: 0.078–0.298 and 0.047–0.441, respectively). On the paretic side, 10 and 8 patients after stroke showed significant TA-TA and MG-LG coherences in the beta to low-gamma bands, respectively (ranges of peak coherence: 0.034–0.234 and 0.029–0.228, respectively).

There was very little TA-LG coherence at frequencies above 10 Hz in healthy controls. Only 1 healthy control showed low significant TA-LG coherence in the beta to low-gamma bands (ranges of peak coherence: 0.015–0.065). The TA-LG coherence on the non-paretic side was typically similar to the paretic side at frequencies around 20 Hz up to about 30–40 Hz, and was lower than TA-TA and MG-LG coherences (Figure 2). In the beta to low-gamma bands, 8 and 7 patients after stroke showed significant TA-LG coherences on the non-paretic and paretic sides, respectively

(ranges of peak coherence: 0.013–0.204 and 0.021–0.223, respectively).

3.2. Differences in the coherence areas between patients after stroke and healthy controls

We also plotted the pooled EMG-EMG coherences of all paired EMG signals for all healthy controls and all patients after stroke in Figure 3A. The pooled TA-TA and MG-LG coherences were smaller at frequencies around the beta to low-gamma bands on the paretic side as compared to those on the non-paretic side and in healthy controls. The pooled TA-LG coherence was smaller at frequencies around the beta to low-gamma bands in healthy controls as compared to those on both the paretic and non-paretic sides in patients after stroke.

The areas under the coherence curves of all paired EMG signals for the frequency ranges in the beta and low-gamma bands in healthy controls and patients after stroke are shown in Figure 3B. For the beta band, the areas under the TA-TA and MG-LG coherence curves on the paretic side were significantly lower than those on the non-paretic side ($p = 0.032$ and $p = 0.049$, respectively) and compared to healthy controls ($p = 0.046$ and $p = 0.015$, respectively). The TA-TA and MG-LG coherence areas did not significantly differ between the non-paretic side and healthy controls ($p = 0.572$ and $p = 0.890$, respectively). The areas under the TA-LG coherence curves for the beta band on the paretic and non-paretic sides were both significantly higher than in healthy controls ($p = 0.020$ and $p = 0.024$, respectively) but did not significantly differ between the paretic and non-paretic sides in patients after stroke ($p = 0.635$).

For the low-gamma band, there were no significant differences in the areas under the

coherence curves between the paretic side and healthy controls and between the non-paretic side and healthy controls (TA-TA $p = 0.222$ and $p = 0.820$, MG-LG $p = 0.528$ and $p = 0.847$, TA-LG $p = 0.281$ and $p = 0.216$, respectively). The areas under the TA-TA, MG-LG, and TA-LG coherence curves in the low-gamma band did not significantly differ between the paretic and non-paretic sides in patients after stroke ($p = 0.123$, $p = 0.462$, and $p = 0.478$, respectively).

3.3. Relationships between coherence areas and clinical functions

The area under the TA-TA coherence curve in the beta band on the paretic side positively correlated with gait speed ($r = 0.627$, $p = 0.039$) (Figure 4A). In the low-gamma band, the area under the TA-TA coherence curve on the paretic side tended to negatively correlate with the swing time symmetry ratio ($r = -0.591$, $p = 0.056$). In contrast, the area under the MG-LG coherence curve in the beta and low-gamma bands on the paretic side did not significantly correlate with any clinical function. The area under the TA-LG coherence curve in the beta band on the paretic side negatively correlated with the paretic ankle PF muscle strength ($r = -0.788$, $p = 0.004$) (Figure 4B), and tended to negatively correlate with the paretic ankle DF muscle strength ($r = -0.539$, $p = 0.087$). In the low-gamma band, the area under the TA-LG coherence curve on the paretic side tended to negatively correlate with gait speed ($r = -0.591$, $p = 0.056$) and paretic ankle PF muscle strength ($r = -0.573$, $p = 0.066$). On the non-paretic side, the areas under the coherence curves of all paired EMG signals in the beta and low-gamma bands did not significantly correlate with any clinical function.

4. Discussion

In the present study, the EMG-EMG intramuscular (TA-TA) and synergistic muscle (MG-LG) coherences in the beta band were reduced during gait on the paretic side in patients after stroke. The TA-TA coherence in the beta band on the paretic side positively correlated with gait speed. In this study, we first demonstrated that the EMG-EMG coherence between agonist-antagonist muscles (TA-LG) in the beta band was increased on both sides during gait in patients after stroke and that this coherence on the paretic side negatively correlated with paretic ankle PF muscle strength.

The TA-TA and MG-LG coherences in the beta band on the paretic side in patients after stroke were significantly lower than those on the non-paretic side and in healthy subjects during gait. The present results were consistent with previous results in patients after SCI (Hansen et al., 2005; Barthélemy et al., 2010, 2015) and stroke (Nielsen et al., 2008). Asymmetrical SMC activation was observed during gait in patients after stroke, and this was induced by the reduction in the SMC activation in the affected hemisphere (Miyai et al., 2002). Because EMG-EMG coherence in the beta band can detect SMC excitability changes following transcranial direct current stimulation (Power et al., 2006), the changes in SMC activation may be reflected in the reduced TA-TA and MG-LG coherences during gait on the paretic side in the present study. Therefore, these results indicated that an EMG-EMG coherence analysis can be a reliable physiological marker of the strength of the descending neural drive from the SMC during gait in patients with CNS disorders (Hansen et al., 2005; Nielsen et al., 2008; Barthélemy et al., 2010, 2015). Furthermore, it is a noteworthy approach due to its convenient measures that only require the recording of EMG signals.

The TA-TA coherence in the beta band on the paretic side during gait positively correlated with gait speed in patients after stroke. This relationship was consistent with a recent previous result in patients after SCI (Barthélemy et al., 2015) and reflected a previous result that the SMC activation in the affected hemisphere correlated with gait performances in patients after stroke (Miyai et al., 2002). Furthermore, the TA-TA coherence correlated with the ankle joint kinematics in patients after SCI (Barthélemy et al., 2010) and children with cerebral palsy (Petersen et al., 2013; Willerslev-Olsen et al., 2015). Therefore, these results indicated that an intramuscular coherence during gait can be a clinically relevant measure that is a good predictor of the gait function in patients with CNS disorders.

Patients after stroke had higher TA-LG coherences on both the paretic and non-paretic sides compared to healthy subjects during gait, whereas the significant TA-LG coherence is not generally observed during gait in healthy subjects in the present and previous studies (Halliday et al., 2003). The lack of this coherence in healthy subjects may indicate that there is a very small common descending neural drive to agonist-antagonist muscles at the ankle joint during intact walking because the ankle muscles are activated reciprocally throughout the gait cycle (Perry and Burnfield, 2010). However, the plastic changes in the neural pathways connecting the SMC to the agonist-antagonist muscles that underlie recovery have been demonstrated after SCI in monkeys (Nishimura et al., 2009). Similarly, in human subjects after SCI, the strength of the descending neural drive to agonist-antagonist muscles is increased to generate functional walking (Norton and Gorassini, 2006). Furthermore, the EMG-EMG coherence between agonist-antagonist muscles in the beta to low-gamma bands

correlated with the amplitude of corticospinal conduction in patients after SCI (Norton and Gorassini, 2006). These results suggested that the increase in the common corticospinal drive to agonist-antagonist muscles may be one of the neural mechanisms that underlie the increased muscle coactivation (Hansen et al., 2002; Geertsen et al., 2013), which is frequently observed during gait in patients after stroke (Rosa et al., 2014). The reorganization of the descending neural drive to agonist-antagonist muscles on the paretic side was likely induced to compensate for the reduction in the normal descending neural drive to individual and synergistic muscles on the paretic side following a lesion in the CNS (Norton and Gorassini, 2006; Nielsen et al., 2008; Nishimura et al., 2009). The descending neural drive to agonist-antagonist muscles on the non-paretic side was increased during gait to compensate for the paretic instability (Rosa et al., 2014) because this drive was increased during voluntary muscle co-contraction to improve the stability (Hansen et al., 2002; Geertsen et al., 2013).

We demonstrated that the increased EMG-EMG coherence between agonist-antagonist muscles in the beta band on the paretic side significantly correlated with paretic ankle PF muscle weakness. Paretic ankle PF muscle weakness causes gait instability and is a limiting factor of gait speed in patients after stroke because PF muscle activities enhance stance limb stability (Nadeau et al., 1999a, 1999b). Therefore, increasing ankle muscle coactivation on the paretic side might be required during gait to compensate for the paretic instability from the paretic ankle PF muscle weakness in patients after stroke. Similar to patients after SCI (Norton and Gorassini, 2006), patients after stroke who have paretic ankle PF muscle weakness may exhibit an enhancement of the descending neural drive to agonist-antagonist muscles during gait

to help to provide postural stability and restore functional walking.

EMG signals during gait can originate from the brain or from the spinal reflex. EMG-EMG coherence is only found in the lower-frequency band (less than 10 Hz) in patients after complete SCI, suggesting that the origin of lower-frequency band coherence is likely to be spinal (Norton et al., 2003). In contrast, the lack of significant relationship between EMG-EMG coherence in the beta and low-gamma bands and spasticity indicates that the EMG-EMG coherence in these frequency bands is not strongly related to the spinal reflexes. Beta band (15-30 Hz) oscillatory SMC activation plays a key role in motor control (van Wijk et al., 2012), and beta band EMG-EMG coherence is commonly thought to originate from the SMC (Grosse et al., 2002; Fisher et al., 2012). Low-gamma band (30-45 Hz) synergistic muscle coherence was observed during voluntary muscle contraction (Kattla and Lowery, 2010), which indicates that the origin of this band coherence is also likely to be cortical (Grosse et al., 2002). In addition, EMG-EMG coherence in these frequency bands is reduced in patients with CNS disorders, providing evidence that it is supraspinally mediated (Petersen et al., 2013; Barthélemy et al., 2015). In the present study, the beta band coherence was well correlated to clinical functions, which was consistent with a recent result in patients after SCI (Barthélemy et al., 2015). These results suggested that beta band coherence is likely to play a key role in locomotor control and to correlate well with clinical functions in adult patients with CNS disorders. In contrast, gamma band coherence has been found to correlate well with gait parameters in children, including gait kinematics in healthy children (Petersen et al., 2010) and impaired toe elevation in children with cerebral palsy (Petersen et al., 2013).

There were several limitations in the present study. First, we could not include information on the kinematic and kinetic parameters during over-ground walking because we only measured clinical gait performances. Thus, the relationships between EMG-EMG coherence and biomechanical gait parameters (e.g., ankle joint kinematics) remain unclear in patients after stroke. Further studies are needed to investigate these relationships and determine whether EMG-EMG coherence is linked to functional gait disabilities, such as foot drop, in patients after stroke, as has been shown in patients with other CNS disorders (Barthélemy et al., 2010; Petersen et al., 2013). While EMG-EMG coherence between agonist-antagonist muscles is not generally observed during gait in healthy subjects (Halliday et al., 2003; Norton and Gorassini, 2006), it is increased during voluntary muscle co-contraction (Hansen et al., 2002; Norton and Gorassini, 2006; Geertsen et al., 2013). EMG-EMG coherence between agonist-antagonist muscles has not been investigated during voluntary muscle co-contraction in patients after stroke. Therefore, it remains unclear how different motor tasks (e.g. voluntary muscle contraction and movements such as gait, which require both voluntary and involuntary muscle control) influence descending neural drive in patients after stroke. Furthermore, the present observational study did not elucidate how the changes in the neural pathways connecting the SMC to the agonist and/or antagonist muscles that correspond to the degree of functional recovery occurred in patients after stroke. Further studies are required to investigate the longitudinal changes in the intramuscular, synergistic muscle, and agonist-antagonist muscle EMG-EMG coherences during gait in patients after stroke.

5. Conclusions

Reduction in the descending neural drives to the individual and synergistic muscles through the corticospinal tract were observed on the paretic side during gait in patients after stroke. The strength of the descending neural drive to individual muscle on the paretic side correlated with gait speed. Significant descending neural drives to the agonist-antagonist muscles on both the paretic and non-paretic sides were observed during gait in patients after stroke, and the increased strength of this drive on the paretic side correlated with paretic ankle muscle weakness, which may indicate reorganization to compensate for the paretic instability during gait. This reorganization may be important for functional gait restoration in patients after stroke with paretic ankle muscle weakness.

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Table 1. Characteristics of the subjects

	Patients *n* = 11	Controls *n* = 9	*p*
Age (years)	59.27 ± 11.58	55.78 ± 3.87	0.365
Height (cm)	163.36 ± 10.22	165.00 ± 8.50	0.706
Weight (kg)	63.95 ± 11.48	60.39 ± 10.53	0.483
Sex (*n*): male/female	7 / 4	6 / 3	0.999
Affected side (*n*): right/left	4 / 7		
Time post-stroke (years)	5.85 ± 2.09		
Brunnstrom recovery stage (*n*): I/II/III/IV/V/VI	0/0/4/3/4/0		
Cutaneous sensation (points)	5.09 ± 4.09		
Position sense (number of correct answers)	7.36 ± 3.35		
Modified Ashworth scale (*n*): 0/1/1+/2/3/4	0/4/5/1/1/0		
Ankle muscle strengths (Nm/kg)			
DF on the paretic side	0.23 ± 0.13		
PF on the paretic side	0.38 ± 0.15		
Functional Ambulation Category (*n*): 1/2/3/4/5	0/0/0/3/8		
Gait speed (m/s)	0.58 ± 0.21	0.55 ± 0.04	0.637
Swing time symmetry ratio	1.53 ± 0.34		
Stride time coefficient of variation	4.80 ± 1.18		

The data are reported as mean ± standard deviation or *n*. A Functional Ambulation Category score of 4 indicates that the patient can ambulate independently on level surfaces, but requires supervision or physical assistance to negotiate stairs, inclines, or non-level surfaces, and the score of 5 indicates that the patient can ambulate independently on non-level and level surfaces, stairs, and inclines. DF: dorsiflexor, PF: plantar flexor.

Figure Legends

Figure 1. Rectified electromyography (EMG) signals during gait on the paretic side in a single representative patient after stroke. Each EMG signal was segmented into epochs of 300-ms data segments that corresponded to the fixed period of paired muscle activities. The EMG activities of the paired tibialis anterior (TA) muscle during the initial swing phase, the medial and lateral gastrocnemius (MG and LG) muscles during the mid-to-terminal stance phase, and the overlapping co-activity of the proximal end of the TA muscle and the LG muscle during the initial-to-mid stance phase were used in the TA-TA, MG-LG, and TA-LG coherence analyses, respectively. The vertical dashed lines and filled triangles indicate foot strike events, and these times were used as trigger points. The open triangles indicate foot-off events.

Figure 2. Representative examples of typical patterns of EMG-EMG coherence during gait. The horizontal dashed lines indicate the 95% confidence limit of coherence (0.042). The vertical dashed lines indicate the frequency range of the beta (15–30 Hz) and low-gamma (30–45 Hz) bands. The phase spectrum was calculated as the argument of the cross-spectrum (Halliday et al. 1995) for the estimation of the timing relationships between the EMG signals, which is illustrated in the subplot that is inserted in the coherence plot. The phase spectrum is defined over the range [$-\pi$, $+\pi$], and the y axis is marked in radians. The phase spectrum is only valid in the frequency band in which the coherence is significant, and hence, only those regions are indicated in the phase plots.

Figure 3. (A) Pooled EMG-EMG coherences of each paired EMG signal during gait for all healthy controls and all patients after stroke. The 95% confidence limit of pooled coherence is given as a horizontal dashed line. The vertical dashed lines indicate the frequency range of the beta (15–30 Hz) and low-gamma (30–45 Hz) bands. (B) Comparisons of the area under the coherence curve of each paired EMG signal for the frequency ranges of the beta and low-gamma bands during gait between the patients after stroke (paretic and non-paretic sides) and healthy controls and between the paretic and non-paretic sides. For the beta band, the areas under the TA-TA and MG-LG coherence curves on the paretic side were significantly lower than those on the non-paretic side and compared to healthy controls (*$p < 0.05$), and the areas under the TA-LG coherence curves for the beta band on the paretic and non-paretic sides were both significantly higher than in healthy controls (*$p < 0.05$). For the low-gamma band, there were no significant differences in the areas under the coherence curves between the patients after stroke (paretic and non-paretic sides) and healthy controls and between the paretic and non-paretic sides. *n.s.* no significant.

Figure 4. (A) Correlation between the TA-TA coherence in the beta band on the paretic side and gait speed. (B) Correlation between the TA-LG coherence in the beta band on the paretic side and the paretic ankle plantar flexor (PF) muscle strength.

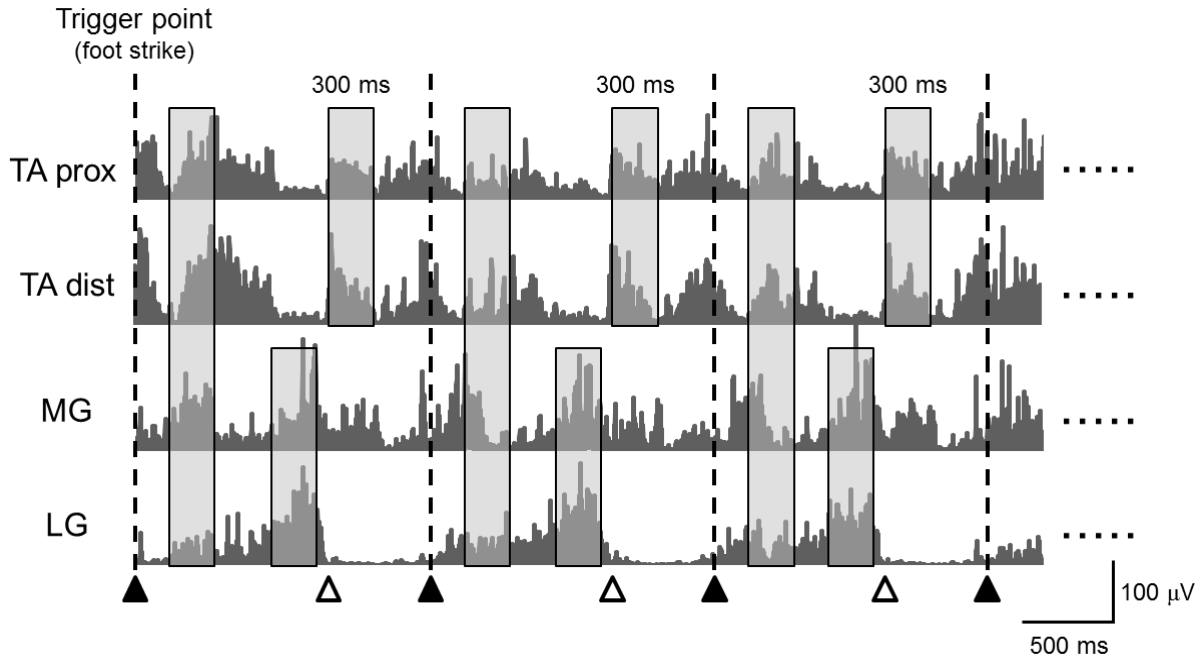
Trigger point
(foot strike)
300 ms
300 ms
300 ms
TA prox
TA dist
MG
LG
100 μV
500 ms

Figure 1

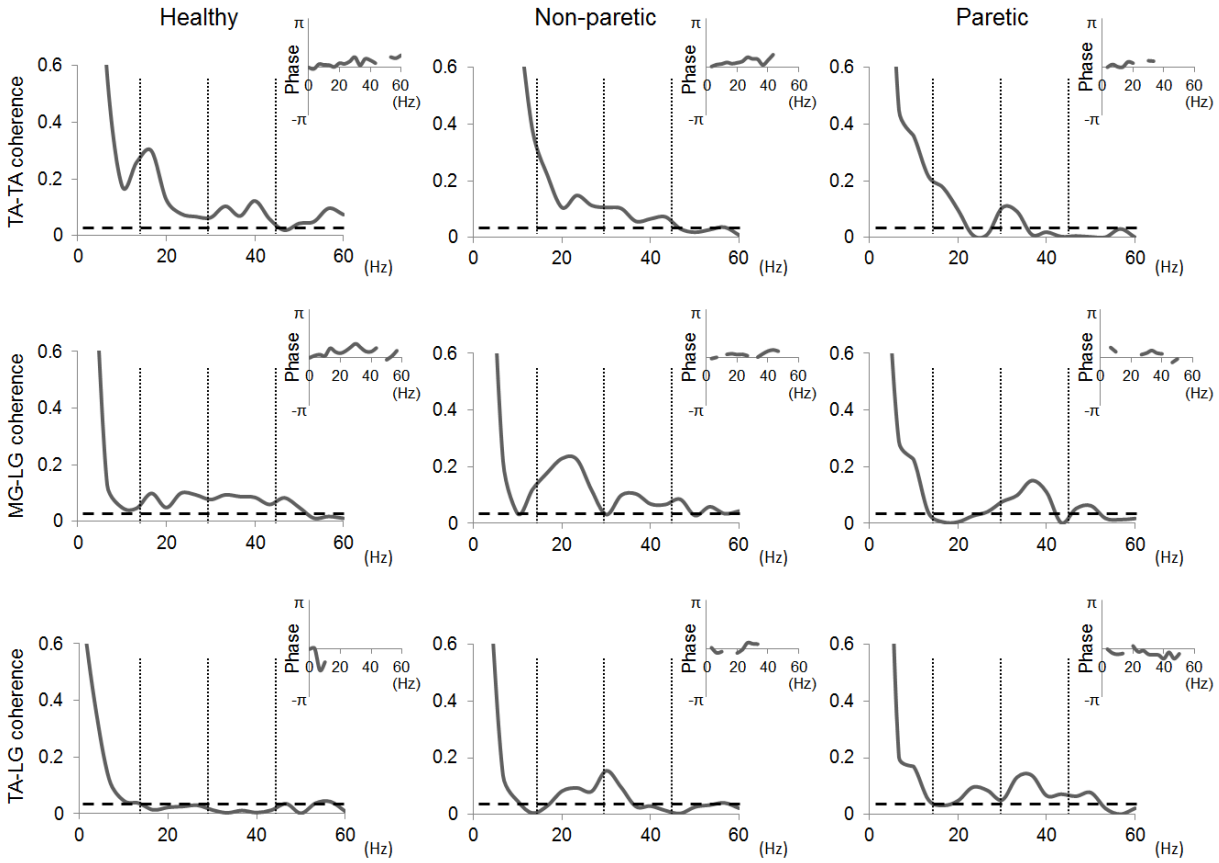
Healthy
Non-paretic
Paretic
TA-TA coherence
MG-LG coherence
TA-LG coherence
Phase
(Hz)
π
-π
0
20
40
60
0.2
0.4
0.6

Figure 2

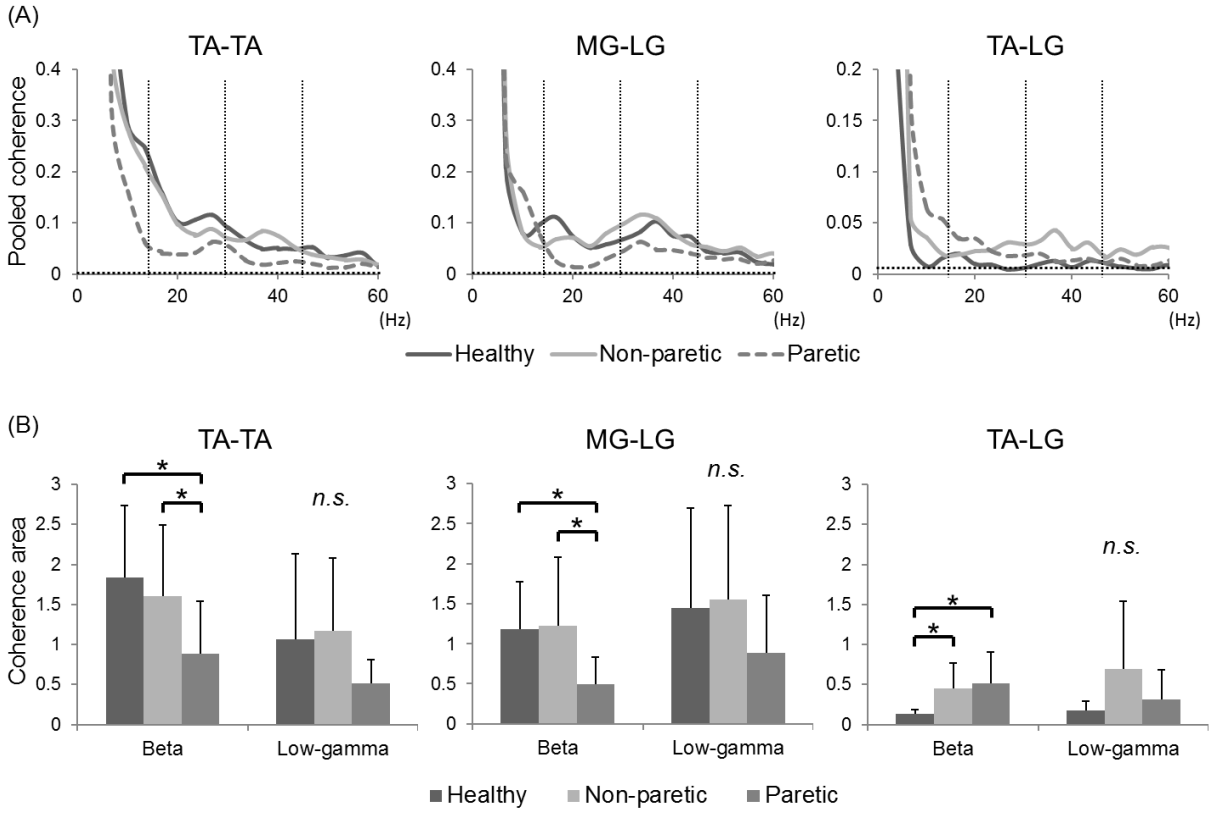
(A)
TA-TA
MG-LG
TA-LG
Pooled coherence
(Hz)
Healthy
Non-paretic
Paretic
(B)
Coherence area
n.s.
Beta
Low-gamma

Figure 3

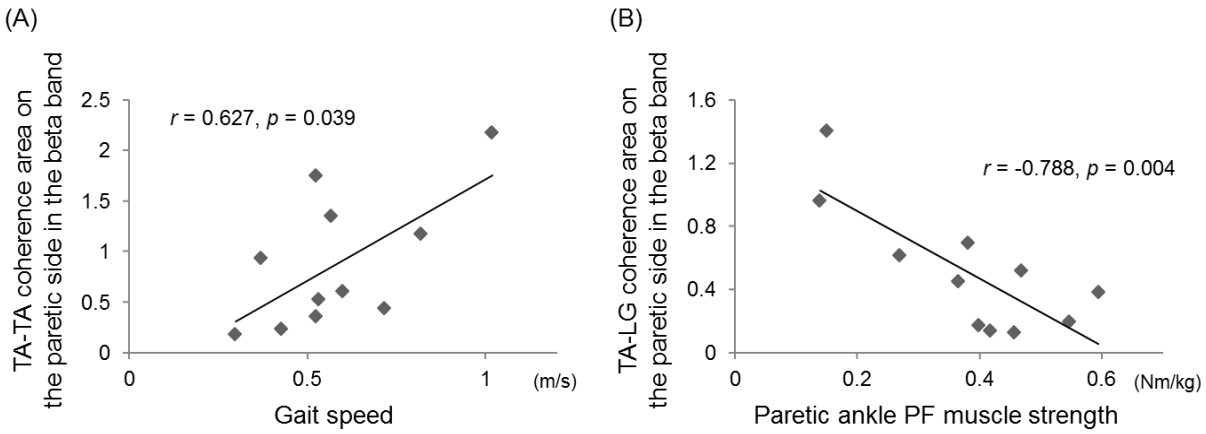
(A)
TA-TA coherence area on the paretic side in the beta band
r = 0.627, p = 0.039
2.5
2
1.5
1
0.5
0
0
0.5
1
(m/s)
Gait speed
(B)
TA-LG coherence area on the paretic side in the beta band
r = -0.788, p = 0.004
1.6
1.2
0.8
0.4
0
0
0.2
0.4
0.6
(Nm/kg)
Paretic ankle PF muscle strength

Figure 4