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# Failure of normal development of central drive to ankle dorsiflexors relates to gait deficits in children with cerebral palsy.

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**Abstract**

Neurophysiological markers of the central control of gait in children with cerebral palsy (CP) are used to assess developmental response to therapy. Here we measure the central common drive to a leg muscle in children with CP. We recorded EMGs from the Tibialis Anterior (TA) muscle of 40 children with hemiplegic CP and 42 typically-developing age-matched controls during static dorsiflexion of the ankle and during the swing phase of treadmill walking. The common drive to TA motoneurones was identified through time and frequency domain cross-correlation methods. In control subjects, the common drive consists of frequencies between 1 and 60 Hz with peaks at beta (15-25 Hz) and gamma (30-45 Hz) frequencies known to be caused by activity within sensori-motor cortex networks: this drive to motoneurones strengthens during childhood. Similar to control subjects, this drive to the least affected TA in the CP children tended to strengthen with age, although compared to the control subjects it was slightly weaker. For CP subjects' of all ages the most affected TA muscle common drive was markedly reduced compared both to their least affected muscle and to controls. These differences between the least and most affected TA muscles were unrelated to differences in the magnitude of EMG in the two muscles but positively correlated with ankle dorsiflexion velocity and joint angle during gait. Time and frequency domain analysis of on-going EMG recruited during behaviourally relevant lower limb tasks provides a non-invasive and important measure of the central drive to motoneurones in subjects with CP.

## Introduction

Can the developmental outcome of children with pre-natal brain lesions causing cerebral palsy (CP) be improved and if so what would be the neurophysiological correlates of such an improvement? (Blauw-Hospers et al. 2007). In individuals diagnosed with hemiplegic cerebral palsy (CP) the ability to walk is impaired and loss of locomotor capability may greatly affect these subjects' ability to participate in everyday activities such as education and fitness activities (Lepage et al. 1998). Maintaining or even improving mobility throughout development in these children is a therapy goal of great importance. However, attempts at optimizing gait training, for example, are hampered by our lack of knowledge of the neural mechanisms involved in the control of gait and how they change during motor development and the effect of early brain lesion on these changes. Normal human lower limb muscle activation and walking involves activity in multiple neural networks that are hierarchically organised (Hultborn and Nielsen 2007; Rossignol 2006). In studies of healthy and neurologically impaired subjects, the strong corticospinal drive to Tibialis Anterior (TA) muscle during gait has received particular attention because loss of TA activation is a universal feature of the lower limb upper motoneurone syndrome (see Nielsen 2003 for review).

The CP syndrome emerges as the result of developmental adaptations to early brain lesions that involve central motor pathways and as such the activity within the neural networks that provide drive to spinal motoneurones is of crucial importance in understanding the pathophysiology of CP. A neurophysiological measure of the central drive to spinal motoneurones involved in lower limb muscle activation and gait is required and changes in the central drive in children developing with CP needs to be understood.

Through time and frequency domain analysis of pairs of EMG signals the common drive to motoneurones can be detected without experimental perturbation (Farmer 1998). Common drive is detected over a broad frequency range between 1 and 60 Hz (De Luca et al. 1993; Farmer et al. 1993a; Halliday et al. 1995). Beta (15-25 Hz) and gamma (30-45 Hz) frequencies, which are in excess of the mean motor unit firing rate, are of particular interest, since they are strongly related to oscillatory corticospinal drive from the sensory-motor cortex (Brown et al. 1998; Conway et al. 1995; Kilner et al. 2000; Mima and Hallett 1999). Recently, the oscillatory central common drive to spinal motoneurones during tonic leg muscle activation (Perez et al. 2006; Ushiyama et al. 2011) and during walking has been measured in adults using EMG-EMG (Halliday et al. 2003) and EEG-EMG coherence analysis (Petersen et al. 2012). In adult subjects common drive to motoneurones is reduced by lesions of the corticospinal pathways projecting to upper (Farmer et al. 1993b; Smith et al. 1999) and lower limb muscles (Hansen et al. 2005; Nielsen et al. 2008). Furthermore, in a recent study of subjects with spinal cord lesions reduction in common drive to the TA muscle during walking was linked to the degree of foot drop (Barthelemy et al. 2010).

The common drive to upper limb human motoneurones undergoes a developmental increase both during static and dynamic muscle activation (Deutsch et al. 2011; Farmer et al. 2007; James et al. 2008). Recently it was shown that the common drive to motoneurones controlling the Tibialis anterior (TA) muscle in the beta (15-25 Hz) and gamma (30-45 Hz) frequency bands increases with age in healthy children during static dorsiflexion of the TA muscle and during the dynamic swing phase of walking during which TA is active (Petersen et al. 2010). It was suggested that this age-related increase in common drive reflects the functional maturation of the central neural networks responsible for control of the ankle joint during walking.

In the present study we build on these findings and ask what effect early acquired brain lesions causing hemiplegic CP have on the central drive to spinal motoneurone pools and its emergence over the course of childhood and early adolescence.

We hypothesise that children with hemiplegic cerebral palsy will show loss and failure of developmental emergence of central common drive to their TA motoneurones during static muscle activation and during walking. We expect that this will be most evident for their most affected muscle and that this loss of drive will correlate with deficits in the control of the ankle joint during walking.

## Methods

*Subjects*

Forty children with cerebral palsy (mean age= 10 years; age range 4-15 years; 26 male and 14 female) participated in the study. All children were diagnosed with congenital spastic hemiplegia (19 subjects: right hemiplegia and 21 subjects: left hemiplegia) and classified according to the Gross Motor Classification System (GMFCS), which is validated for use in CP subjects and describes five levels of impairment (Palisano et al. 1997). Classification was performed by a pediatric neuro-physiotherapist (MKD). In this study only children with mild-moderate hemiplegia at GMFCS levels I and II were included (Level I, n=36, Level II, n=4). The study was approved by the local ethics committee (H-B-2009-017) and all procedures were conducted within the standards of the Helsinki declaration. Prior to all experiments all parents received written and verbal information, and consent for participation was obtained from the parents and the child. Two subjects were excluded from further analysis due to cross-talk in the EMG measurements (see below). Six subjects had undergone lengthening of the Achilles tendon a minimum of one year prior to the study. An analysis was performed excluding these subjects, but since this did not change any conclusions, data from all subjects is presented. Subjects who had received Botulinum toxin injections into the most affected calf muscle were included providing no injections had been given within 6 months of the recordings. No subjects had received botox injections into the TA muscle. Twenty-one children had been treated with a Botulinum toxin between 6 month and 7 years prior to the study (median= 12 month). Two subjects were taking baclofen at the time of the study, one subject was taking Levetiracetam to prevent epileptic seizures, one subject was taking an LHRH antagonist (Procren) and one was taking sertraline as treatment for ADHD.

Data from static muscle activation (n=36, mean age= 9.4 years; age range 4-15 Years; 21 male and 15 female) and walking (n=42, mean age= 9.5 years; age range 4-15 Years; 24 male and 18 female) in typically developing subjects was used to compare with the CP subjects. The common drive developmental profile of this group has previously been published (Petersen et al. 2010). For the purpose of further analysis, all children (CP and controls) were split into three different age groups: 4-7 yrs, 8-11 yrs and 12-15 yrs.

*Experimental procedures*

Two sets of experiments were performed in all subjects. First, we examined static muscle activation of the TA muscle. The children were asked to sit comfortably on a plastic box that could be adjusted according to height. With the left or right foot in front of them, keeping an angle of 100 deg. in both the knee and the ankle joint they were asked to produce a non-fatiguing weak static contraction of the TA muscle for 1 minute against the hand of the experimenter who opposed the movement. The experimenter monitored the EMG signal online. Two to three minutes of rest were allowed before another trial was initiated. The hemiplegic subjects were able to produce EMG activity in both legs (see for example, figure 1). However, it should also be noted that the CP subjects reported that it took more effort to complete the task with the most affected leg and the root mean square (RMS) EMG values were lower (see results). The second part of the experiments consisted of 5 minutes of treadmill walking. The children were asked to choose their own walking speed. Details of this can be found in table 1. After 5-10 minutes of familiarization, EMG measurements and 3-D kinematic data was collected. All children had previous experience of treadmill walking, and did not experience any difficulties regarding this task, however most held on to the handlebar in front of the treadmill with one or both hands for safety.

*EMG recordings*

Bipolar EMG recordings were obtained from two sets of non-polarizable Ag-AgCL electrodes (Blue Sensor, AMBU, Denmark) placed at the proximal and distal end of the TA muscle respectively. In the control children we recorded only from the left leg TA muscle, whereas recordings in the hemiplegic subjects were obtained from both left and right TA muscles and were designated with respect to the side of the hemiplegia as the most affected (MA) and least affected (LA) muscles, respectively. In all cases the inter electrode pair distances were two cm. Details on the distance (influenced by limb size) between the two sets of electrode pairs can be found in table 1. The signal was amplified (GAIN =1000) and band bass filtered (10 Hz to 1 KHz) with a Wireless EMG system (Zerowire EMG, Aurion S.l.r, Italy) and sampled at 2KHz (Using a micro 1401 AD converter and spike 2 software, Cambridge Electronic Design, UK) and stored on a PC for further analysis. A pressure resistive sensor placed under the heel of both feet was used to monitor the time of heel contact in the case of treadmill walking. In three hemiplegic subjects the sensor was placed under the medial part of the fore foot since these subjects failed to make heel contact during walking. It was ensured in all cases that the heel trigger was activated with the first contact between the foot and the ground with each step. The heel contact data were used as triggers for the EMG epochs used in the frequency domain analysis. In the static muscle activation experiment we included 60 seconds of EMG data. For the experiment on treadmill walking we used a total of 300 steps for each leg (EMG epochs) for each subject. Each epoch consisted of 500-600ms of data corresponding to the EMG activity observed prior to heel strike. We avoided using EMG from the time of heel strike and onwards to exclude heel strike artefacts from the analysis. Cross-talk between the bipolar EMG recordings was recognized through visual inspection of the EMG and through calculation of time and frequency domain analysis. Cross-talk contamination is easily identified in the cumulant density function from the presence of very narrow peaks (< 2 ms) and in the coherence estimates from the presence of coherence at all frequencies represented in the data (see Fig. 1 in Hansen et al. 2005). All recordings with central peaks in the cumulant density function lasting less than 5 ms or with coherence over the interval 0-150 Hz were consequently omitted from further analysis. It should be noted that the risk of cross-talk increases with reduced muscle size and hence shorter inter-electrode differences and with increased motor unit size. This issue was addressed by measuring inter-electrode distances (see table 1). The results of the present study show opposite effects to those expected from EMG cross-talk: there is lack of coherence in the youngest (i.e. those with the smallest inter-electrode distance) and in the MA TA muscle (expected to have the largest motor units).

*Kinematic recordings and analysis*

Six infrared Qqus cameras (Qualisys, Sweden) were used for kinematic recordings. Markers were placed on both legs on 1) the caput fibulae, 2) the lateral malleolus and 3) the lateral side of the 5th metatarophalangeal joint. The data were collected at a rate of 200 Hz on a PC and stored for further analysis. Based on 30 randomly selected steps, we calculated the mean amount of ankle dorsiflexion performed during the early swing phase $\mu\Delta\varphi$, the standard deviation (S.D.) of this and the mean time $\mu\Delta t$ this movement took. From these parameters we calculated the mean velocity of the dorsi-flexion movement $\mu\Delta\varphi/\mu\Delta t$ and the coefficient of variation (COV) of the dorsiflexion movement S.D/$\mu\Delta\varphi$

*Frequency domain and statistical analysis.*

Frequency domain analysis of the data was undertaken using the methods set out in detail by Halliday *et al.* (1995). Briefly, the practice of full wave rectification of surface EMG signals was adopted. This approach has been shown to maximize the information regarding timing of motor unit action potentials (MUAP) whilst suppressing information regarding MUAP waveform shape (Boonstra and Breakspear 2012; Halliday and Farmer 2010; Myers et al. 2003). As a precursor to undertaking population analysis of the data the two rectified TA EMG signals were normalized to have unit variance (Halliday and Rosenberg 2000). Rectified and normalized EMG signals are assumed to be realizations of stationary zero mean time series, denoted by $x$ and $y$. The results of analysis of individual records generated estimates of the auto-spectra of the two EMGs $fxx(\lambda)$, $fyy(\lambda)$, and their cross-spectra $fxy(\lambda)$. We then estimated three functions that characterize the signals' correlation structure: coherence, $|R_{xy}(\lambda)|^2$; phase, $\varphi_{xy}(\lambda)$; and cumulant density, $q_{xy}(u)$. Coherence estimates are bounded measures of association defined over the range [0, 1]; cumulant density estimates are not bounded, and phase is defined over the range $[-\pi, +\pi]$. For the present data, coherence estimates provide a measure of the fraction of the activity in one surface EMG signal at any given frequency that can be predicted by the activity in the second surface EMG signal. In this way, coherence estimates quantify the strength and range of frequencies of common rhythmic synaptic inputs distributed across the motoneurone pool. The timing relations between the EMG signals are estimated from the phase. The cumulant density provides an unbounded time-domain representation of the EMG-EMG correlation structure analogous to the motor unit cross-correlogram (Halliday et al. 1995)

Pooled estimates provide a single time or frequency domain measure that describes the correlation structure across a number of data sets (Amjad et al. 1997). Like individual coherence estimates, pooled coherence estimates provide a normative measure of linear association on a scale from 0 to 1 (Halliday & Rosenberg, 2000). Similarly, pooled cumulant density estimates provide a measure of the time-domain correlation across a number of records. Pooled spectra provide a normalised average spectra.

The interpretation of pooled estimates is similar to those for individual records, except any inferences relate to the population as a whole. Details of pooled coherence analysis and on setting of confidence limits can be found in (Amjad et al. 1997). The approach used here to calculate pooled coherence estimates was to pool individual coherency estimates (Farmer et al. 2007; Halliday and Rosenberg 2000). The individual coherency estimate for record $i$ was denoted as $R^i_{xy}(\lambda)$, where this has been calculated from $L_i$ segments of data. This coherency function is a complex quantity, the corresponding coherence is its the magnitude squared.. The pooled coherence across $k$ records, at frequency $\lambda$ is then:

$$\left| \frac{\sum_{i=1}^{k} L_i \, R^i_{xy}(\lambda)}{\sum_{i=1}^{k} L_i} \right|^2$$

Estimates of the above pooled coherence provide a single parameter describing the correlation structure, as a function of frequency, within the $k$ records in a single population. This can be considered analogous to single coherence estimate calculated from $\sum_{i=1}^{k} L_i$ segments of data.

Inherent within pooled coherence framework is the Chi-Squared $\chi^2$ extended difference of coherence test with the null hypothesis no difference in coherence at a given frequency. Like coherence the $\chi^2$ test is applied separately at each frequency of interest (see Amjad et al., 1997). Changes in the correlation structure between two different subject populations, can be asecertained by undertaking a $\chi^2$ extended difference of coherence test on the populations to be compared. The resulting $\chi^2$ difference test, thus provides a metric of ammount of pooled coherence difference at each frequency between the two populations (Farmer et al. 2007).

Estimates of pooled coherence, pooled spectra, pooled cumulant density functions and pooled phase were used to summarize the EMGs and the EMG-EMG correlation structure in each group of subjects. Estimates of pooled coherence provide a single parameter describing the correlation structure, as a function of frequency, within the records in a single population, where the total number of records to be used equates to the number of subjects for each group.

In addition to pooled statistics the peak values of EMG-EMG coherence in the beta and gamma frequency range were collected along with the duration and magnitude of the central peak in the EMG-EMG cumulant density function and RMS EMG magnitude. The central peak was calculated as the total time where the central peak was above the upper 95 % confidence limit.

Data were tested for normality before analysis using the Kolmogorov-Smirnov test. Data were rank transformed since all peak coherences were found to be normally distributed. For the comparison of peak coherence values, cumulant density measures, and leg kinematic data between the LA and MA muscle and data from typically developing control subjects a 2-way factorial ANOVA general linear model was calculated using Sigmaplot 11, with age ranges: 4-7 years, 8-11 years and 12-15 years as one factor and muscle: MA, LA and control as the other factor.

For the comparison of MA/LA ratios of beta and gamma coherence, RMS EMG amplitude and kinematic measures across the three age groups a 1-way ANOVA was calculated. Multiple pair wise comparisons were performed using Tukeys t-test. All values are given as mean ± 95 % confidence intervals. For correlation analysis we used Pearson product moment correlations. Multiple linear regression analysis was used to account for the effect of age or EMG RMS amplitude on the correlations between peak coherences and kinematic parameters

## Results

### *Static muscle activation*

During static activation all CP subjects were able to produce EMG in the Most Affected (MA) and Least Affected (LA) TA muscles. A typical example is shown in figure 1 (A and B) in which EMGs from the LA and MA TA muscles were recorded in a 12 year old subject during static ankle dorsiflexion. The corresponding power spectra and output from the time/frequency analysis are displayed in this figure. The $chi^2$ difference of coherence measure (Fig 1L) calculated for the two muscles emphasizes that the main differences in the common drive between the LA and MA TA muscles are at 10, 16-22 and 24-40 Hz, with the highest coherence values obtained from the LA TA muscle. The corresponding time domain measures of synchrony show a central peak at time zero with broad side lobes indicative of broad-peak synchrony in the MA TA muscle (Fig 1K). The LA muscle (Fig 1M) shows a narrower central peak with a peak value of double that of the MA muscle. From the phase plots (Fig. 1H and J) it is seen that the two EMGs were in phase over the frequency range up to 50 Hz for the LA TA (Fig. 1J) whereas this was only the case for frequencies up to 10 Hz for the LA TA (Fig. 1H).

Using the technique of pooled coherence and $Chi^2$ comparisons the common drive to the muscles during static activation was quantified for the MA and LA sides in all subjects (figure 2). The subjects were divided into 3 age groups: 4-7 years (n=7; Fig 2A & 2B), 8-11 years (n=17; Fig 2D & 2E) and 12-15 years (n=14; Fig 2G & 2H). In keeping with the results illustrated for the individual subject there were marked MA vs. LA differences in pooled coherence (Fig 2C, 2F & 2I). The $chi^2$ difference of coherence between MA and LA muscles for the older age groups (8-11 and 12-15 years) showed marked differences in the range 10-50 Hz ($Chi^2$: 75-125). The comparison for the younger 4-7 year age group showed a less impressive MA and LA difference ($Chi^2$: 20 in range 10-50 Hz and 50 at 5 Hz). The interaction between age and the effects of the CNS lesion was further explored through $Chi^2$ comparisons and through calculation of the correlation between age and peak coherence (see Fig 3).

In figure 3 is shown $Chi^2$ differences for within side MA vs LA comparisons across age groups. The three age groups were compared against one another: 4-7 vs. 8-11 years (Fig. 3A & 3B); 4-7 years vs. 12-15 years (Fig. 3C & 3D) and 8-11 years vs. 12-15 years (Fig 3E & 3F). For the MA muscle coherence there was an increase in common drive when comparing the youngest (4-7 years) age against the oldest (12-15 years) age group ($Chi^2$: 40-50 in frequency range 15-40 Hz). Some small changes in common drive were observed when comparing the MA coherence between 4-7 and 8-11 years age groups and also when comparing the 8-11 years age group with those of 12-15 years age group ($Chi^2$: 10-20 for frequency range 15-40 Hz). The $Chi^2$ differences were overall much smaller than those observed in the same subjects when comparing the LA muscle coherence strength between the different age groups. For the LA muscle there was a marked increase in common drive in the range 15-50 Hz when comparing the youngest age group against the two older groups ($Chi^2$: 40-125 for frequency range 15-40 Hz). The largest difference between the coherence values was observed for age ranges 4-7 years vs. 12-15 years. These results demonstrated that it was between the ages 4-7 and 8-11 years that there was a maximal increase in the development of the common drive to the LA muscle.

Figure 3 G & H display peak coherence (mean ± 95 % confidence intervals) for the three age groups in the beta (15-25 Hz) and gamma frequency bands (30-45 Hz) for the MA and LA TA muscle in comparison to that of the TA muscle in typically developing children (control group). Peak values are given in table 2

A significant effect of age group ($F(2,103)=7.9$, $p<0.001$) and muscle ($F(2,103)=39.6$, $p<0.001$) was found for peak beta coherence, with no interaction between the two parameters ($F(4,103)=1.1$, $p=0.34$). For peak gamma coherence an effect of age group ($F(2,103)=15.6$, $p<0.001$) and muscle ($F(2,103)=15.59$, $p<0.001$) was found, with no significant interaction between the two parameters ($F(4,103)=1.0$, $p=0.39$).

Pair wise comparisons across age ranges showed significantly lower levels of peak beta coherence in the 4-7 yrs age group compared to the 8-11 yrs and ($p=0.005$) and the 12-15 yrs age groups ($p<0.001$), respectively. No significant difference was observed between the 8-11 and the 12-15 yrs age groups ($p=0.68$)

Pair wise comparisons across muscle showed significantly lower levels of peak beta coherence in the MA TA muscle compared to the LA ($p<0.001$) and the control TA muscle ($p<0.001$), respectively. No significant difference was observed between the LA and the control TA muscle ($p=0.68$)

Pair wise comparisons across age ranges showed significantly lower levels of peak gamma coherence in the 4-7 yrs age group compared to the 8-11 yrs and ($p<0.001$) and the 12-15 yrs age groups ($p<0.001$), respectively. No significant difference was observed between the 8-11 and the 12-15 yrs age groups ($p=0.63$)

Pair wise comparisons across muscle showed significantly lower levels of peak gamma coherence in the MA TA muscle compared to the LA ($p<0.001$) and the control TA muscle ($p<0.001$), respectively. significantly lower levels of gamma coherence was observed between the LA and the control TA muscle ($p=0.08$)

Higher amplitudes of EMG RMS were found for the LA side compared to the MA side ($P<0.001$, for ratio MA/LA see Fig 3I). In the CP subjects for both the coherence and RMS EMGs, the ratio for the MA and LA muscles (MA/LA) was calculated for each subject. The results are presented for each of the 3 age groups in Fig 3I. The MA/LA ratio for the beta band coherence decreased with increasing age group ($F(2,35)=3.6$, $p=0.04$). The gamma coherence ratio MA/LA did not change significantly with increasing age group (F(2,35)=1.3, p=0.29). The MA/LA ratio for the RMS EMG increased with increasing age group (F(2,35)=6.4, p=0.004). When the ratio MA/LA was examined for individual subjects the tendency for RMS EMG to increase with age was confirmed (r=0.46, P=0.004). The coherence MA/LA ratios for individual subject's showed an effect of reduction with increasing age for beta frequencies (r= -0.40, P=0.01) and a tendency in this direction for gamma frequencies (r= -0.25, p=0.13). Thus whilst the RMS EMG values for the MA muscle approach those of the LA muscle with increasing age the relative modulation of the EMG due to common drive either does not increase for gamma frequencies or for beta frequencies decrease. To summarize during static TA muscle activation there are differences in beta and gamma band coherence between the MA muscle and the LA muscle with a reduction of age-related increases in coherence in the MA muscle.

*Muscle activation during walking*

Figure 4 illustrates for a single subject (same subject as figure 1) the common drive to the TA muscle during gait. Rectified and averaged EMG from the MA and LA TA muscles during the swing phase of gait is shown (Fig 4 A and B). The heel strike occurred at 0 ms. Both MA and LA TA muscles showed modulation of the EMG activity throughout the swing phase. We focused on the EMG activity prior to the heel strike, indicated by shaded areas which correspond to the first peak of EMG activity where the forefoot is lifted to clear the toes above the ground during the swing phase. Power spectra recorded from the two electrodes on the left and right sides, coherence and phase plots for the EMG-EMG correlation are shown in Fig 4 C-J. For the MA muscle there is coherence at low frequencies with little coherence at frequencies in excess of 10 Hz. For the LA muscle there is significant coherence at all frequencies between 1 and 45 Hz. The difference in common drive (higher magnitude coherence in the LA muscle) between MA and LA muscles is quantified by the $Chi^2$ difference plot (Fig. 4L) in which the primary differences between the two muscles during gait are a low coherence frequencies (<5 Hz and at 10 Hz) and in the range 17-27 Hz. Figure 4 K and M show the corresponding MA and LA cumulant densities for this subject, from these it can be seen that the overall level of EMG-EMG synchrony in the MA TA muscle is less than 50% of that of the LA TA muscle. Note the longer duration of the central peak of synchronization during gait as compared to static contraction. This is explained by the synchronizing effect of the EMG envelope during gait (cf. Hansen et al. 2005; Nielsen et al. 2008).

The pooled coherence data for all CP subjects during walking are shown in figure 5. As for the static contractions the data are presented for the MA and LA TA muscle across 3 age groups: 4-7 years (n=7; Fig. 5A & 5B), 8-11 years (n=17; Fig. 5D & 5E) and 12-15 years (n=14; Fig 5G & 5H). In comparison to the MA muscle, the values of coherence in the LA muscle across a broad frequency range (1-50 Hz) at each age were greater and this was shown clearly in the $Chi^2$ comparisons (Fig. 5C, 5F and 5I). The $Chi^2$ coherence difference was least marked for the MA versus LA comparison in the 4-7 years age group ($Chi^2$: 150 at 3 Hz and 10-50 for range 10-40 Hz. The most marked differences between the MA and LA muscles were identified for the older age groups: 8-11 and 12-15 years, with particularly marked differences for the 4-7 vs. 8-11 year group comparison at low <10 Hz frequencies ($Chi^2$: ~200) as well as frequencies between 10 and 50 Hz ($Chi^2$: 50-150).

The effect of age was explored further through $Chi^2$ comparisons and through calculation of the correlation between age and peak coherence (Fig. 6). As with static contraction for the LA muscle of CP subjects there was a similar effect of age to that observed in typically developing subjects performing the same task (see Petersen *et al.*, 2010). The youngest age group (4-7 years) showed less gamma band (~40 Hz) common drive compared to the 8-11 and 12-15 year age groups, Fig 6 B and D ($Chi^2$: 25 for range 25-50 Hz). In the gamma frequency range there was little difference in common drive between the two older age groups (Fig 6 F). Using $Chi^2$ analysis no evidence of a clear age related increase in the beta frequency band was observed for gait. Interestingly the $Chi^2$ comparison detected differences for the MA TA muscle in favor of the oldest group when compared to the two younger groups (see Fig 6C and 6E, $Chi^2$: 20-50 at 35 Hz), suggesting that weak gamma common drive during gait developed late for the MA muscle.

Figure 6 G & H show peak coherence (mean ± 95 % confidence intervals) for the three age groups in the beta (15-25 Hz) and gamma frequency bands (30-45 Hz) for the MA and LA TA muscle in CP subjects and for the TA muscle of typically developing children. Peak values are given in table 2. No significant effect of age range ($F(2,109)=2.3$, $p=0.11$), but a significant effect of muscle ($F(2,109)=24.4$, $p<0.001$) was found for peak beta coherence, with no interaction between the two parameters ($F(4,109)=0.39$, $p=0.82$).

For peak gamma coherence a significant effect of both age range ($F=10.2$, $p<0.001$) and muscle ($F=36.0$, $p<0.001$) was found, with no significant interaction between the two parameters ($F(4,109)=1.0$, $p=0.46$).

Pair wise comparisons across muscle showed significantly lower levels of peak beta coherence in the MA TA muscle compared to the LA (p<0.001) and the control TA muscle (p<0.001), respectively. No significant difference was observed between the LA and the control TA muscle (p=0.97)

Pair wise comparisons across age ranges showed significantly lower levels of peak gamma coherence in the 4-7 yrs age group compared to the 8-11 yrs and (p=0.02) and the 12-15 yrs age groups (p<0.001), respectively. No significant difference was observed between the 8-11 and the 12-15 yrs age groups (p=0.13)

Pair wise comparisons across muscle showed significantly lower levels of peak gamma coherence in the MA TA muscle compared to the LA (p<0.001) and the control TA muscle (p<0.001), respectively. No significant difference was observed between the LA and the control TA muscle (p=0.63)

In the CP subjects the ratio of the coherence and RMS EMG between the MA and LA muscles during walking was calculated for each subject. The results are presented for each of the 3 age groups in Fig 6I. The MA/LA ratio for the beta and gamma band coherence ranges showed a tendency to decrease with increasing age (see Fig 6I) but these did not reach statistical significance (F(2,35)=0.75, p=0.48 and F(2,35)=1.0, p=0.39). The MA/LA ratio for the RMS EMG showed a tendency to increase between the youngest and oldest age groups but this did not reach statistical significance (F(2,35)=1.1, p=0.33). When the ratio MA/LA was examined for individual subjects the tendency for RMS EMG to increase with age was confirmed (r=0.18, P=0.28). The coherence MA/LA ratios for individual subject's showed little affect of subjects' age (r= -0.03, P=0.85 for beta and r= -0.22, p=0.19 for gamma). Thus there was a weaker tendency for MA/LA ratio to increase for RMS EMGs and decrease for coherence with increasing age during walking when compared to static muscle activation. To summarize during walking differences between the MA and the LA muscles in beta and gamma band coherence with a loss of age-related increases in coherence in the MA were found.

*EMG-EMG synchronization during static muscle activation and walking*

Figure 7 (upper part) shows pooled cumulant density plots obtained during static activation for the MA, LA and control TA muscle across all three age groups: 4-7 yrs (Fig. 7 A, B & C), 8-11 years (Fig. 7 D, E & F) and 12-15 years (Fig. 7 G, H& I). Peak cumulant magnitudes and peak cumulant durations are given in table 3. The peak size showed an overall effect of age group (F(2,109)=15.8, p<0.001) and muscle (F(2,109)=23.2, p<0.001) with no significant interaction between the two parameters (F(4,109)=0.8, p=0.53).

Pair wise comparisons showed significantly smaller peaks for the 4-7 yrs age group compared to the 8-11 yrs and (p=0.02) and the 12-15 yrs age groups (p<0.001), respectively. No significant difference was observed between the 8-11 and the 12-15 yrs age groups (p=0.34)

Pair wise comparisons across muscle showed significantly smaller peaks in the MA TA muscle compared to the LA (p<0.001) and the control TA muscle (p<0.001), respectively. No significant difference was observed between the LA and the control TA muscle (p=0.99)

Pair wise comparisons showed significantly longer peak duration the 4-7 yrs age group compared to the 12-15 yrs age groups (p<0.001). No significant difference was observed between the 8-11 and the 4-7 (p=0.06) and 12-15 yrs age groups (p=0.34), respectively

Pair wise comparisons across muscle showed significantly longer peak duration for the MA TA muscle compared to the LA (p=0.002) and the control TA muscle (p=0.02), respectively. No significant difference was observed between the LA and the control TA muscle (p=0.61)

Figure 7 (lower part) shows pooled cumulant density plots obtained during walking for the MA, LA and control TA muscle across all three age ranges: 4-7 yrs (Fig. 7 J, K & L), 8-11 years (Fig. 7 M, N & O) and 12-15 years (Fig. P, Q & R). Peak sizes and durations are given in table 3. The peak size showed no significant effect of age group (F(2,109)=0.002, p=0.99) but an overall effect of muscle (F(2,109)=42.8, p<0.001) with no significant interaction between the two parameters (F(4,109)=0.69, p=0.60) was observed.

Pair wise comparisons across muscle showed significantly smaller peaks in the MA TA muscle compared to the LA (p<0.001) and the control TA muscle (p<0.001), respectively. No significant difference was observed between the LA and the control TA muscle (p=0.75)

No differences (p>0.05) were observed for the peak duration and the effect of gait modulation on the peak duration renders it meaningless

*Kinematic recordings*

There was a significant effect of age group (F(2,109)=3.6, p=0.03) and leg (F(2,109)=19.1, p<0.001) when comparing the ankle joint dorsiflexion movement ranges (Fig 8A). A significant higher movement range was found for the LA and control ankle joint compared to the MA leg for the two oldest age groups (8-11 yrs; p<0.001 & p=0.011, 12-15 yrs; p<0.001 & p=0.01).

There was not a significant effect of age group (F(2,109)=2.3, p=0.11) but a significant effect of leg (F(2,109)=34.4, p<0.001) when comparing the ankle joint dorsiflexion movement velocities (Fig 8B). A significant higher movement velocity was found for the LA and control ankle joint compared to the MA leg for the all three age groups (4-7 yrs; p=0.013 & p=0.004, 8-11; p>0.001 & p<0.001, 12-15 yrs; p<0.001 & p<0.001).

The COV of the dorsiflexion movement decreased with age for the LA side (r=0.56, p<0.001) but not for the MA side (r=0.28, p=0.085) showing a similar effect for the LA side as for that of the controls (Petersen et al. 2010). No significant relationship between MA or LA COV of the dorsiflexion movement and peak MA or LA beta and gamma coherence was observed (p>0.05) nor was the MA/TA beta or gamma coherence ratio correlated with the MA/LA COV ratio (p>0.05)

The functional significance of the difference in coherence between the LA and MA TA muscle was further explored. Because of inter-subject differences and the effects on coherence of age we calculated the ratio peak coherence magnitude for beta and gamma frequency ranges (see Fig 3I and 6I) and compared this to the ratio of ankle joint movement range and the ratio of ankle joint velocity. Comparison between the beta coherence ratio and the ankle dorsiflexion angle ratio and movement velocity ratio (Fig 8C, D) revealed positive relationships independent of the effects of age and RMS EMG (r=0.57, p<0.001; r=0.61, p<0.001, respectively). No relationship was observed between either the MA/LA gamma coherence ratio (r=0.08, p=0.64 & r=0.11, p=0.5, respectively) or the MA/LA RMS EMG ratio (r= 0.17, p=0.32 & r=0.24, p=0.15, respectively) and the MA/LA ratios for range and velocity of joint movement (Fig 8E-H). No significant (p>0.05) relationships were observed between the MA/LA coherence ratios obtained during static contraction and kinematic parameters.

## Discussion

We have shown that the common drive to the most affected TA muscle during static dorsiflexion and walking in children with CP is reduced as compared to the least affected TA muscle and typically developing control subjects. The reduction of common drive during gait in the CP children was related to deficits in their ability to lift the foot in the swing phase of gait.

*Methodological considerations*

Cross-talk between recording electrodes will always be a concern for analysis of coherence between EMG recordings from adjacent muscles or as in the present study from the same muscle. To minimise the influence of cross-talk we ensured that the distance between recording electrodes was as large as possible. In previous studies we have ensured a distance of more than 10 cm between electrodes, which exceeds the length of individual muscle fibres in the adult TA muscle. It was not possible to separate the electrodes by an as long distance especially in the smaller children in this study (Table I). We do not know the exact length of TA muscle fibres in the different age groups, but if there is a relatively proportionate scaling to body size, the distance between electrodes was considerably longer than the fibre length even in the youngest (smallest) children. It may also be argued that the youngest children had the shortest distance between electrodes but the least coupling between the recordings in both the time and frequency domains. Cross-talk due to sampling of activity from too closely located electrodes would have been expected to produce the opposite result. To further minimize any influence from cross-talk, all data showing either very narrow peaks in the cumulant density function (less than 2 ms) or equal and significant coherence at all frequencies were deemed to be influenced by cross-talk and therefore omitted from further analysis. All recordings that were used for the analysis thus showed coherence for only restricted frequency band and cannot easily be explained by cross-talk.. It should also be noted that coherence in a similar restricted frequency band and central peaks of synchrony in the time domain with a similar duration as observed for surface EMG recordings in the present study have been observed in needle and wire recordings of the activity of individual motor units (Hansen et al. 2005; Farmer et al. 2003).

*Central motor pathways underlying common drive in CP*

Based on studies of patients with CNS lesions, primate physiology and MEG/EEG-EMG coherence it is recognized that motor unit synchronization and beta and gamma rhythm common drive to upper (Baker et al. 1997; Brown et al. 1998; Conway et al. 1995; Datta et al. 1991; Farmer et al. 1993a; Farmer et al. 1993b; Halliday et al. 1998; Mima and Hallett 1999; Salenius et al. 1997) and lower limb motoneurones (Gross et al. 2000; Hansen and Nielsen 2004; Hansen et al. 2002) are the result of oscillatory activity in cortical networks. Other peripheral feedback mechanisms may play a supportive but not essential role in maintaining EMG-EMG and EEG-EMG coherence (Farmer et al. 1993a; Hansen et al. 2002; Kilner et al. 2004; Pohja and Salenius 2003). In healthy adults the duration of single TA motor unit synchrony during static muscle activation is ~13 ms between TA motor units (Datta et al., 1991). In subjects who have suffered stroke damage to central motor pathways or spinal cord damage short-term synchrony is lost and may be replaced by longer duration (~29 ms) broad-peak synchrony (Datta et al. 1991). In the CP subjects the central cumulant peak size was smaller for the MA TA muscle both during static muscle activation and during walking supporting the results of Rose & McGill (2005) in which CP subjects were shown during static contraction to have reduced short-term synchronization compared to controls. Spinal cord lesions in cat produce a loss of short-term synchrony with the emergence of broad peak synchrony, which results from lesion-induced increased drive to the motoneurone pool from synchronized polysynaptic inputs (Kirkwood et al. 1982). In CP subjects the combined results of the loss of higher frequencies of coherence coupled with smaller central cumulant peaks of longer duration during static muscle activation suggests that for the MA muscle motoneurone activation is achieved through polysynaptic pathways rather than from directly projecting corticospinal pathways. The RMS EMG amplitude was larger for all age groups in the LA TA muscle compared to the MA TA muscle. However, taking into account individual differences in the CP subjects through calculation of the ratio MA/LA for coherence and RMS EMG amplitude we were able to show that for static muscle activation with increasing age, in contrast to the coherence values, the RMS EMG ratio between the MA and LA muscle normalized. We suggest therefore that RMS EMG levels during static muscle activation cannot explain the developmental pathophysiology of CP without taking into account the failure of the modulatory effects on motoneurone activity of common drive to develop.

*The relationship between common drive and TA muscle activation during walking*

Tibialis Anterior is the prime dorsiflexor of the ankle and its activation is essential in allowing the toes to clear the ground during the swing phase of gait. The importance of central drive for normal TA muscle function is evident clinically and in neurophysiological studies (Barthelemy et al. 2010; Halliday et al. 2003; Hansen et al. 2005; Nielsen et al. 2008; Petersen et al. 2001). It has recently been shown that during the swing phase of gait the EEG is coherent with TA muscle EMG at frequencies in the range 24-40 Hz (high beta-gamma range) and at 10 Hz (Petersen et al. 2012). These results show that during the swing phase of gait the TA muscle EMG synchronizes with EEG over the leg area of sensory-motor cortex indicating that during this period of gait TA EMG is also integrated (synchronized) within a cortical oscillatory network. Taken together these findings support the view that as for static TA activation during walking the beta and gamma drives to the muscle are the result of oscillatory synchrony within cortical circuits that include the leg area of the primary motor cortex.

Impaired central drive to TA results in a dropped foot and a gait pattern characterized by toe rather than heel strike. Interestingly 24-40 Hz common drive to thigh muscles has been shown to increase following treadmill training and improvement of locomotion skills (Norton and Gorassini 2006). During normal gait the common drive is present in the early and late part of the swing phase with a maximum right before the foot is placed on the ground in very late swing phase (Halliday et al. 2003). Therefore, measurement of common drive provides important information about the corticospinal involvement in the control of the TA muscle at a time where precise control of the ankle joint is required during human walking. Gamma range common drive (~35-55 Hz) has been described in strongly contracting hand muscles (Brown et al. 1998; McAuley et al. 1997) and is coherent with cortical rhythms (Brown et al. 1998). Our previous study and the results of the present study support those of Omlor *et al.* (2007) which showed a switch from beta to gamma band drive during dynamic force output for upper limb muscles. Omlor *et al.* (2007) suggested that gamma range EEG-EMG coherence underpins binding of the attentional, visual, somatosensory information necessary for control of dynamic force output as opposed to static force output. We suggest that such integrated dynamic force control of the ankle joint during gait is essential for co-coordinated walking and that failure of development of gamma range common drive to TA muscle during walking may be a pathophysiogical underpinning of the increased clumsiness and excess falls seen in CP children. In our recent study on normally developing children we found an increase in gamma band coherence with age that was associated with a reduction in the step to step variability (COV) (Petersen et al. 2010). In the present study a similar relationship was not found for CP children for either the most or least affected leg, although COV decreased with age for the LA side but not for the MA side. This lack of correlation is in all likelihood explained by low values and large inter-individual variability of common gamma drive levels in the CP subjects. We did find, however, a significant relation between the LA/MA ratio of beta coherence and the range and velocity of dorsiflexion in the swing phase of walking. The LA/MA ratio gives a measure of the difference in function between the two legs within each individual and thus greatly reduces inter-subject variability. The significant correlation of beta coherence with the functional kinematic parameters, corrected for age and EMG magnitude suggests that this measure of central drive to TA motoneurones is of functional significance for the gait ability of the children. Furthermore the MA/LA ratios of beta and gamma coherence for static muscle activation did not correlate with the functional kinematic parameters. Static muscle activation is used widely in the measurement of motor unit synchrony however our finding signifies that the common drive should also be measured during functionally relevant conditions.

We do not as yet have data showing increases in EEG-EMG coherence during static TA activation and during walking across childhood or in subjects with CP. However, for upper limb muscles the increases in EMG-EMG synchrony and coherence seen in childhood are mirrored by an increase in beta and gamma EEG-EMG coherence during childhood (Graziadio et al. 2010; James et al. 2008). We have suggested therefore that the developmental increases in TA EMG-EMG synchrony and coherence in static activation and walking across childhood reflect that the TA muscle receives increased oscillatory drive from motor cortex networks. We now suggest that the failure of the MA TA muscle to show increases in beta and gamma range coherence across childhood is evidence that in CP there is a failure of development of oscillatory motor cortex networks and a failure to integrate TA EMG activity through the mechanism of oscillatory synchrony with these cortical networks.

*Conclusion*

We conclude that children with CP show reduced oscillatory beta and gamma common drive to spinal motoneurones that innervate the MA TA muscle during static contraction and gait. The relation between the MA/LA ratio of beta and gamma coherence during gait and the kinematics of gait suggests that the time and frequency domain analyses of EMGs may in the future provide pathophysiologically meaningful and functionally relevant measures of the effect of gait training and other therapeutic interventions on the cortical drive to spinal motoneurones during gait in children with CP. The ease with which these techniques may be applied makes them ideal for longitudinal studies of training interventions in which mechanistic understanding of neuro-plastic changes in central networks is required.

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## Author contributions

T.H.P. and J.B.N. designed the experiment. T.H.P. and M.K.-D. collected the data. T.H.P. and S.F.F. analysed the data. T.H.P.,S.F.F. and J.B.N. interpreted the data and drafted the manuscript. All experiments were performed at the Helene Elsass Center.


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**Table 1.** Summary of data from the three different age groups. All values are given as mean± 95% CI. Inter electrode distance between the proximal and distal electrode pair placed above the least (LA) and most (MA) affected muscle. Treadmill walking speed in km/h.

**Table 2.** Summary of peak coherence values for the MA, LA and control TA muscle across the three different age groups. Peak coherence in the beta (15-25 Hz) and gamma (30-45 Hz) frequency band are given for static muscle activation and for walking. All values are given as mean± 95% CI. Please refer to text for detailed statistics.

**Table 3.** Summary of cumulant density estimates for the MA, LA and control TA muscle across the three different age groups. Peak durations and peak sizes band are given for static muscle activation and for walking. All values are given as mean± 95% CI. Please refer to text for detailed statistics

**Figure 1.** Data from one hemiplegic CP subject (12 yrs of age). Raw EMG traces obtained from electrodes placed at the proximal and distal part of the MA (A) and LA(B) TA muscle. Power spectra constructed from the rectified EMG signals from the MA (C & D) and LA muscle (E & F). Coherence estimates from MA (G) and LA (I) muscle, the dashed lines denote upper 95% confidence limits. Phase estimates from MA (H) and LA (J) muscle. Cumulant density plots from MA (K) and LA (M) solid lines around zero denotes upper and lower 95% confidence limits. (L) display the extended $chi^2$ test of difference of coherence between MA and LA. The dashed line denotes the upper 95% confidence limit on the assumption of independence.

**Figure 2.** Pooled estimates of coherence from all hemiplegic CP subjects. Pooled coherence estimates from the MA side are shown for three different age groups 4-7 yrs (A), 8-11 yrs (D) and 12-15 yrs (G). Pooled coherence estimates from the LA side are show for the three different age groups 4-7 yrs (B), 8-11 yrs (E) and 12-15 yrs (H). Results from the extended $chi^2$ test for difference of coherence are shown for the three age groups 4-7 yrs (C), 8-11 yrs (F) and 12-15 yrs (I)

**Figure 3.** Statistical comparisons of pooled coherence using the extended $chi^2$ test for difference of coherence. Comparisons of 4-7 yrs vs. 8-11 yrs for the MA muscle (A) and LA muscle (B). Comparisons of 4-7 yrs vs. 12-15 yrs for the MA muscle (C) and LA muscle (D). Comparisons of 8-11 yrs. vs. 12-15 yrs for the MA side (E) and LA side (F). Comparisons of peak beta band coherence (G) and peak gamma band coherence. (H) from MA muscle, LA muscle and control group (data from Petersen *et al.* 2010) across the three different age groups. Ratios (MA/LA) for peak beta coherence, peak gamma coherence and EMG RMS amplitude across the three different age groups (I). Error bars denote 95% confidence intervals. Please refer to text for detailed statistics.

**Figure 4.** Data from one hemiplegic CP subject (12 yrs of age). Rectified and averaged EMG from 300 individual steps from electrodes placed at the proximal and distal part of the MA (A) and LA (B) TA muscle. Heel strike at 0 ms. Shaded areas represent the EMG segments analysed. Power spectra constructed from the rectified EMG signals from the MA (C & D) and LA muscle (E & F). Coherence estimates from MA (G) and LA (I) muscle, the dashed lines denote upper 95% confidence limits. Phase estimates from MA (H) and LA (J) muscle. Cumulant density plots from MA (K) and LA (M) solid lines around zero denotes upper and lower 95% confidence limits. (L) display the extended chi$^2$ test of difference of coherence between MA and LA. The dashed line denotes the upper 95% confidence limit on the assumption of independence.

**Figure 5.** Pooled estimates of coherence from all hemiplegic CP subjects during walking. Pooled coherence estimates from the MA side are shown for three different age groups 4-7 yrs (A), 8-11 yrs (D) and 12-15 yrs (G). Pooled coherence estimates from the LA side are show for the three different age groups 4-7 yrs (B), 8-11 yrs (E) and 12-15 yrs (H). Results from the extended chi$^2$ test for difference of coherence are shown for the three age groups 4-7 yrs (C), 8-11 yrs (F) and 12-15 yrs (I)

**Figure 6.** Statistical comparisons of pooled coherence obtained during walking using the extended chi$^2$ test for difference of coherence. Comparisons of 4-7 yrs vs. 8-11 yrs for the MA muscle (A) and LA muscle (B). Comparisons of 4-7 yrs vs. 12-15 yrs for the MA muscle (C) and LA muscle (D). Comparisons of 8-11 yrs. vs. 12-15 yrs for the MA side (E) and LA side (F). Comparisons of peak beta band coherence (G) and peak gamma band coherence (H) from MA muscle, LA muscle and control group (data from Petersen *et al.* 2010) across the three different age groups. Error bars denote 95% confidence intervals. Ratios (MA/LA) for peak beta coherence, peak gamma coherence and EMG RMS amplitude across the three different age groups (I). Please refer to text for detailed statistics.

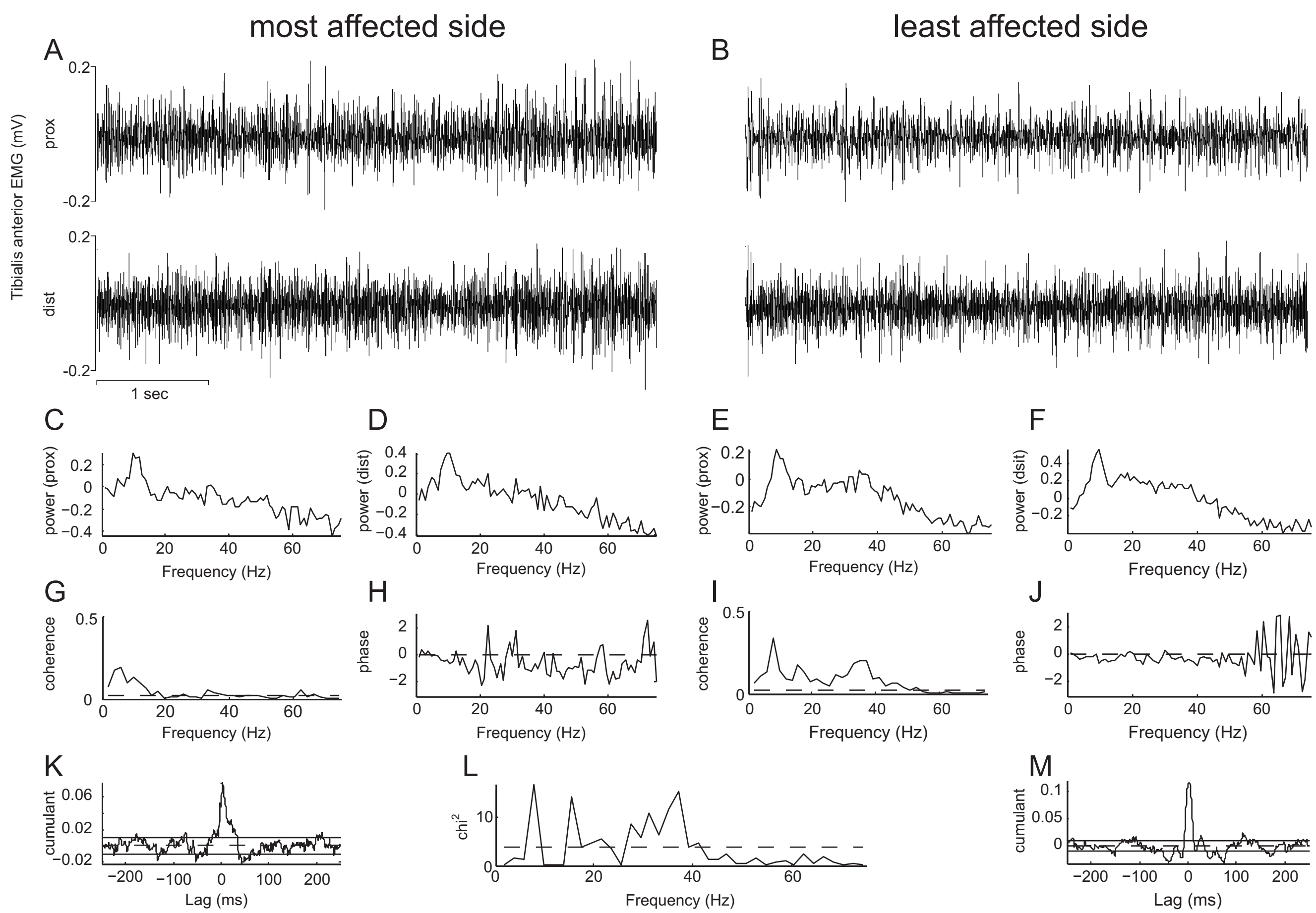
**Figure 7.** Pooled cumulant density plots are shown for the LA, MA and control TA muscle for the three age groups. 4-7 yrs (A,B, C & J, K, L), 8-11 yrs (D, E, F & M, N, O), 12-15 yrs (G,H, I & P, Q, R) for static muscle activation (upper part) and walking (lower part), respectively. Peak magnitudes and peak durations are given in table 3. Please refer to text for detailed statistics.

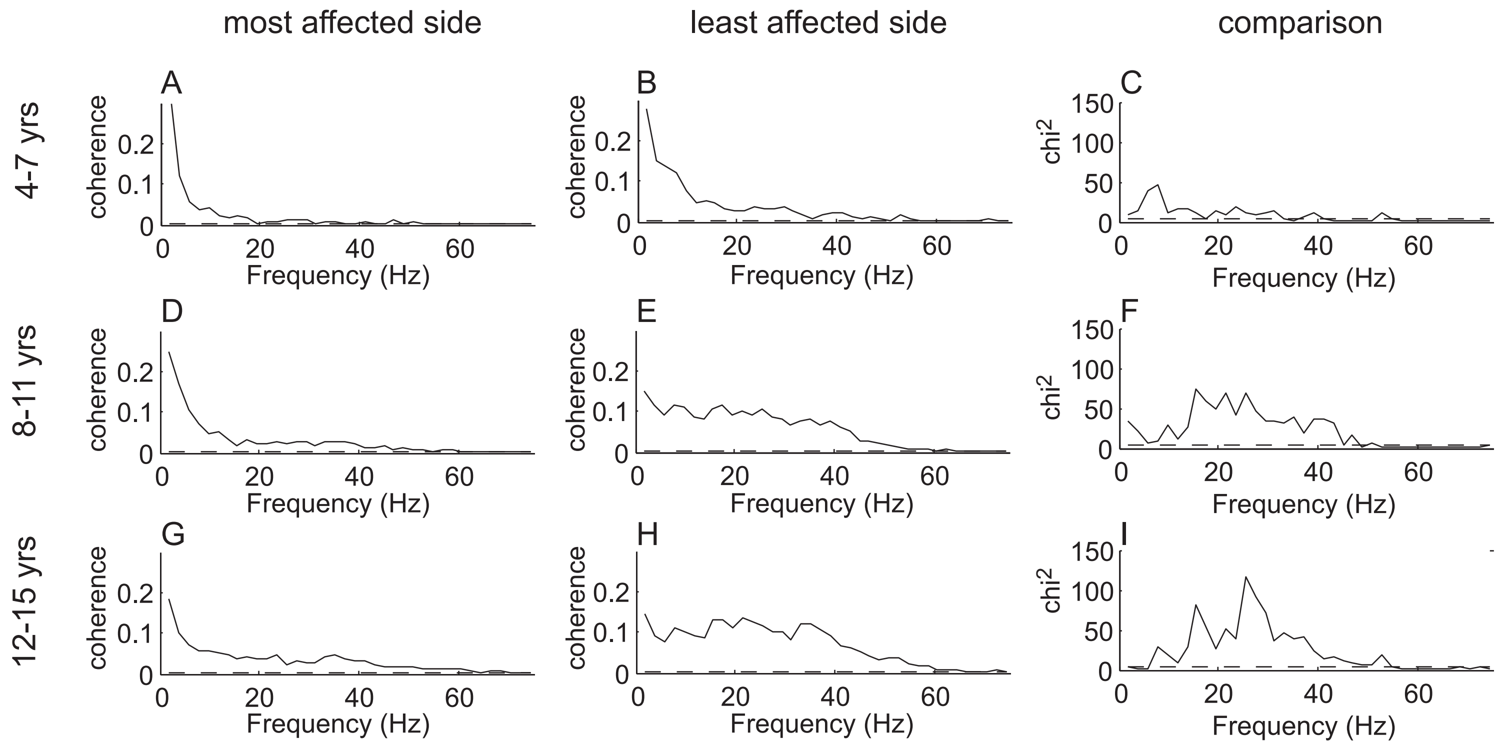
**Figure 8.** Kinematic data for the MA, LA and control ankle joint movements and correlations with EMG results. Dorsiflexion movement ranges for the ankle joint (A). Dorsiflexion movement velocity (B). Correlation between peak beta coherence ratio and dorsiflexion movement range ratio (C) and dorsiflexion movement velocity ratio (D). Correlation between peak gamma coherence ratio and dorsiflexion movement range ratio (E) and dorsiflexion movement velocity ratio (F). Correlation between RMS EMG amplitude ratio and dorsiflexion movement range ratio (G) and dorsiflexion movement velocity ratio (H). Please refer to text for detailed statistics on A & B.

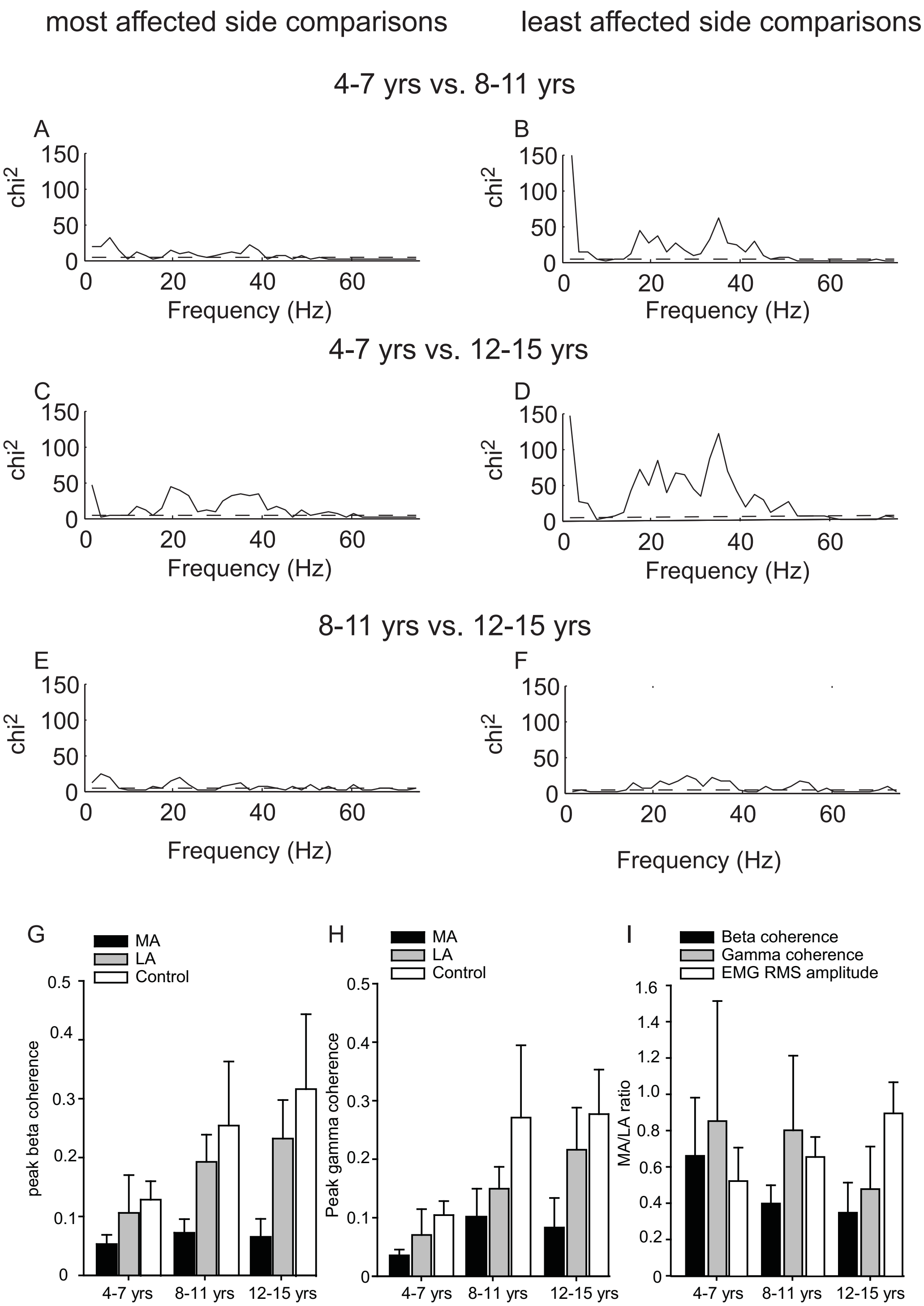
| | 4-7 years (n=7) | 8-11 years (n=17) | 12-15 years (n=14) |
|---|---|---|---|
| Electrode dist. MA (cm) | 7.0±0.7 | 10.6±0.6 | 12.5±1.0 |
| Electrode dist. LA (cm) | 7.4±0.4 | 10.8±0.5 | 12.5±0.9 |
| Walking speed (km/h) | 1.9± 0.4 | 2.5±0.2 | 2.8±0.2 |

| Coherence estimates | Static contraction | | | Walking | | |
|---|---|---|---|---|---|---|
| | CP MA side | CP LA side | Control | CP MA side | CP LA side | Control |
| 4-7 yrs, peak beta | 0.05±0.02 | 0,11±0.06 | 0.13±0.03 | 0.09±0.03 | 0.16±0.07 | 0.15±0.03 |
| 8-11 yrs, peak beta | 0.07±0.02 | 0.18±0.04 | 0.25±0.11 | 0.08±0.02 | 0.19±0.03 | 0.21±0.06 |
| 12-15 yrs, peak beta | 0.07±0.03 | 0.24±0.07 | 0.32±0.13 | 0.11±0.04 | 0.20±0.04 | 0.20±0.04 |
| 4-7 yrs, peak gamma | 0.04±0.01 | 0.07±0.04 | 0.11±0.02 | 0.05±0.02 | 0.09±0.05 | 0.08±0.02 |
| 8-11 yrs, peak gamma | 0.08±0.03 | 0.15±0.04 | 0.27±0.12 | 0.05±0.01 | 0.13±0.04 | 0.16±0.06 |
| 12-15 yrs, peak gamma | 0.11±0.07 | 0.21±0.07 | 0.27±0.08 | 0.07±0.05 | 0.16±0.04 | 0.18±0.03 |

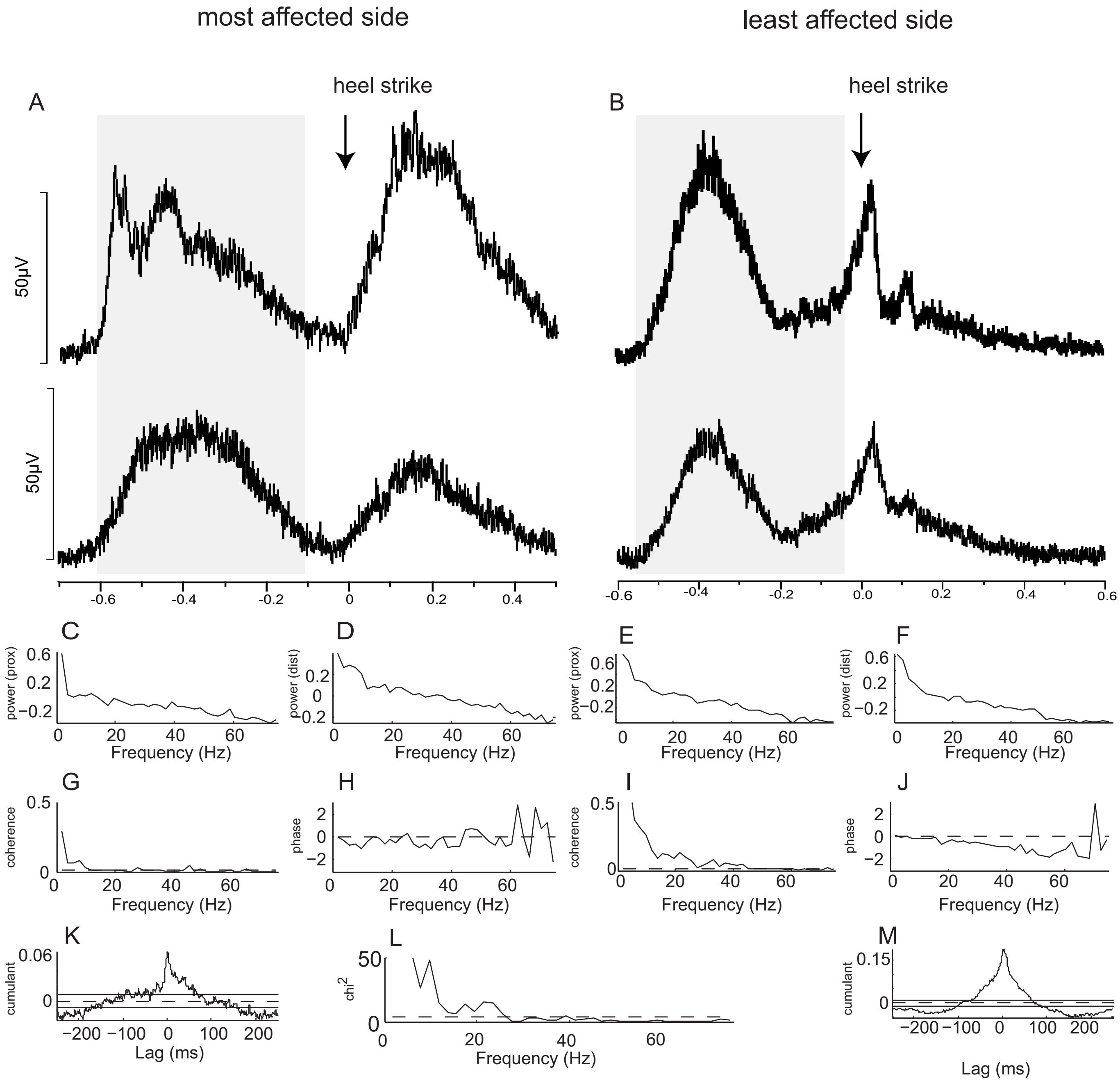
| Cumulant estimates | Static contraction | | | Walking | | |
|---|---|---|---|---|---|---|
| | CP MA side | CP LA side | Control | CP MA side | CP LA side | Control |
| 4-7 yrs, peak size | 0.047±0.014 | 0.083±0.043 | 0.068±0.015 | 0,169±0.042 | 0,269±0.078 | 0,295±0.046 |
| 8-11 yrs, peak size | 0.066±0.015 | 0.110±0.016 | 0.159±0.065 | 0,155±0.023 | 0,254±0.036 | 0,328±0.041 |
| 12-15 yrs, peak size | 0,072±0.020 | 0,144±0.042 | 0.167±0.053 | 0,166±0.030 | 0,242±0.051 | 0,329±0.052 |
| 4-7 yrs, peak width (ms) | 42±20 | 26±12 | 24±4 | 128±29 | 136±23 | 147±22 |
| 8-11 yrs, peak width (ms) | 31±7 | 22±3 | 21±4 | 147±22 | 121±14 | 121±19 |
| 12-15 yrs, peak width(ms) | 23±6 | 18±2 | 19±2 | 128±22 | 106±26 | 167±23 |


most affected side
least affected side
A
B
Tibialis anterior EMG (mV)
prox
dist
0.2
-0.2
1 sec
C
D
E
F
power (prox)
power (dist)
power (dsit)
Frequency (Hz)
G
H
I
J
coherence
phase
K
L
M
cumulant
chi2
Lag (ms)

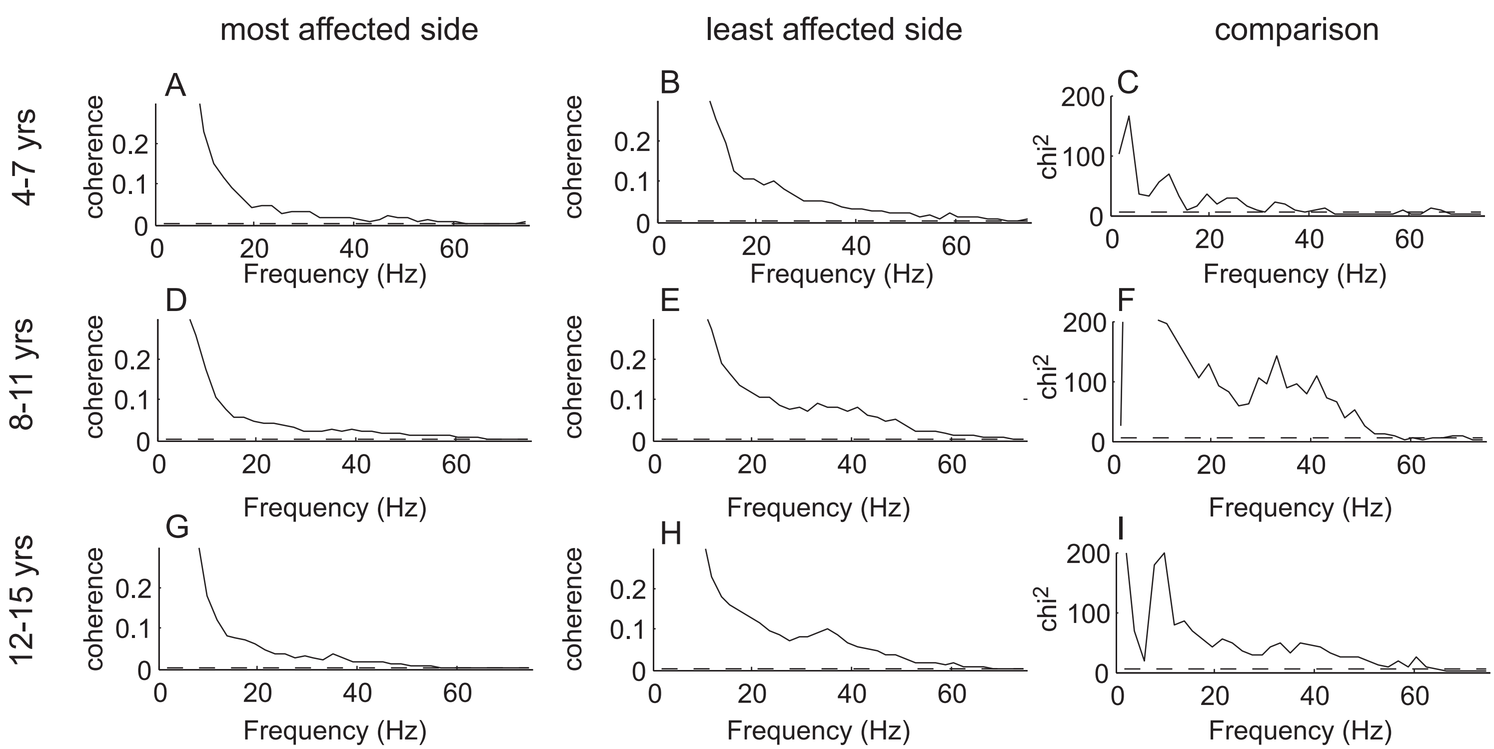

most affected side
least affected side
comparison
4-7 yrs
8-11 yrs
12-15 yrs
A
B
C
D
E
F
G
H
I
coherence
chi2
Frequency (Hz)
0
0.1
0.2
0
50
100
150
0
20
40
60



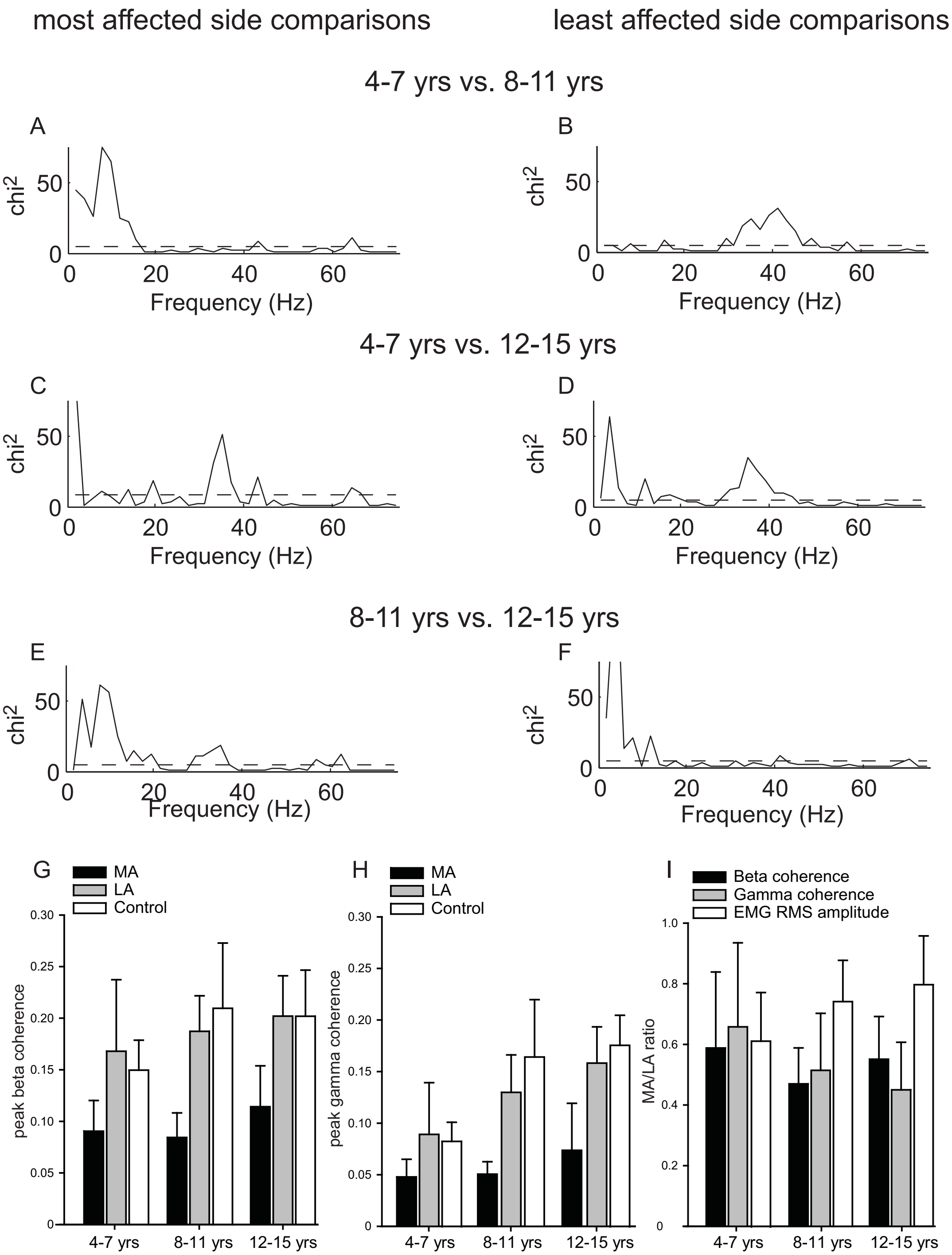
most affected side comparisons
least affected side comparisons
4-7 yrs vs. 8-11 yrs
A
B
4-7 yrs vs. 12-15 yrs
C
D
8-11 yrs vs. 12-15 yrs
E
F
chi2
Frequency (Hz)
G
MA
LA
Control
peak beta coherence
H
Peak gamma coherence
I
Beta coherence
Gamma coherence
EMG RMS amplitude
MA/LA ratio
4-7 yrs
8-11 yrs
12-15 yrs

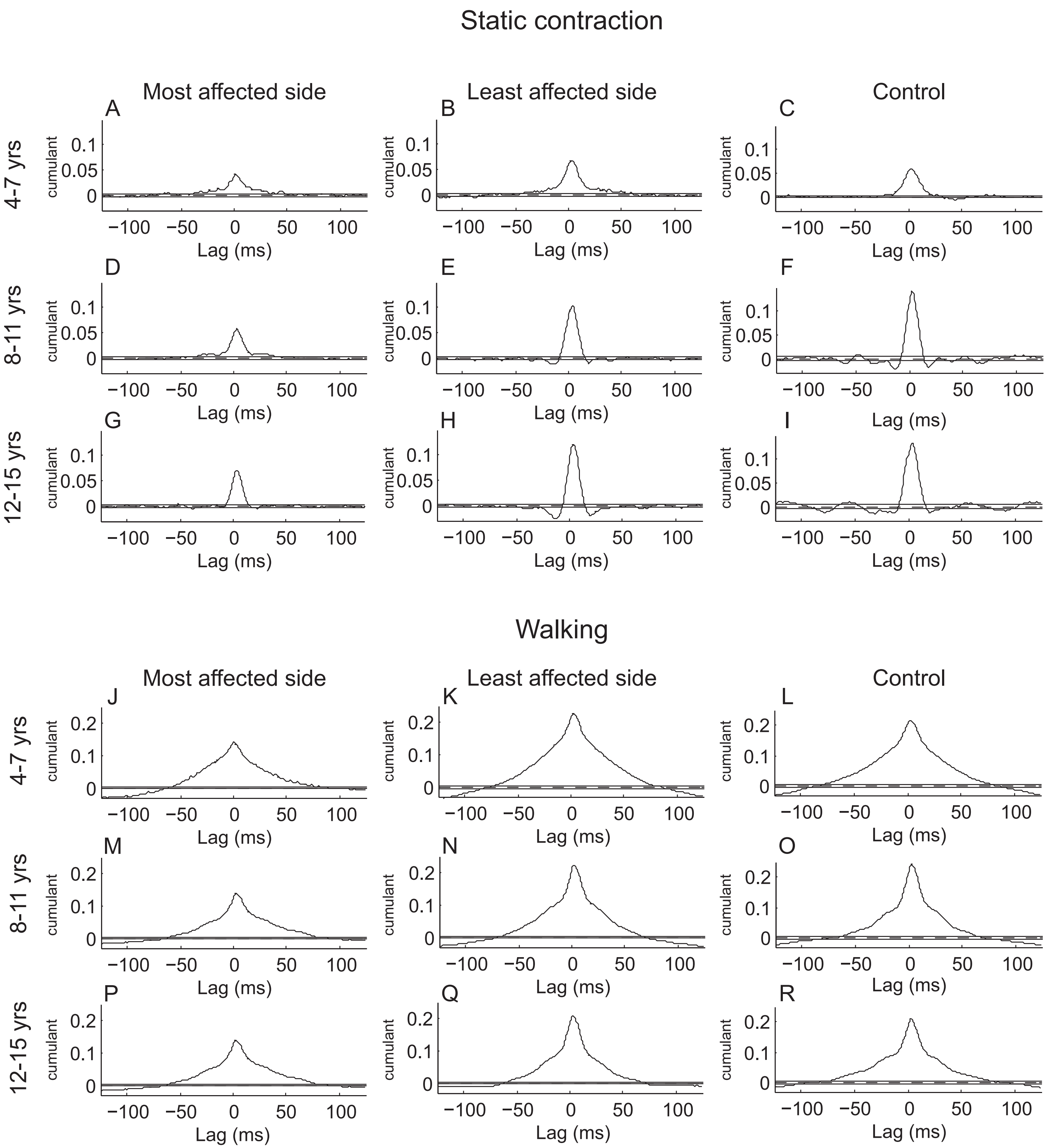


most affected side
least affected side
heel strike
heel strike
A
B
50µV
50µV
-0.6
-0.4
-0.2
0
0.2
0.4
-0.6
-0.4
-0.2
0.0
0.2
0.4
0.6
C
D
E
F
power (prox)
power (dist)
power (prox)
power (dist)
Frequency (Hz)
G
H
I
J
coherence
phase
coherence
phase
Frequency (Hz)
K
L
M
cumulant
chi2
cumulant
Lag (ms)
Frequency (Hz)
Lag (ms)

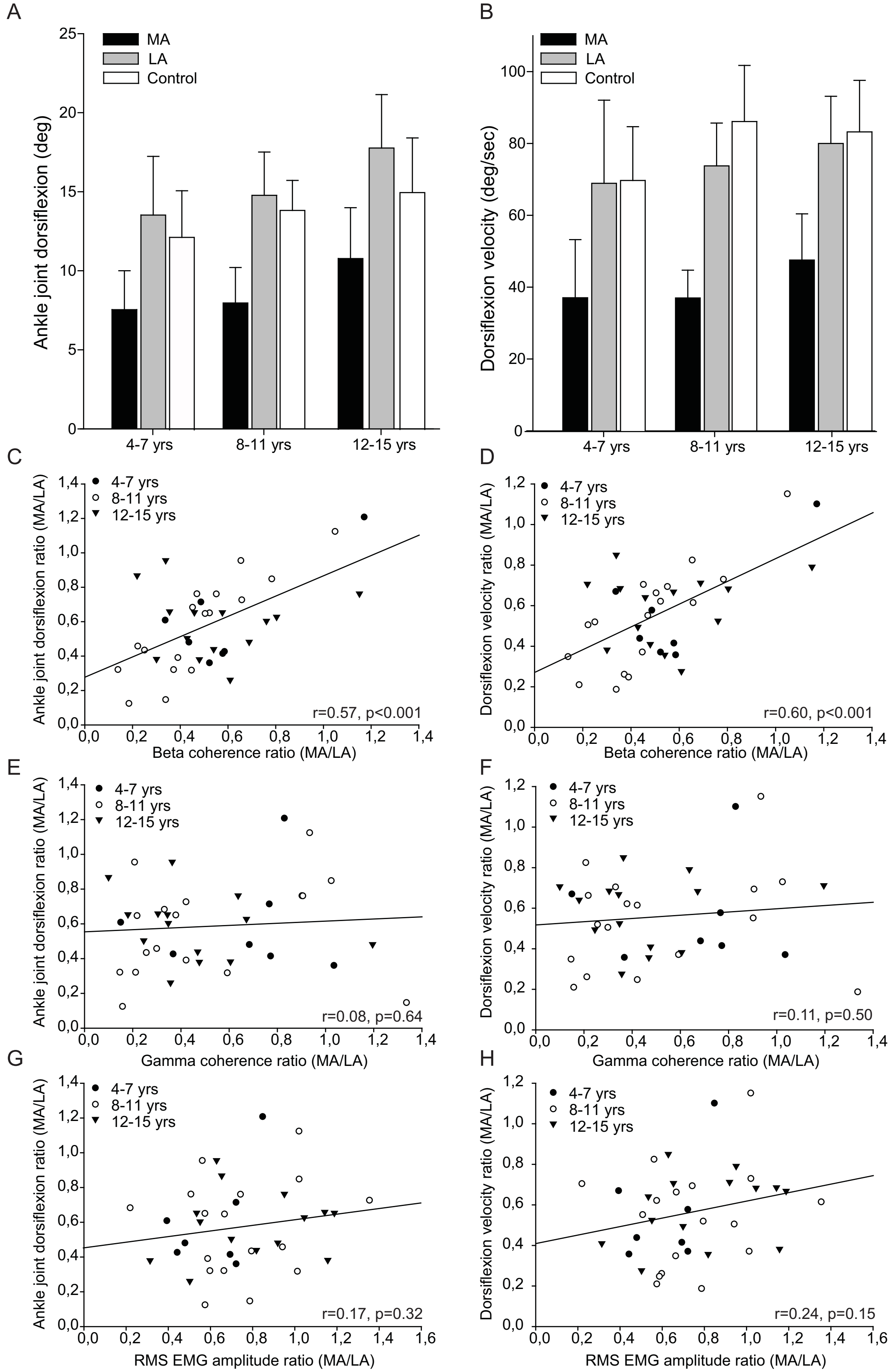


most affected side
least affected side
comparison
4-7 yrs
8-11 yrs
12-15 yrs
A
B
C
D
E
F
G
H
I
coherence
chi2
Frequency (Hz)


most affected side comparisons
least affected side comparisons
4-7 yrs vs. 8-11 yrs
A
B
chi2
Frequency (Hz)
4-7 yrs vs. 12-15 yrs
C
D
8-11 yrs vs. 12-15 yrs
E
F
G
MA
LA
Control
peak beta coherence
4-7 yrs
8-11 yrs
12-15 yrs
H
peak gamma coherence
I
Beta coherence
Gamma coherence
EMG RMS amplitude
MA/LA ratio



Static contraction
Most affected side
Least affected side
Control
4-7 yrs
8-11 yrs
12-15 yrs
A
B
C
D
E
F
G
H
I
cumulant
Lag (ms)
Walking
Most affected side
Least affected side
Control
J
K
L
M
N
O
P
Q
R


A
MA
LA
Control
Ankle joint dorsiflexion (deg)
4-7 yrs
8-11 yrs
12-15 yrs
B
Dorsiflexion velocity (deg/sec)
C
4-7 yrs
8-11 yrs
12-15 yrs
Ankle joint dorsiflexion ratio (MA/LA)
r=0.57, p<0.001
Beta coherence ratio (MA/LA)
D
Dorsiflexion velocity ratio (MA/LA)
r=0.60, p<0.001
Beta coherence ratio (MA/LA)
E
r=0.08, p=0.64
Gamma coherence ratio (MA/LA)
F
r=0.11, p=0.50
Gamma coherence ratio (MA/LA)
G
r=0.17, p=0.32
RMS EMG amplitude ratio (MA/LA)
H
r=0.24, p=0.15
RMS EMG amplitude ratio (MA/LA)