Modulation of Soleus H-Reflexes During Gait in Children With Cerebral Palsy

Maike Hodapp,1 Cornelia Klisch,1 Volker Mall,2 Julia Vry,2 Wiltrud Berger,1 and Michael Faist2

Department of Neurology and Clinical Neurophysiology, University Hospital Freiburg; and Department of Neuropediatrics and Muscular Disorders, Children’s University Hospital, University of Freiburg, Freiburg, Germany

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INTRODUCTION

Short-latency reflexes of the major leg muscles are profoundly modulated throughout the step cycle in adults. Soleus Hoffmann (H-) reflexes show a maximum in the stance phase and a minimum in the swing phase during walking and running (Capaday and Stein 1986, 1987). In addition to the rhythmic part of the modulation a general reflex depression also occurs during locomotion, compared with free standing or sitting (Brooke et al. 1991; Capaday and Stein 1986, 1987). In young children before the complete maturation of the corticospinal tract, an intact spinal cord and brain stem may be sufficient. In contrast, tonic depression depends on an intact, fully mature corticospinal tract (Hodapp et al. 2007). It was concluded that spinal reflexes are suppressed in a task-specific manner during locomotion in parallel with the maturation of the corticospinal tract. This suggests the task-specific supraspinal control of spinal reflexes is not fully established in infancy.

In children with cerebral palsy (CP), a coactivation of antagonistic leg muscles during the stance phase of gait is present (Berger 1998). The electromyographic (EMG) pattern observed during locomotion in older CP children is similar to the pattern observed in younger healthy children (Berger et al. 1984; for review, see Forsberg 1999; Myklebust 1990). This has been ascribed to a lack of maturation of the corticospinal tract in CP, and it has been concluded the immature locomotion pattern persists in CP children. Although it is well known that the leg muscle EMG activation pattern is disturbed in CP children, it is unknown if the modulation of spinal reflexes is also affected.

Bilateral spinal lesions in adults commonly result in a severe disturbance of the rhythmic part of the reflex modulation; however, this is partially preserved after unilateral cerebral lesions (Faist et al. 1999; Yang et al. 1991). It is unknown if the reflex modulation is also affected after a bilateral cerebral lesion or if the spinal level of the lesion is the relevant factor. Because the rhythmic part of the modulation is already present in young children before the complete maturation of the corticospinal tract, an intact spinal cord and brain stem may be sufficient. In contrast, tonic depression depends on an intact, fully mature corticospinal tract (Hodapp et al. 2007). CP children with spastic diplegia suffer from a bilateral supraspinal lesion of the pyramidal tract that occurs before the maturation of the CNS is complete. If supraspinal structures are involved in the tonic, but not rhythmic, age-dependent reflex depression, it may be hypothesized, that in CP the tonic depression with age is disturbed while the rhythmic part of the modulation remains unaffected.

To test this hypothesis, we compared H-reflex modulation during gait in CP children and in healthy children. To account for the age-dependent development that occurs in healthy children up to the age of 13, we investigated two groups of CP children aged 6–11 and 15–16. The development of H-reflex modulation during locomotion in children with CP may give important information both about mechanisms involved in reflex modulation and the anatomic level at which this modulation is generated.

Hodapp M, Klisch C, Mall V, Vry J, Berger W, Faist M. Modulation of soleus H-reflexes during gait in children with cerebral palsy. J Neurophysiol 98: 3263–3268, 2007. First published October 3, 2007; doi:10.1152/jn.00471.2007. In healthy adults, soleus H-reflexes are rhythmically modulated and generally depressed during gait compared with rest. From ages 6 to 13 yr, there is a progressive increase in the tonic inhibition of H-reflexes during walking, especially during the stance phase of the step cycle. In adults, rhythmic modulation and tonic depression are severely disturbed after bilateral spinal lesions but remain partly preserved after unilateral cerebral lesions. Children with diplegic cerebral palsy (CP) suffer from a bilateral supraspinal lesion of the corticospinal tract that occurs before the maturation of the CNS is complete. If supraspinal structures are involved in the tonic, but not rhythmic, age-dependent reflex depression, it could be hypothesized that the tonic reflex depression with age is disturbed in CP, whereas the rhythmic part of the modulation remains unaffected.

To test this hypothesis, soleus H-reflexes were assessed during gait in 16 CP children aged 5–11 and 15–16 and compared with 25 age-matched healthy children walking at similar velocities. Although the rhythmic part of the modulation pattern was present in CP, there was no significant tonic reflex depression with age, thus reflecting a lack of maturation of the corticospinal tract. It is argued the rhythmic part of the modulation may be generated on a spinal or brain stem level and is therefore not affected by the bilateral supraspinal lesion, whereas the tonic depression that occurs with maturation of the CNS is under supraspinal control. In conclusion, the supraspinal structures affected in CP are therefore likely involved in this age-dependent tonic depression.

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METHODS

A total of 16 CP children (mean age: 10.6 yr; range: 5–16) participated in the study. They were divided into two subgroups with 11 younger children aged 5–11 and the other group with 5 older children aged 15–16. All of the children had a leg-dominated spastic tetraplegia but were functional walkers, at least with support such as a walking frame or crutches. The severity of motor impairment was classified according to the Gross Motor Classification System (GMFCS), which consists of five levels of impairment (Palisano et al. 1997). GMFCS ranged from 1 to 3 of 5 (GMFCS °I: n = 4, °II: n = 4, °III: n = 8, °IV: n = 0, °V: n = 0). The distribution of the GMFCS values between younger and older CP children was similar (°I: n = 3 vs. 1, °II: n = 3 vs. 1, °III: n = 5 vs. 3). The control group consisted of 25 age-matched healthy children (mean: 11.9 yr; range: 6–16) without any history of neurological or orthopedic disease. These children represent a subgroup from the previous study, which investigated the age dependency of H-reflexes during gait (Hodapp et al. 2007). The younger subgroup comprised 14 children aged 6–11, the older group 11 children aged 15–16. Parents or guardians provided written informed consent on behalf of their children. The study was approved by the ethics committee of the University of Freiburg.

General experimental arrangement

H-reflexes were investigated during walking on a split-belt treadmill. Force-measuring platforms placed under each belt allowed for the assessment of the time course of the stance and swing phases of gait. EMG activity of the soleus muscle was recorded with pairs of surface electrodes (diameter: 0.9 cm, inter-electrode distance: 2 cm) placed in a longitudinal direction above the bellies of the respective muscles. The CP children were investigated at a walking velocity at which they felt comfortable (mean: 1.4 km/h, range: 0.4–2.5 km/h). At the beginning of the experiment, they were asked to walk on the treadmill while the velocity was increased step-wise. When the children reported the velocity at which they felt comfortable and believed they were able to walk for a few minutes, this velocity was chosen. Initially, all 25 children of the healthy control group were investigated at a slow walking velocity of 1.2 km/h. The experimental procedure was repeated at a walking velocity of 3 km/h in only 24 children, because one child did not want to walk again. All 24 children reported that the 3 km/h was the more comfortable walking velocity.

H-reflexes

Soleus H-reflexes were elicited with the cathode placed in the popliteal fossa stimulating the tibial nerve. At the beginning and end of each experimental session, the stimulus thresholds and the maximal amplitudes of H-reflexes (Hmax) and M responses (Mmax) were assessed during free standing with the weight distributed equally on both legs. The stimulus intensity at which Hmax was obtained during standing was used as the reference for the stimulus intensity that was chosen to elicit H-reflexes during gait. To ensure H-reflexes on the ascending part of the H-reflex recruitment curve (cf. Crone et al. 1990), the stimulus intensity applied to elicit H-reflexes during gait was chosen to be just below, the stimulus intensity (~0.9 times) required to elicit Hmax during standing (cf. Hodapp et al. 2007). Choosing the stimulus intensity with reference to Hmax allows for inter-individual comparison of the reflex size during gait. This chosen stimulus intensity was sufficient to elicit an M response in all subjects. The effective stimulus intensity applied at the tibial nerve during gait was determined by this M response during the gait condition. The amplitude of the M response was kept constant to ensure that the effective stimulus intensity applied at the nerve remained constant throughout the gait experiments. Reflexes were obtained during 8 different phases of the step cycle. At least 12 reflexes were elicited in every phase in a randomized sequence (for details, see Faist et al. 1996). The size of each H-reflex was measured as a peak-to-peak amplitude of the nonrectified EMG trace, and the mean H-reflex was calculated for each of the eight phases of the step cycle investigated. To allow for inter-individual comparison, the H-reflex size was normalized by expressing it as a percentage of the amplitude of Mmax.

Soleus background EMG during gait

The amplitude of the H-reflex is essentially dependent on the EMG activity of the same muscle. For each of the eight step phases investigated, the background EMG activity of the soleus muscle was assessed by the rectified and averaged EMG, which in turn was expressed as a percentage of the mean EMG activity during the whole step cycle. This normalization allows for inter-individual comparison of the background EMG modulation pattern during the step cycle.

Statistical analysis

First, single subject’s mean values were calculated for reflex size (n = 12) and background EMG for each of the eight gait phases (with each phase corresponding to 12.5% of the step cycle). Second, the mean reflex size and background EMG of all eight phases were calculated. In healthy children, this was performed for both walking velocities. To test for changes in reflex size between the stance and swing phases, a mean stance and mean swing phase reflex size was calculated for each subject and walking velocity. Step phases close to the transition of stance to swing and swing to stance (phases 1, 5, and 8) were not considered for this part of the analysis. Accordingly, the mean stance phase reflex size was calculated from the reflexes obtained during phases 2–4. The mean swing phase reflex size was calculated from the reflexes obtained during phases 6 and 7. To quantify the extent of reflex modulation during gait, the modulation index was calculated according to Yang et al. (1991). In brief, the minimum reflex during the swing phase is subtracted from the maximum reflex during the stance phase. This difference is expressed as a percentage of the maximum reflex during stance.

For healthy children and CP children, group mean values and SE were calculated for reflex sizes, background EMG, and modulation index. To investigate for the possibility of age-dependent changes, children were divided into two age groups: one group aged 5–11 and 15–16 yr. H-reflex amplitudes during stance phase, mean EMG values and values for the Yang modulation index were distributed normally. To test for differences between healthy children and CP children, an ANOVA was used. A multivariate ANOVA was used to test for an interaction of age with the differences for the stance phase between healthy children and CP children. H-reflex amplitudes during the swing phase were not distributed normally. Accordingly, for the H-reflex amplitudes during the swing phase and during the entire step cycle a nonparametric Mann-Whitney U test was used.

RESULTS

H-reflexes during standing and stimulus intensities

For all 16 CP children investigated, the mean (±SE) size of the maximal soleus H-reflex amplitude (Hmax) obtained during quiet standing without support was 50.4 ± 5.9% of Mmax. The mean Hmax in the younger children aged 5–11 was 51.3 ± 8.4%, which is similar to the value of 48.3 ± 5.1% obtained for the group of older children aged 15–16. The mean size of the maximal soleus H-reflex amplitude (Hmax) for all 25 age-matched healthy children was 50.3 ± 5.9% of Mmax. The mean Hmax in the younger children aged 6–11 was 49.8 ± 7.3%, and for the group of older children aged 15–16, it was 50.9 ± 9.9%. There were no significant differences between the age groups.
or between CP children and the control group. The mean stimulus intensity applied during gait was almost identical, with 0.87 ± 0.04 and 0.86 ± 0.07 times of the $H_{\text{max}}$ stimulus intensity for the younger and older group of CP children and with 0.86 ± 0.04 and 0.86 ± 0.06 for the younger and older group of the healthy children.

**H-reflexes during gait in children aged 5–11**

Figure 1A illustrates the mean H-reflex amplitudes obtained during gait in the younger children aged 5–11 [CP: $n = 11$, mean walking velocity 1.4 (range: 0.4–2.5) km/h; healthy children: $n = 14$, walking velocity 1.2 km/h]. In CP children and in healthy children, H-reflexes showed a similar rhythmic modulation during the step cycle with the maximum in midstance. The mean H-reflex size over the entire step cycle (27.6 ± 5.9 vs. 17.6 ± 2.9% of $M_{\text{max}}$) showed no significant differences ($P = 0.21$). Furthermore, no statistically significant differences emerged when the stance phase (35.6 ± 7.3 vs. 27.2 ± 4.5% of $M_{\text{max}}$; $P = 0.32$) and swing phase (17.9 ± 6.1 vs. 7.6 ± 1.4% of $M_{\text{max}}$; $P = 0.25$) were calculated separately (Fig. 1B). No significant differences were found, neither for the modulation index (74.0 ± 6.0 vs. 80.6 ± 2.8%; $P = 0.30$) nor for the absolute values of the background EMG during gait (0.23 ± 0.07 vs. 0.35 ± 0.05 mV; $P = 0.16$). Soleus EMG-activity was similarly modulated throughout the step cycle in both groups, apart from higher amplitudes observed in CP children at the beginning of the stance phase; this could be explained by the presence of cloni in three of the children (Fig. 1C).

**H-reflexes in children aged 15–16**

Figure 2A illustrates the mean H-reflex amplitudes obtained during gait in CP children ($n = 5$) at 1.5 (range: 1.1–2.0) km/h and in healthy children ($n = 11$) at 1.2 km/h aged 15–16. H-reflexes showed a rhythmic modulation during the step cycle with a maximum in the second half of the stance phase, similar to that recorded in healthy children. The mean H-reflex size over the complete step cycle (22.8 ± 5.5 vs. 11.3 ± 2.0% of $M_{\text{max}}$; $P < 0.05$) and during the stance phase (36.6 ± 1.6 vs. 11.3 ± 2.0% of $M_{\text{max}}$; $P < 0.01$) showed significant differences. The differences between the mean H-reflex size during the swing phase only showed a trend (10.2 ± 3.2 vs. 5.4 ± 1.2% of $M_{\text{max}}$; $P = 0.08$; see Fig. 2B). Differences were also significant if compared with healthy children walking at 3.0 km/h ($P < 0.05$). No significant differences were found, neither for the modulation index (79.0 ± 6.1 vs. 72.1 ± 5.2% $P = 0.44$) nor for the absolute values of soleus EMG activity (0.31 ± 0.18 mV vs. 0.29 ± 0.06 mV; $P = 0.96$, see Fig. 2C).

**Effect of age on reflex modulation**

During quiet standing, $H_{\text{max}}$ was almost identical in both groups and it was independent of age. It has to be noted that in both groups, CP and healthy children, the reflexes during gait were elicited with a stimulus intensity of 0.87 times the $M_{\text{max}}$ and in healthy children ($n = 14$, walking velocity 1.2 km/h, age 15–16) vs. healthy controls (at 1.2 km/h, age 15–16). There was no significant difference if compared with healthy children walking at 3.0 km/h ($P < 0.05$). No significant differences were found, neither for the modulation index (79.0 ± 6.1 vs. 72.1 ± 5.2% $P = 0.44$) nor for the absolute values of soleus EMG activity (0.31 ± 0.18 mV vs. 0.29 ± 0.06 mV; $P = 0.96$, see Fig. 2C).
Accordingly, in contrast to healthy children, there seems to be no age-dependent development of H-reflex modulation during gait in CP. Multivariate ANOVA revealed significant differences for age in the healthy children ($P < 0.01$) but not in CP ($P = 0.94$). For the Yang modulation index in the ANOVA no significant differences for age were shown, neither in healthy ($P = 0.13$) nor in CP children ($P = 0.61$).

**DISCUSSION**

This study demonstrates that the rhythmic part of the soleus H-reflex modulation during gait is already present in CP children at the age of 6 years and is similar to healthy children. This may be surprising because this modulation has been shown to be disturbed in patients with bilateral incomplete spinal lesion for H-reflexes (Yang et al. 1991), stretch reflexes (Sinkjaer et al. 1996), and tendon jerk reflexes (Faist et al. 1999).

A second result of the present study is that CP children do not show the age-dependent tonic suppression of H-reflexes during the stance phase of walking that occurs in parallel with the maturation of the corticospinal tract in healthy children. The fact that the reflex modulation pattern of the older children with developmental disorder resembles the pattern of the younger healthy children may indicate that the immature patterns in CP children fail to be suppressed during development due to defective corticospinal pathways.

**Methodological considerations**

The size of the H-reflex is essentially dependent on the background EMG of the same muscle (Edamura et al. 1991). If reflexes were simply a function of background EMG, one would expect the larger reflexes in CP children to be reflected by a larger background EMG. However, the EMG in the CP group is either smaller or similar, and therefore cannot account for the discrepancy. Interestingly, $H_{\text{max}}$ during quiet standing was identical in healthy and CP children and also not dependent on age; hence, any differences in reflex modulation during gait must be related to factors other than background EMG or differences in stimulus intensity.

Finally, the differences in reflex size could also be influenced by walking velocity. In healthy children, it is evident that with faster walking velocity, the reflex amplitudes increase in the stance phase, whereas they are further depressed in the swing phase (Hodapp et al. 2007). One may argue that the healthy children had smaller reflexes simply because their relative speed was lower compared with CP children. However, even if the results of the healthy children walking at 3.0 km/h were compared with the results of CP children walking at a mean velocity of 1.4 km/h, the reflexes in CP children were still significantly larger. Accordingly, walking velocity alone cannot explain the results obtained.

**Age-dependent development**

The rhythmic modulation throughout the step cycle was present even in the youngest CP children examined. Soleus H-reflexes in healthy children have been shown to decrease during walking with age, whereas $H_{\text{max}}$ during quiet standing remained unchanged (Hodapp et al. 2007). This age-dependent effect occurs in parallel with the maturation of the CNS. Furthermore, this effect appears to be task specific, i.e., it only occurs during locomotion when the central pattern generator is
active. In the present study, older CP children especially showed higher amplitudes during gait compared with age-matched healthy children, whereas $H_{\text{max}}$ during quiet standing was similar in both groups. This may represent a lack of maturation of the gait reflex pattern in CP.

Locomotor patterns of older CP children resemble the early gait patterns of young children. The immature patterns fail to be suppressed during development (for review, see Forssberg 1999; Myklebust 1990). The maintenance of an infantile pattern has been shown for several parameters. The EMG activity of CP children tested at various ages reveals a striking similarity to that of relatively younger healthy children with a coactivation of antagonistic leg muscles (Berger et al. 1984; Leonard et al. 1991; Unnithan et al. 1996) and large biphasic stretch reflex potentials in the gastrocnemius muscle at foot contact (Berger et al. 1984; Leonard et al. 1991). Additionally, in CP children aged 12–16, soleus H-reflex amplitudes did not decrease during voluntary dorsiflexion in contrast to healthy age-matched controls. This has been argued to be due to an impaired reciprocal inhibition (Leonard et al. 1990).

Central motor conduction times for the upper limb obtained with transcranial magnetic stimulation during childhood reach adult values before the related motor performance is accomplished (Fietzek et al. 2000; Heinen et al. 1998). Eyre et al. (2000) demonstrated in neonates that direct corticospinal projections are established as early as 26 wk of postconceptional age. They suggested the perinatal damage to the corticospinal pathway in CP secondarily leads to disrupted development of spinal motor centers or malfunction of spinal interneurons due to altered corticospinal input. This may explain the alterations in corticospinal projections in adult CP patients reported by Brouwer and Ashby (1991) as well as the lack of reflex depression observed during gait in the present study.

Spinal versus supra-spinal source of gait reflex modulation

The question arises as to which part of the reflex modulation during gait is influenced by supraspinal centers and which part is generated on a spinal level. Two components of reflex modulation during gait may be focused in the discussion of this topic. First, the tonic general reflex depression throughout the step cycle that occurs with age, and second, the rhythmic part of the modulation that is already present in healthy children probably even before the age of 6 (Hodapp et al. 2007). In CP children, the general depression of H-reflexes during gait with age is lacking. One may suspect that this suppression is generated or transmitted by the supraspinal parts of the corticospinal tract. These supraspinal parts are damaged bilaterally in CP children before the development of the CNS is accomplished. After bilateral spinal lesion (e.g., from traumatic spinal cord injury), this tonic depression is also reduced (Yang et al. 1991). However, in patients with unilateral cerebral lesions caused by stroke, the depression during the stance phase is still present on the affected side though less marked on the unaffected side (Faist et al. 1999). It can therefore be concluded, that tonic reflex depression is clearly reduced after bilateral spinal and bilateral supraspinal lesions of the corticospinal tract. This may lead to the suggestion that bilateral or ipsilateral supraspinal projections are required for the tonic reflex depression during gait.

The rhythmic part of the reflex modulation pattern is not different in CP children compared with age-matched controls. However, this pattern is disturbed after bilateral spinal lesions (Faist et al. 1999; Yang et al. 1991). Accordingly, there are clear differences in rhythmic modulation between bilateral spinal and bilateral supraspinal lesions. This may lead to the suggestion that the rhythmic pattern is generated on a spinal and/or brain stem level.

Conclusions

The rhythmic part of the reflex modulation during gait is mainly unaffected in CP children, whereas it is severely disturbed in adult patients suffering from a spinal lesion. This may lead to the suggestion that the rhythmic part of the reflex modulation is generated on a brain stem or spinal level, which is unaffected in CP. Furthermore, it can be posited that the lack of general gait reflex suppression with age in CP is due to a disturbed supraspinal control caused by the bilateral cerebral lesion. The functional relevance of these pathophysiological findings should be addressed in future studies. One interesting question may be if the disturbed reflex pattern during gait can be influenced by training.

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