



Late developmental deficits in force control in children with hemiplegia

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Received ■ ■ ■; accepted 19 June 2004

DOI: 10.1097/01.wnr.0000137491.55172.0b

Differences related to development were investigated using a finger isometric force task in children with cerebral palsy and control children. The increase in force and force control observed in controls did not take place in patients. In the younger subset of patients (< 10 years) the force produced by the non-affected hand was greater than in either hand of young controls. This effect was not observed in the older subset of patients (< 10 years). Older

controls also differed from younger controls in that they used higher frequency feedback loops. In contrast, older patients failed to show this increase. Moreover, the failure occurred both in the affected and non-affected hand, indicating that abnormalities involve the force control system of both sides. *NeuroReport* 15:000–000 © 2004 Lippincott Williams & Wilkins.

Key words: Cerebral palsy; Corticospinal tract; Development; Isometric task; Upper limb

INTRODUCTION

Cerebral palsy (CP) is defined as damage to the developing CNS, which is non-progressive in nature [1]. Subtypes of CP however, develop and change over time. Clinically, a decrease in motor performance with age is seen in many children with CP [2]; however, these motor deficits of older children with CP have been described mostly in terms of locomotion and little is known whether there is deterioration in manual force control. The available studies on hand function in CP have focused on the grip-lift force synergies in children [3,4]. However, in these studies the emphasis was not on absolute force generation but on the ability of the child to anticipate the force needed to lift a particular object and to coordinate the lift and grip forces. In contrast, studies on developmental aspects of force generation in CP over a wide range of force levels are not available to our knowledge.

The increased impairments in motor control of older children with CP are usually attributed to secondary musculoskeletal pathology [5] and more rarely to central control mechanisms, which fail to develop [6,7]. In a developmental study on force control in typically developing children we showed that the decrease in variability during isometric finger contractions followed a time course of corticospinal maturation, leading to changes in motor control strategy after 10 years of age [8]. Corticospinal tract degeneration has been documented in children with spastic hemiplegia [7,9,10], and this may lead to severely impaired manipulative skills. In view of the importance of the cortical

control over finger movements an age-related impact on force regulation of the finger flexors in CP is to be expected.

Performance of skilled finger movements relies upon the integrity of the corticomotoneuronal system and specifically on direct monosynaptic input from the cortex to spinal alpha-motoneurons [11]. CNS damage in early life can affect subsequent brain development and lead to patterns of brain organization and function that differ greatly from normal [12]. It is hypothesized that abnormalities in the developmental process may explain the pattern of behavioral impairments in the older children with CP. Based on modern neurobiological insights functional outcome is partly determined by the initial structural damage and partly by the interactions of the impaired system with its environmental influences. Since the young system has sufficient plasticity, compensation will occur in undamaged areas. Therefore, if one component of the system is damaged the whole system will change. For example, corticospinal projections in several mammalian species develop transient ipsilateral projections early in development. In normal development these projections are predominantly eliminated when maturity is reached [13]. In contrast, in children with early unilateral brain damage, fast conducting ipsilateral corticomotoneuronal projections are preserved [11]. Central changes in CP do not exclude that peripheral factors may also be important in the deterioration of motor control.

During normal development the muscles grow and become stronger until adulthood [8]. This is very different in CP. Ito *et al.* [14] reported a selective atrophy of type II muscle fibers during development in CP. Moreover, during

growth there is a progressive fibrosis and the number of sarcomeres does not increase as rapidly as for children without CP. The changes in mechanical factors on spasticity are likely to increase over time. This is substantiated by Dietz [15], who suggested that in younger children the reflex or neural component of spasticity may predominate, whereas in older children changes in muscle elastic properties may contribute to the increased resistance felt during passive movements. Friden and Lieber [16] recently demonstrated changed length-tension relationships of muscle fibers and increased elastic modulus of muscle fibers (stiffness) in subjects with chronic spasticity. Based on these facts it is likely that the net force relatively decreases with age compared to control children.

To gain insight in age related changes in force and force control in children with spastic hemiplegia, a longitudinal design is best but this is not always feasible especially when a large age range is involved. In the present study we therefore controlled very carefully that the groups were well matched (by means of comparable inclusion criteria such as CP classification and severity, affected side and gender) to allow a valid exploratory analysis of two age groups by means of a cross-sectional design.

MATERIALS AND METHODS

Subjects: Twenty children classified as hemiplegic according to Hagberg [17] participated in this study. Their age ranged between 5 and 15 years of age (mean (\pm s.d.) 9.6 ± 3.4 years): half of them ($n=10$) were under 10 (mean 6.6 range 5–9 years) and half ($n=10$) >10 years of age (mean 12.5; range 11–15 years). In both age groups right and left-sided hemiplegia, and gender were evenly distributed (all 50%). The children were mildly impaired. To be included in the study they had to be able to actively extend the fingers and wrist of the affected arm. Children in both groups did not suffer from severe limited range of motion and had comparable values for passive motion of elbow and wrist extension (elbow: 180.0 and 176.6° , wrist: 78 and 66° for the under- and over-ten group, respectively). All children were able to walk without walking aids (besides ankle-foot orthosis), attended mainstream education in the special school belonging to the rehabilitation center and experienced no problems understanding the instructions. The parents gave informed consent and the Medical Ethic Committee of Stichting Revalidatiecentra Limburg approved the study. Twenty age-matched children (10 in each age-group) with motor performance above the 15th percentile on a test for motor impairment [18] participated as control subjects.

Methods: The methods used have been described in detail elsewhere [8]. To perform the tasks, the children were seated on an adjustable chair, forearms resting on the table, in front of a monitor, on which visual feedback was given. The subject was asked to apply force with his/her index and middle finger positioned onto the end of a lever, as fast as they could do accurately. The aluminum levers transmitted the force onto a force transducer. To measure the force a high-quality strain gauge (Sokki Kenkyujo; type CLS-20KA) was used. This gauge is temperature compensated and highly linear. An amplifier (Burstner; type 9154) delivered its

output to a 12-bit AD-converter (DAS800). The computer sampled the signal at a rate of 1000 Hz.

First the maximum voluntary contraction (MVC) was measured. Then five different levels of constant force –12, 24, 36, 48 and 60% of MVC, duration 10 s/level, were recorded 5 times. An auditory start and stop signal was used. For all tasks a random design was used. All children were given a training session.

Analysis: Absolute error was calculated as the absolute deviation of the generated force (N) from the target force. Time to peak force was defined as the time (s) from the starting signal until the moment the target was reached. In addition a power spectral density analysis (PSDA) was performed. The grand average of the resulting spectra over all trials and subjects was calculated to form an overall spectrum with bands of 1 Hz. Relative spectra were calculated by dividing the summed energy per band by the total power. For statistical testing, the bands were clustered, based on assumed origin of the energy (1–6, 7–12, 13–18, 19–24, 25–30 Hz, respectively). The dependent variables were evaluated by means of a general linear model, repeated measures design, with age (2 levels) and group (2 levels) as between subject variables, and percentage of MVC (5) as within subject variable. Alpha was set at 5% (two-tailed).

RESULTS

MVC: A main effect of group ($F(1,36)=15.33$, $p<0.001$), age ($F(1,36)=10.82$, $p=0.002$) and hand ($F(1,36)=23.84$, $p<0.001$) and an interaction effect of group \times age ($F(1,36)=30.78$, $p<0.001$) and group \times hand ($F(1,36)=58.18$, $p<0.001$) emerged. Figure 1 depicts these effects, showing that overall, controls were stronger than the patients and that patients were stronger in their non-affected hand (NAH) compared to their hemiplegic hand. Moreover, the interactions revealed that younger patients were stronger in their NAH than in their affected hand (AH) but also stronger compared to the control children. The opposite pattern is seen in the older patients. Unexpectedly, they generated less force than the younger patients both in the AH and NAH.

Absolute error: Participants complied with the tasks well. No statistical differences in absolute error were found between the patients and controls, nor between the younger and older children. The main effect of force level showed that more errors were made when higher forces were generated ($F(4,144)=13.36$, $p<0.001$).

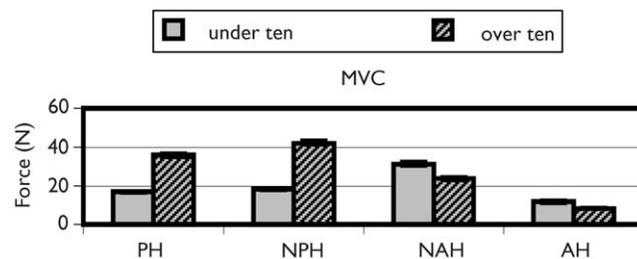


Fig. 1. Maximum Voluntary Contraction (MVC) for controls (PH: preferred hand, NPH: non-preferred hand) and patients (NAH: non-affected hand and AH: affected hand).

Time to peak: For all hands it appeared to be difficult to reach the highest force level ($F(4,144)=37.82, p=0.001$) and AH was slower than the NAH ($F(1,36)=5.72, p=0.02$). However, a rather unexpected third order interaction emerged (group \times hand \times force level \times age ($F(4,144)=4.13, p<0.001$; Fig. 2a,b) indicating that the difference found between patients and control was caused by the older patients. It took the older patients more time to generate higher force levels.

Power spectral density analysis: The PSDA revealed a main effect for force level ($F(4,144)=122.38, p<0.0001$), showing a clear increase in power with force. Statistical analysis exposed differences between the age groups in all the frequency ranges outside the 19–24 Hz band. While in the young children the energy was centered in the lowest frequencies, with age it was more distributed the other frequency ranges. However, interaction effects revealed significant differences in the distribution of energy over the frequency bands between the hands of the patients and controls with age. At the lowest frequency bands (1–6 Hz) an interaction emerged between hand and group and age ($F(1,37)=5.89, p<0.02$). The relative power in the 1–6 Hz range was lowest in the preferred hand (PH) and not much different for the non-preferred hand (NPH), NAH and AH

in the younger children. In the older children less energy was found in the 1–6 Hz band, although this was less evident in the AH. In the 7–12 Hz range a group by age effect was found ($F(1,37)=9.41, p<0.01$) revealing *no* difference between young patients and controls (Fig. 2c). Conversely, the energy distribution in the 7–12 Hz range in the older control group showed a clear increase, which did not occur in either hand of the older patient group (Fig. 2d). After the age of 10, the energy in this range was twice as high in the controls. However, virtually no increase in the energy in this frequency range was observed in the older patients. A comparable, though smaller effect can be seen in the 25–30 Hz cluster (Fig. 2d).

DISCUSSION

The current study focused on differences in force production and force control mechanisms between two age groups of children with CP. Our initial hypothesis was that a decrease of force generation would occur in the affected hand of the older children with CP. A second expectation based on our earlier work [8] was that children with CP around 10 years of age would fail to change their control strategies from predominately long loops to faster control loops [8]. Both of these hypotheses were confirmed, although new facts also emerged.

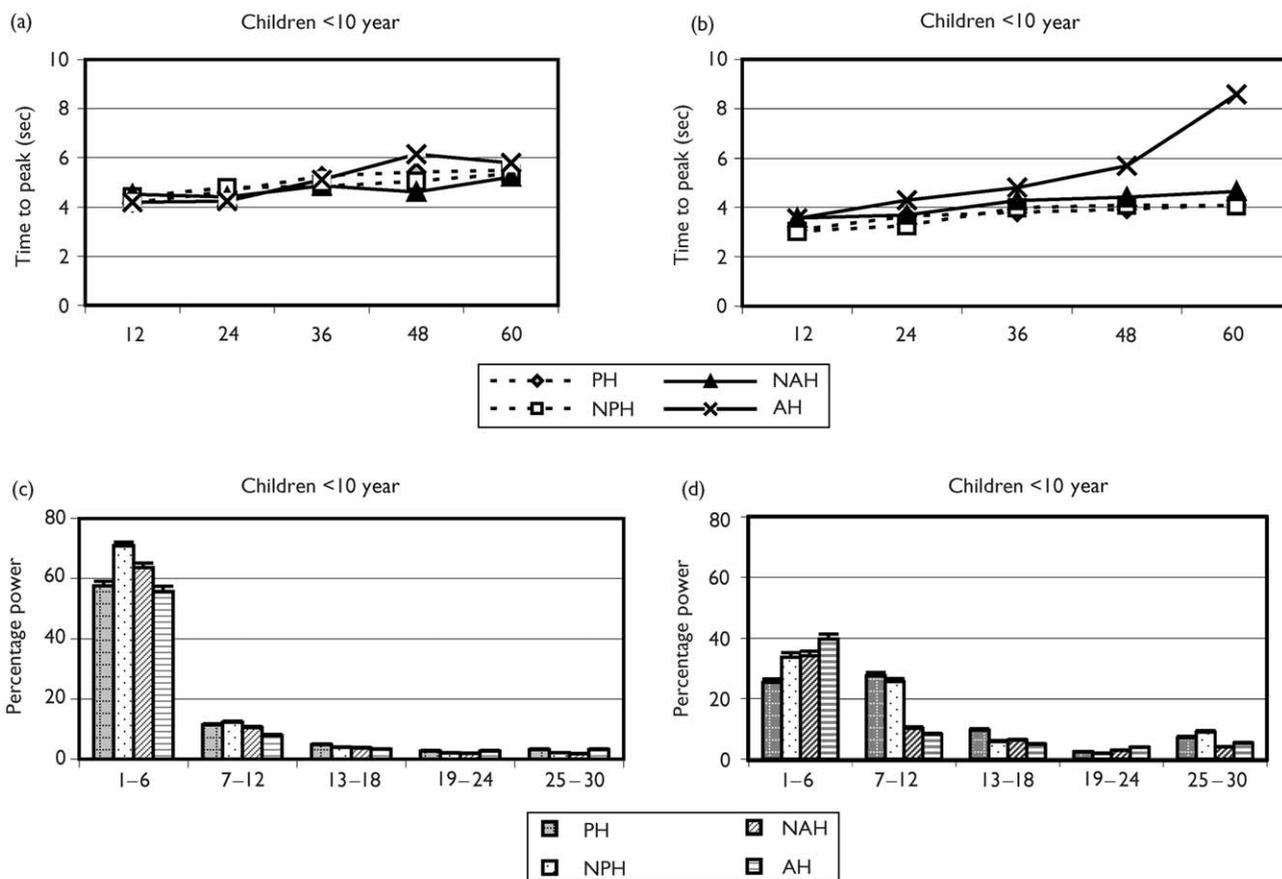


Fig. 2. Effect of age for patients and controls. Panel A and C depict results of children under ten, panel B and D of the children over ten years of age. Panel A and B show differences between time to peak at all force levels for the preferred (PH), non-preferred (NPH), non-affected (NAH) and affected hand (AH). Panel C and D show the PSDA of the clustered frequency bands.

For the older patients, the data revealed that the affected hand did not necessarily become stronger with age. Secondly, they were slower in generating forces. Thirdly, the shift to a broader range of frequencies in the force trace did not occur. The failure to improve muscle force with age may be linked to spasticity-related structural changes in the muscle [2,15]. Alternatively, they may involve a failure of cortical motor output. In the first case, if there were an increase in structural muscle changes with age, one would expect the range of motion to decrease as well. However in this study the young and older children with CP had no significant differences in passive range of motion in the forearm. Furthermore, there are several studies that show a lack of correlation between spasticity and muscle force [6,19,20]. Therefore, one should probably look into reduced cortical output to explain the reduction of force with age.

The results with the non-affected hand corroborate the idea of a central origin since an age related deficit was found in this hand as well, despite the lack of spasticity or structural changes. In young patients the non-affected hand is stronger than the average of the controls, presumably because it has to compensate for the dysfunction of the affected hand in daily tasks. Moreover, in young children the non-affected hand showed time to peak values and frequency spectra as expected for their age. This was not the case in the older patients. Their non-affected hand was weaker compared to the controls and no frequency shift was found in the power spectra of their force trace. In typically developing children, Deutsch and Newell [21] found that improvement of performance is associated with a broader power spectrum across the frequency range and they proposed that age-related enhancements in motor performance are primarily due to a more appropriate tuning of the neuromotor system to task constraints. The PSDA in the present study showed that both young patients and younger controls had most energy in the 1–6 Hz range, indicating that they relied upon on-line control through recurrent signals from muscles and from visual feedback (1–6 Hz range) [8]. As neural maturation and development proceed, controls show a shift to the 7–12 Hz range suggesting that they add faster, most probably anticipatory, control strategies to their repertoire, which rely more upon corticospinal gain setting. Patients do not show this change in the 7–12 Hz range in either hand with age.

The data may indicate that the symptoms of older patients are not only caused by the initial damage to the brain but also by differences in developmental or reorganization processes. There may be a specific time window for these developmental changes, one of which is related to the normal maturational time course of the corticospinal tract. If children with CP skip these developmental stages, they will show a relative regression in motor function.

Following early unilateral brain damage, reorganization leading to enhanced participation of the motor areas in the unaffected hemisphere has been identified [11]. A speculative explanation for the present findings could be that children with CP use their unaffected cortex to control both hands [11]. This sharing of brain areas could be sufficient for the easier control strategies used by the young children, but not for the more sophisticated control strategies used by the older children, which demands increased activity of the motor output in the higher frequency ranges. This developmental failure, causing non-optimal cortical output to

both hands could lead to an increasing deficit in voluntary muscle activation. Other authors have previously mentioned that failure in the central drive is a probable option for reduced motor output [7,20,22]. The inability of individuals with CP to recruit the available motor units or to attain maximal discharge rates can be measured by using percutaneous neuromuscular electrical stimulation [23]. It was demonstrated this way that children with CP had a profound deficit in voluntary activation of the m. quadriceps and the m. gastrocnemius. However, no data is available on voluntary activation levels in the non-affected arm of children with CP.

Another possible explanation for an age-related decrease in force generation, besides central factors, is that older patients have severe disuse in both hands. So far, we are not familiar with any studies describing such relative disuse, leading to loss of strength in the non-affected hand.

CONCLUSION

Whatever the mechanisms underlying this growing into deficit, it is evident that age-dependent loss of force in both hands is an important challenge for clinicians treating CP. It would be interesting to investigate whether early strength-training and/or forced use, are capable of countering the expected loss in force with age.

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