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Fatigue Resistance During a Voluntary Performance Task Is Associated With Lower Levels of Mobility in Cerebral Palsy

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Abstract

Objectives—To investigate muscle fatigue of the knee flexors and extensors in people with cerebral palsy (CP) compared with those without motor disability during performance of a voluntary fatigue protocol and to investigate the relationship with functional mobility.

Design—A case-control study.

Setting—A biomechanics laboratory.

Participants—Ambulatory subjects with CP (n=18; mean age, 17.5y) in Gross Motor Function Classification System (GMFCS) levels I, II, and III and a comparison group of age-matched subjects (n=16) without motor disability (mean age, 16.6y).

Interventions—Not applicable.

Main Outcome Measures—The voluntary muscle fatigue protocol consisted of concentric knee flexion and extension at 60° a second for 35 repetitions on an isokinetic dynamometer. Peak torque for each repetition was normalized by the maximum peak torque value. Muscle fatigue was calculated as the rate of decline in normalized peak torque across all repetitions, represented by the slope of the linear regression. Self-selected and fast gait velocities were measured as well as the Pediatric Outcomes Data Collection Instrument (PODCI).

Results—Greater fatigability (slope) was observed in the comparison group for both knee flexors and extensors than in the group with CP. Within CP, lower knee extensor fatigue (slope) was associated with lower functioning GMFCS levels and lower levels of activity and participation as measured by the PODCI transfers and basic mobility.

Conclusions—Even after adjusting for maximum peak torque, the knee flexors and extensors of participants with CP were observed to be less fatigable than age-matched peers without motor disability. The lower rate of muscle fatigue was also associated with lower functional mobility in CP. These results may be related to strength or activation differences and/or muscle property alterations. Future investigations are warranted.

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Keywords

Muscle fatigue; Muscle spasticity; Muscle strength; Quadriceps muscle; Rehabilitation

Measures of physiologic capacity, such as lower-extremity muscle strength, have been correlated with functional measures in people with CP and other disabilities.¹⁻³ However, neither muscle strength nor measures of physical function have been shown to be related to psychosocial aspects of QOL, such as comfort and happiness.⁴ Self-reported physical fatigue, on the other hand, has been significantly associated with QOL measures of psychosocial well being, such as bodily pain, limitations in physical and emotion role function, and low life satisfaction in adults with CP.⁵ Furthermore, adults with CP report fatigue as a main cause of the deterioration or cessation of their walking ability.⁶⁻⁸ However, these studies assessed fatigue using questionnaires and interviews and did not attempt to differentiate among the different types of fatigue.

Previous objective clinical measures of fatigue in people with CP were focused primarily on the cardiorespiratory system. Although it has been well documented that children and adolescents with CP have lower $\dot{V}O_2$ max than their typically developing peers, most authors concluded that local muscle factors, such as muscle fatigue, were responsible for the lower $\dot{V}O_2$ max and limitations in activity.⁹⁻¹¹ Following this same argument, Lundberg¹⁰ and Hoofwijk et al⁹ suggested that spastic muscles may have decreased venous return and inhibited muscle lactate clearance during exercise, thereby increasing muscle fatigue and leading to a decrease in $\dot{V}O_2$ max values.

There are different definitions of muscle fatigue in the literature. *Muscle fatigue* is defined here as a reduction in force output that occurs during sustained voluntary activity.¹² *Fatigue resistance*, or the ability to withstand fatigue, is also referred to as *muscle endurance* in the literature. Muscle fatigue can occur at any point along the activation process, from the central nervous system to the level of the motor neuron. Techniques that use electric stimulation (ie, twitch interpolation, electrically elicited contractions) are capable of isolating peripheral aspects of muscle fatigue from central aspects. For example, Stackhouse et al¹³ investigated peripheral muscle fatigue of the quadriceps and triceps surae through the use of electrically elicited contractions in children with CP. In that study, the quadriceps, but not the triceps surae, were observed to be less fatigable compared with a control group. However, in their study, the influence of the central nervous system was removed. Because muscle activity depends on the integration of the entire chain of events, muscle fatigue as assessed through voluntary performance may occur at both central and peripheral sites simultaneously.¹⁴

Because muscles adapt to the amount and type of neural stimulation being imposed on them, secondary effects of spasticity on muscle tissue can also have a profound impact on the ability to generate and maintain muscle force. Muscle abnormalities such as alterations in muscle fiber size and fiber type distribution, excessive collagen accumulation, and increased muscle stiffness (elastic modulus) of spastic muscle cells have also been reported in CP.¹⁵⁻²⁰ These alterations of muscle properties can have significant implications for essential aspects of muscle performance, such as the ability to generate force and to sustain force output. In CP and other motor disorders, different muscle groups can be affected to varying degrees; therefore, these changes may be muscle-specific, rather than generalizable across all muscles.

Isokinetic fatigue protocols for the knee flexors and extensors have been extensively developed in the healthy adult population^{21,22} and have been modified for use with children²³ and with other neurologic populations such as multiple sclerosis.²⁴ An advantage of isokinetic dynamometry is that it provides a safe, controlled environment in which a muscle or group of

muscles can be isolated with stabilization of other joints.²⁵ An isokinetic fatigue protocol similar to the ones mentioned was developed recently by the authors²⁶ for use in children and young adults with mild-to-moderate CP and was shown to be feasible for testing the knee flexors and extensors.

The primary purpose of this study was to determine whether muscle fatigue in the knee flexors and extensors in people with CP differs from those without a motor disability during the performance of a voluntary fatigue test. A secondary purpose of the study was to determine the relationship of muscle fatigue to functional level, walking velocity, and activity/participation as measured by the PODCI. The quadriceps and hamstrings muscle groups were chosen because of the importance of these muscles in gait and function.¹⁻³ We hypothesized that people with CP would have greater levels of muscle fatigue than nondisabled peers and that muscle fatigue would be inversely related to functional level, walking velocity, and activity and participation.

METHODS

Participants

A group of 18 participants with CP and a comparison group of 16 participants without motor disability between the ages of 10 and 25 years were recruited for the study. An attempt was made to ensure that sex and age distributions were similar across groups. Participant characteristics are listed in table 1. Participants with CP were ambulatory with or without assistive devices. They were excluded if they had orthopedic surgery within 12 months prior to the testing, received botulinum toxin injections to the quadriceps or hamstrings within 6 months prior to the testing, or complained of existing knee pain.

The study was approved by the human studies committee at our institution. Written informed consent from each participant over 18 years of age was obtained. Parental consent forms for participants younger than 18 years of age were obtained from their parents or legal guardians.

Fatigue Testing

An isokinetic dynamometer^a was used to record torque of the knee flexors and extensors during maximum voluntary exertions throughout the available passive ROM. Participants performed 8 to 12 submaximal concentric, reciprocal knee flexion and extension repetitions to familiarize themselves with the task. The fatigue protocol consisted of reciprocal, maximal concentric knee extension and flexion at 60° a second for 35 repetitions and has been published elsewhere.²⁶ During pilot testing, peak torque during the fatigue test for both knee extension and flexion showed a consistent pattern of decline during the first 30 to 40 repetitions and then began to level off in subjects with and without CP who were asked to complete 100 repetitions. This pattern has been demonstrated for the knee extensors during similar protocols in other studies.^{27,28} Therefore, 35 repetitions were chosen for this protocol. Strong verbal encouragement on every repetition as well as visual biofeedback of torque production was provided to encourage maximal effort on all repetitions. Data were gravity-corrected, and only the constant velocity portion was used for calculation. The following calculations were made separately for knee flexion and extension repetitions. For each subject, peak torque was measured as the highest value achieved during each repetition. Maximum peak torque for each subject was measured as the single highest peak torque value across all repetitions. Peak torque for each repetition was then normalized by the maximum peak torque value. Normalized peak torque data were averaged for each group, and muscle fatigue was calculated as the rate of decline in

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normalized peak torque across all repetitions, represented by the slope of the linear regression.²¹ The first repetition was excluded from analysis because it is usually unreliable.

Functional Measures

Each subject was assigned a GMFCS level as a measure of functional mobility, restricted to I, II, or III because of the ambulatory requirements of the study. Although the GMFCS was not originally intended for those over 12 years of age, it has been shown to be reliable²⁹ and stable over time in adults with CP.³⁰ Activity and participation were assessed with the PODCI.³¹ The PODCI questionnaire was completed by the parents of participants under 18 or by the participants themselves who were 18 or older (American Academy of Orthopaedic Surgeons/Pediatric Orthopaedic Society of North America, Version 2.0). The PODCI was designed to assess self-reported physical function and psychosocial aspects of health status deemed relevant to musculoskeletal disability. Five scales were computed with a percent score from 0 (worst) to 100 (best).

Gait velocity was assessed using a stop watch during level walking over a 10-m distance. Subsequent marks were placed 2m from the starting point and 2m from the ending point, thus allowing a 6-m timed middle section for the test. Each subject was tested at a comfortable walking speed and a fast walking speed. Velocity was calculated as meters a second divided by the participant's height. Two trials at each speed were averaged.³²

Statistical Analysis

Comparisons between the 2 groups (with and without CP) and the 2 muscle groups (knee flexors and extensors) were made using independent and paired *t* tests, respectively. Within the group with CP, Pearson *r* correlation procedures were used to determine the relationship of gait velocity and PODCI scores with the slope for the knee flexors and extensors. Spearman ρ correlations were used to determine the relationship between GMFCS level and the slope ($\alpha = .05$).

RESULTS

Mean age and weight did not differ across groups, but the comparison group without CP was slightly taller than the group with CP ($t=2.66$; $P=.02$) (see table 1). The average maximum peak torque values of the knee extensors obtained during the fatigue protocol for the group with CP and the comparison group were 54.2 ± 20.8 and 108.4 ± 37.9 Nm, respectively ($t=5.24$; $P<.001$). For the knee flexors, the average maximum peak torque values were 24.2 ± 11.3 and 57.7 ± 21.3 Nm for the group with CP and the comparison group, respectively ($t=5.83$; $P<.001$).

Fatigue

Figure 1 illustrates the group means and SDs of the normalized peak torques over the 35 repetitions for the knee flexors and extensors. The normalized peak torque of the comparison group declined more (greater slope) than the group with CP for both the knee flexors ($t=-2.44$; $P=.02$) and extensors ($t=-4.22$; $P=.001$), indicating greater muscle fatigue of the comparison group. Means and SDs of the slope values for each group are illustrated in figure 2. The magnitude of the slope values are presented as positive values for ease of interpretation. The slope values did not differ between the knee flexors and extensors for either the comparison ($t=-.80$; $P=.434$) or the group with CP ($t=-2.01$; $P=.061$).

Functional Measures

Participants with CP who had greater mobility (eg, lower GMFCS levels) had a greater rate of decline in normalized peak force (greater slope) of the knee extensors ($r=-.50$; $P=.035$). The

transfers and basic mobility scale of the PODCI was directly correlated with the slope of the knee extensors ($r=.61$; $P=.008$). A positive correlation indicates that participants with greater levels of functioning (eg, greater scores on the PODCI) had greater rates of decline. None of the scales related to psychosocial well being (pain and comfort, happiness) were correlated with the slope. Self-selected and fast walking velocities approached significance with the knee extensors only ($P=.08$, $P=.06$, respectively). Correlation coefficients are listed in table 2.

DISCUSSION

Contrary to our hypotheses, the knee flexors and extensors in our sample of participants with CP were observed to be less fatigable than the age-matched comparison group as indicated by the lower rate of decline in peak torque. Furthermore, greater knee extensor fatigue was associated with higher functioning GMFCS levels and greater levels of activity and participation as measured by the PODCI transfers and basic mobility. Counterintuitively, it appears as though lower levels of muscle fatigue of the knee flexors and extensors, as measured by this test, are characteristic of greater disability.

Although knee extensor fatigue was significantly associated with the GMFCS and transfers and basic mobility, it was not associated with any of the other functional measures; however, the relationship with self-selected and fast velocity approached significance (see table 2). Perhaps this is because the transfers and basic mobility scale contain items related to overall physical performance, which would be most closely associated with lower-extremity muscle function. The sports and physical function scale, on the other hand, consists of more challenging and specific performance items, whereas the global functioning scale is very generalized and includes items from both of the aforementioned scales as well as upper-extremity activities and items related to pain and comfort. It should be noted that although we tested participants with CP up to 25 years of age, the PODCI has not been validated in people over 18 years.

The fatigue protocol employed here was designed as a measure of volitional activity, which would be more representative of everyday function versus an electrically elicited fatigue test or an isometric test. Nevertheless, our results are similar to a study that used an electrically elicited fatigue test in which the quadriceps in children with CP were found to be less fatigable than a control group.¹³ Because the muscles were electrically stimulated in that study, only peripheral aspects of muscle fatigue distal to the peripheral motor nerve were assessed. Our study, on the other hand, encompassed both central and peripheral aspects of muscle fatigue, from the central nervous system command to the contractile apparatus of the muscle itself. Therefore, peripheral versus central contributions to the measured fatigue can not be determined from these results. Similarities between the 2 studies should be interpreted within this context.

Several mechanisms can be suggested to explain the lower rate of fatigue in the group with CP, the first of which are maximal torque level (strength) and muscle mass. It has been suggested that males are more fatigable than females^{33,34} and adults are more fatigable than children³⁵ and older adults³⁶ because of greater strength and/or greater muscle mass. In our study, the maximum peak torque values of both muscle groups obtained during the fatigue test were 50% lower in the group with CP than the comparison group. Perhaps the lower capacity for force production in the participants with CP lowers the rate of decline in torque. However, it should be noted that sex and age differences in fatigue caused by absolute strength differences have been refuted by some researchers.^{37,38} Rather, some authors claim that weakness leads to disuse atrophy and increased levels of muscle fatigue³⁹ because of the recruitment of more motor units or the greater frequency of excitation required to perform a given task. As a consequence of recruiting more motor units, the overall fatigability will likely increase because increased numbers of upper threshold units will be recruited, which include more fast fatiguing

fibers. Although these are all plausible theories, the relationship between absolute strength and muscle fatigue is not fully understood and warrants further investigation.

Second, predominance of a particular fiber type can influence muscle fatigue, because type I (slow twitch) fibers are more fatigue resistant, whereas type II (fast twitch) fibers are more fatigable. Although there has been no consensus on fiber type predominance in CP and other spastic disorders, there are several reports of increased type I fibers in CP or atrophy of type II fibers.^{16,18–20} The main results of this study could partially be explained if secondary impairments in CP, such as spasticity, do result in muscle adaptations, which include increased proportions of type I fibers with a greater oxidative capacity.

Third, the issue of voluntary muscle activation must be considered. Recent evidence revealed that children are more susceptible to central fatigue than adults and that the lower peripheral fatigue of the knee extensors was associated with a lower degree of voluntary activation.⁴⁰ Similarly, Stackhouse et al¹³ observed 33% lower voluntary muscle activation of the quadriceps in children with CP ages 7 to 13 years than age-matched typically developing children. Therefore, despite the fact that the subjects with CP were giving a maximal voluntary effort, it is possible that they were not activating all of their motor units secondary to impaired motor pathways. As a result, type I fibers may be preferentially recruited with lower firing rates, thereby contributing to greater fatigue resistance.

Study Limitations

In addition, other potential but unstudied physiologic mechanisms in CP that may affect muscle fatigue are energy metabolism,⁴¹ muscle activation strategies such as cocontraction, and alternate patterns of motor unit recruitment and rate modulation, such as motor unit rotation⁴² and substitution.⁴³ A potential limiting factor is that both participant groups performed the task within their available passive ROM, which varied across subjects, particularly in the group with CP. Therefore, the time to task completion may have been different across subjects and could have influenced results. Clearly more research needs to be done to examine the role of these potential mechanisms and perhaps others on muscle fatigue.

Clinical Significance

Our observations of lower muscle fatigue in CP were contrary to our initial hypothesis and seem to contradict the prevalent complaint or perception of greater fatigue in this population. Measures of muscle fatigue presented here may or may not be related to subjective reports of fatigue. One difference is that this study did not measure the cardiorespiratory contribution to fatigue or perceived exertion. However, it is possible for persons to have greater endurance capacity during voluntary muscle activities and still experience greater subjective fatigue. The physiologic demands of walking and other daily activities require a larger percentage of the muscle's force generating capacity in people with CP and others who are weaker than normal,⁴⁴ increasing the perceived effort of the task. For example, walking may require 80% of a muscle's physiologic capacity in a person with CP compared with 10% in a person without CP. It is the increased load relative to maximum capacity, rather than the absolute load, that results in physiologic burn-out in people with CP as first described by Pimm⁴⁵ and in prevalent complaints of fatigue.^{5,6} Therefore, instead of designing protocols to increase endurance directly, therapeutic strategies should perhaps instead be targeted at increasing strength and thereby reducing the relative effort.

CONCLUSIONS

Participants with CP demonstrated lower fatigue rates for the knee flexors and extensors compared with age-matched peers without motor disability. In addition, lower levels of knee

extensor muscle fatigue were associated with lower levels of function and participation. These results raise the question of whether the fatigue resistance observed in this population is the result of inherent muscle weakness, central fatigue, disordered motor control, or greater reliance on type I or oxidative fibers. More research is needed to explore these mechanisms and the potential effect on muscle fatigue. Furthermore, the influence of weakness on task effort and perceived fatigue warrants greater consideration and may lead to new treatment strategies for reducing the complaints of fatigue in this population, which are strongly linked to walking cessation with advancing age.

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List of Abbreviations

CP	cerebral palsy
GMFCS	Gross Motor Function Classification System
V_{O₂}max	maximal oxygen consumption
PODCI	Pediatric Outcomes Data Collection Instrument
QOL	quality of life
ROM	range of motion

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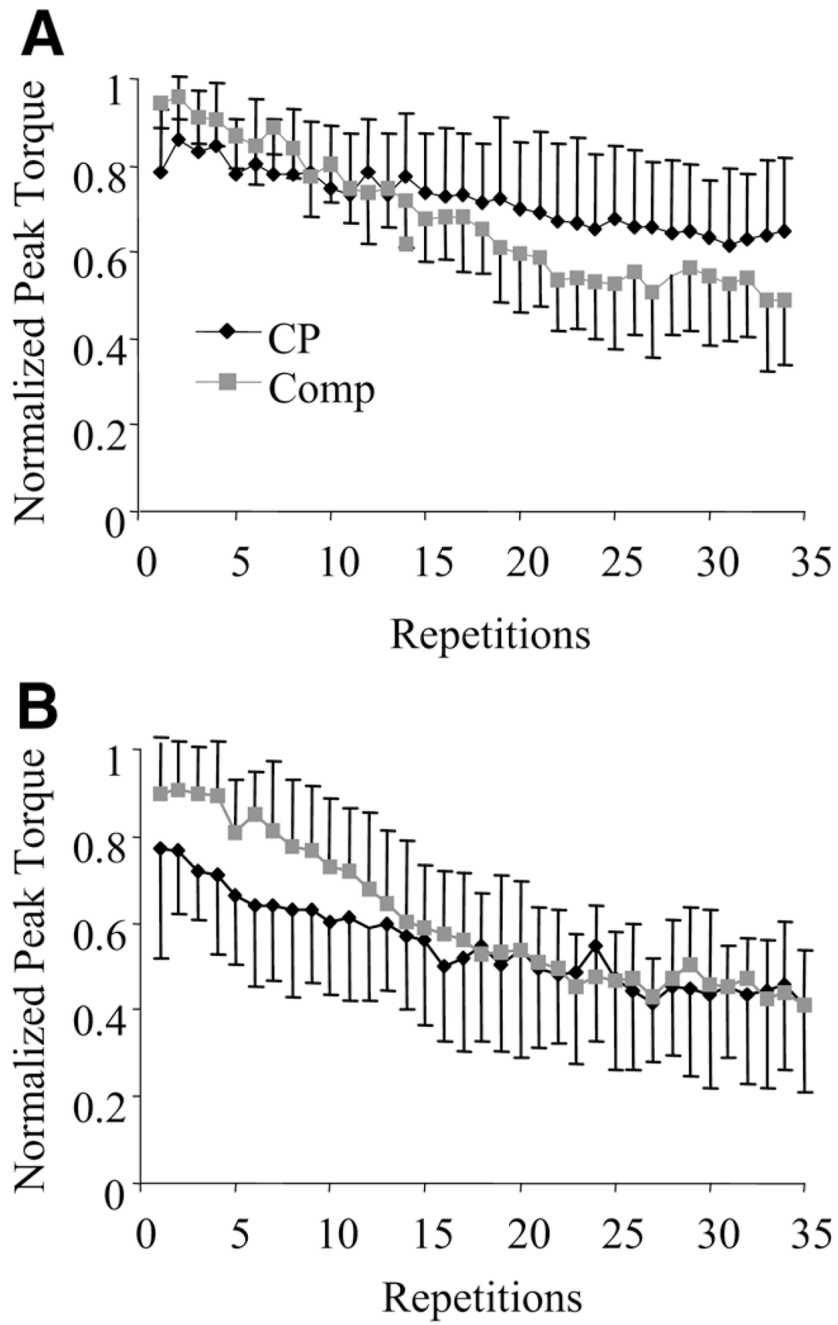


Fig 1. Mean and SD of normalized peak torque data across all repetitions in the CP and the comparison (Comp) groups for (A) knee extensors and (B) knee flexors.

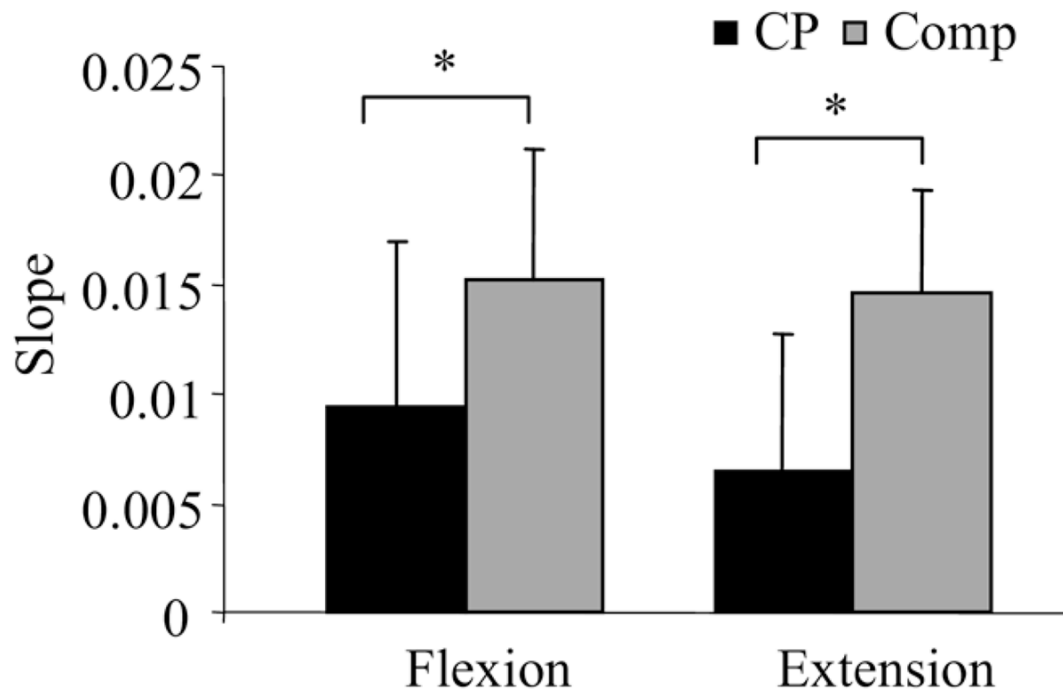


Fig 2. Mean and SD of the slope of the decline in normalized peak torque across repetitions in the CP and comparison (Comp) groups for knee extension and flexion. *Significant difference ($P < .05$).

Table 1

Participant Characteristics

Group	Sex	Age Range (y)	Age \pm SD (y)	Height \pm SD (m)	Weight \pm SD (kg)
CP	13F/5M	10–25	17.49 \pm 5.03	1.52 \pm 0.08	47.57 \pm 9.92
Comparison	13F/3M	10–23	16.61 \pm 4.45	1.59 \pm 0.09*	53.97 \pm 9.72

Abbreviations: F, female; M, male.

* The comparison group was significantly taller than the CP group ($P=0.02$).

Table 2
Correlations of the Slope With Functional Measures

Functional Measures	Slope KE	Slope KF
PODCI sports and physical function	.35	.28
PODCI transfers and basic mobility	.61*	.36
PODCI global functioning	.41	.34
PODCI happiness scale	-.36	-.09
PODCI pain and comfort	.15	-.04
Self-selected velocity	.43	.40
Fast velocity	.45	.38
GMFCS [†]	-.50*	-.24

Abbreviations: KE, knee extension; KF, knee flexion.

* $P < .05$.

[†] Spearman ρ correlation.