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Fatigue in cerebral palsy: a critical review.

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Objective: Fatigue contributes to the deterioration or cessation of walking ability in adults with cerebral palsy (CP). However, conflict exists as to its role. Studies involving functional tasks reported increased, and earlier onset of, fatigue in CP whereas laboratory studies have reported individuals with CP to be more fatigue resistant than their peers.

Methods: A critical review of the literature related to fatigue in CP was conducted.

Results: This review describes factors that contribute to the observed fatigue resistance in laboratory tasks and how a decreased force-production in CP can result in higher energy expenditure to perform the same amount of work as their peers.

Conclusion: More research regarding the process of fatigue and recovery for individuals with CP is needed; specifically studies that focus on functional movements requiring the integration of the whole body, thereby stressing the neuromuscular system in a different way than previously explored.

Introduction

One of the most common impairments experienced by adults with cerebral palsy (CP) is fatigue [1]. However, controversy exists in the available information about individuals with CP and the experience of fatigue. For example, recent laboratory studies have shown individuals with CP to be less fatigable than control participants [2, 3], which is in conflict with reports that fatigue is a chronic and disabling symptom of CP [1]. Locomotion is not usually a considerable cause of fatigue in the neuromuscular system, but for individuals with CP, fatigue becomes an important factor during ambulation over both short and long distances depending on the severity of the motor impairment and the terrain. Thus, in this context adults with CP experience higher levels of fatigue than the general population [4, 5] and, with chronic pain it is estimated that this combination affects 34% of the population with CP [4]. Indeed, a 7-year follow-up study reported that individuals whose walking ability deteriorated reported increased levels of physical fatigue, but no significant differences existed between a sample with CP and the general population in terms of mental fatigue. These results indicate that the fatigue experienced in CP is mainly of physiological origin [5], but the factors responsible are unclear. Thus, the purpose of this review is to synthesize information to explain the conflicting nature of fatigue in CP (with a specific focus on spastic CP), and to describe the characteristics of CP as it relates to fatigue during functional tasks of daily living [6]. It should be noted that this is not a systematic review, rather a critical examination to highlight gaps in our understanding to help design future studies towards a better understanding of the important aspects of fatigue in this population. Furthermore, this review also may help

evaluate current techniques and therapies, and to develop new methods to alleviate fatigue in individuals with CP.

In this review, fatigue is defined as a reduction in muscle force-generating capacity in the neuromuscular system that occurs during prolonged or ongoing activity [7]. The development and maintenance of a given level of force are dependent on the integration of the entire neuromuscular system, and there are several points in the system that can fail and lead to fatigue, and fatigue may occur at more than one site concurrently [8]. Factors contributing to fatigue will be organized into three sections: central factors, peripheral anatomical factors, and peripheral physiological factors.

Reports of fatigue in CP: The conflict

In a controlled isokinetic protocol, the knee flexors and extensors of individuals with CP were shown to be less fatigable compared to a group without disability. However, torque was normalized to the maximum peak torque and this normalized torque declined less in the individuals with CP than in the comparison group [2]. Additionally, individuals who were the least severely affected (as measured by the Gross Motor Function Classification System [9] (GMFCS)) and considered to have higher functional ability had greater rates of decline in their normalized peak force for the knee extensors [2]. One other study demonstrated a significant difference in the decline of normalized peak force after an electrically elicited fatiguing protocol. Children with CP experienced a 42% decline in normalized peak quadriceps femoris force compared to the decline of 52% in the control group [3]. In both of these studies, absolute maximum torque was between 50 to 73% less in individuals with CP, compared to controls, and thus

normalization for comparison between groups could be misleading. As a result of this lower overall strength compared to their peers without a disability [3] normalizing the force reduction that occurs with fatigue to the child's own maximal force capacity removes the functional practicality from the situation. Thus, although children with CP have reduced fatigue compared to non-disabled peers, only part of the picture of fatigue is being recognized in this population. Despite that individuals with CP appear to fatigue less than their non-disabled peers, the measurement of fatigue in the laboratory (i.e. using dynamometry of isolated muscles instead of functional tasks) does not reflect the chronicity of the problem. It is also possible for individuals with CP to have greater resistance to fatigue in the laboratory than the general population but still experience a greater subjective feeling of fatigue, and a greater impact of fatigue on activity, as a result of the inefficient mechanics associated with gait in CP [2]. Therefore, studies comparing fatigue data between individuals with CP and their peers developing typically are confounded by several factors. Specifically, normalization to peak torque can be misleading without also including a comparison in absolute terms (i.e. the use of whole body weight). The normalized data from laboratory studies also may be affected by factors such as co-contraction and variability in the most effective order of activating muscles; both of which have been demonstrated in individuals with CP, but not in peers without CP, causing comparisons between the two groups to be misleading.

A study by Leunkeu and colleagues [10] demonstrated increased fatigue in individuals with hemiplegic CP compared to controls by assessing the decline in the slope of the median frequency of a surface electromyography recording of the vastus lateralis and rectus femoris muscles. In this study, participants with CP required higher

levels of motor unit recruitment along with lower median frequency compared to control participants. This indicated increased skeletal muscle fatigue that has been linked to abnormal muscle function [10]. The authors used a measure of muscle activity to observe the effects of the contraction without relying on an inference from a decline in force production to demonstrate increased fatigue in a sample with CP [10]. These results further highlight the need for caution when using force normalization techniques that can lead to inaccurate conclusions of fatigue resistance in CP. Measures of muscle activity from EMG therefore may be a useful adjunct to measures of force to provide a more complete or accurate description of fatigue.

Further, it is troubling that those individuals who are already weaker than their peers are still experiencing a large reduction in muscle force during fatiguing tasks. This reduction in force has the potential to have a great impact on the capacity to continue performing activity and thus becomes a larger drain on the force reserve needed for continuing activity in individuals with CP compared to their peers. A decline of 42% of their peak torque producing capability with fatigue may have more of an impact on their ability to continue performing daily activities due to a reduced maximal absolute force generating capacity and higher energy expenditure demands. Individuals with CP have weakness that may be due to a variety of factors (discussed in the peripheral factors section), and the demands of walking require a greater percentage of the force generation capacity of the muscle [2] and of the individuals' maximal oxygen consumption for individuals with CP [11]. The increased demands on the muscle relative to its reduced overall capacity are reflected in reports of chronic fatigue in this population. In addition, several studies have documented an increased co-activation/co-contraction of agonist and

antagonist muscles around the same joint in individuals with CP [3, 12, 13]. Small amounts of co-activation are normal; however, too much co-activation increases energy expenditure and as a result could lead to a faster rate of fatigue in both agonists and antagonists [12, 14]. It should be noted that one laboratory study has demonstrated higher hamstring co-contraction, spasticity and reduced hamstring strength to be predictive of fatigue resistance in the hamstring muscles [15]. Additionally, higher quadriceps co-contraction and lower quadriceps strength were predictive of fatigue resistance in the quadriceps muscles [15]. The authors suggest that this relationship may be a result of the muscle adapting to disordered neural inputs; that is, constant co-contraction with movement may act as a training stimulus [15]. It is unknown how this process may translate to functional tasks such as walking, but it should be explored further.

It is possible that during functional activities of daily living, such as walking over long distances, individuals with CP experience a decline in force production greater than that demonstrated in an isolated laboratory setting. Functional tasks require individuals to manage and negotiate their entire body weight, which stresses the neuromuscular system in a different manner than has previously been studied. In addition, recovery from fatigue has not been studied in a population with CP, and important differences may exist between individuals with CP and their non-disabled peers in recovery rate or time that may help explain the conflicting reports of fatigue in this population.

Central sites

The neural factors contributing to fatigue have not been studied extensively in CP, but some studies have indicated disorder in and damage to the corticospinal projections to

the lower motor neurons in individuals with CP [16-18]. Mechanisms of reciprocal excitation of antagonists in CP that contribute to co-activation of muscles around a joint have been proposed in a comprehensive review by Cheney [16]. The first mechanism suggests corticospinal disorganization or abnormal synaptic organization, in which corticospinal neurons co-facilitate the motoneurons of both flexor and extensor muscles around a joint (either monosynaptically or through interneurons) [16]. A second mechanism could be the result of abnormal synaptic organization at the spinal level, where spindle afferents from agonists excite both the agonist and antagonist muscles around a joint [16]. Cheney [16] also described evidence from reflex studies demonstrating a reduction of presynaptic inhibitions acting on muscle spindle afferents as a contributing factor to spasticity in CP [16]. In addition, Heinen et al. [19] demonstrated a lack of inhibitory control in the motor cortex of adolescents with CP. The inability or loss of descending inhibition to antagonist or synergist muscles may contribute to reduced synchronization of motor unit firing and potentially contribute to observed muscle weakness and increased co-contraction in CP [19].

Evidence of corticospinal disorganization was shown by reduced synchronization of motor units in the tibialis anterior (TA) of individuals with CP, hypothesized to be due to a decrease in cortico-motorneuronal connections [17]. Others [18] have inferred abnormal development of projections from the motor cortex to spinal motoneurons that contribute to abnormal patterns of muscle activation in CP. This is manifested as the loss of specificity of the projections from the motor cortex to the motoneuron pools of the lower limb muscles and was demonstrated by similar activation of the TA and the soleus

muscles in individuals with CP as a result of magnetic stimulation intended to produce activation of the TA only [18].

Other evidence of corticospinal tract damage demonstrated that children with CP do not show the tonic suppression of H-reflexes during the stance phase in gait observed in children developing typically [20]. The suppression of the H-reflex happens as the corticospinal tract matures, and it has been hypothesized that the immature pattern persists in children with CP due to corticospinal tract damage [20]. In a laboratory setting, individuals with CP may appear less fatigable than the general population as a result of the inability of the descending tracts to fully transmit the signal to the muscles needed to produce a maximal contraction. However, functionally, a decreased efficiency of the descending signal from the motor cortex through damaged or abnormal projections to agonist and antagonist muscles around a joint can also lead to increased co-activation and increased energy expenditure, a potential cause of fatigue in individuals with CP [12], as discussed above.

In a study of activation and recruitment of motor units in individuals with CP, Stackhouse et al. [3] demonstrated significantly lower voluntary muscle activation ratios and lower force production for children with CP compared to controls, and therefore less muscle fatigue because the muscle was insufficiently activated, this information is summarized in Table I. Rose et al. [17] demonstrated that maximal M-wave amplitudes were similar between a group with CP and a control group, suggesting that the total numbers of available motor units were not different [17] although maximum voluntary contraction (MVC) torque was less in the group with CP for both the TA and gastrocnemius muscles. Additionally, the surface EMG amplitudes during MVC and,

therefore, the levels of neuromuscular activation (NMA) during MVC were significantly smaller in the group with CP. A decrease in NMA with the unaltered M-wave reflects the inability to fully activate all available motor units to sustain the required level of torque.

Elder et al. [21] demonstrated lower mean amplitude of EMG activity from both the plantar flexors (50% lower) and dorsiflexors (40% lower) of children with CP. The reduction in mean amplitude is also thought to reflect incomplete muscle activation either through an inability to activate available motor units or due to the inability to recruit higher threshold motor units [17, 21]. Rose et al. [17] demonstrated an intact relationship between recruitment and firing rate modulation at low to moderate levels of contraction evidenced by increased firing rates and recruitment with increasing voluntary activation of the muscles for both a group with CP and those without. However, the submaximal contractions required more voluntary effort for participants with CP as reflected by the highest target NMA levels corresponding to about 50% of the MVC NMA levels for individuals with CP and approximately 20% of the MVC NMA levels for the controls [17]. A person with CP can produce an equivalent contraction in terms of recruitment and firing rates as a control, but may require full voluntary effort compared to a submaximal effort for the control. Controls can then increase contraction strength by increasing firing rate or recruitment while the person with CP cannot [17] and theoretically, those with CP would experience more fatigue. Rose et al. [17] also calculated a projected maximal firing rate for the TA and gastrocnemius for both groups (Table I) to suggest that maximal firing rates in individuals with CP are reduced by approximately 50% compared to controls, potentially due to impairment of, or a decrease in, the number of cortico-

motoneuronal connections [17], which may be a contributing factor in reports that children with CP are less fatigable than their peers.

[Insert Table I about here]

Skeletal muscles are normally electrically silent when there is no movement [22]. Robertson et al. [22] showed individuals with CP had difficulty in achieving electrical silence after performing a contraction of the TA, and thus required more trials to learn to silence the muscle after activity. Individuals with CP also had difficulty silencing a single motor unit after achieving activation. This demonstrates an inability to inhibit the TA muscle at both the motor unit and gross motor level [22]. The delayed ability to silence motor units after activity may contribute to the co-activation around a joint during reciprocal movements. In the example of gait, the different phases require activation and inhibition of different muscles in a short span of time. Inability to silence motor units after activation during this task could contribute to increased energy expenditure reported in individuals with CP.

Overall it seems that although children with CP may be performing at or near maximal effort, there is also the possibility that not all of their motor units can be activated as a result of impaired motor pathways [17]. It has also been hypothesized that in the case of incomplete activation, type I fibers are preferentially recruited (or there is an inability to recruit higher threshold motor units) [17, 21] at lower firing rates, which may contribute to the observed greater fatigue resistance evidenced in the CP population in laboratory settings using normalized comparisons [2]. However, incomplete activation can result in individuals with CP using more effort to produce a contraction and maintain movement which could result in increased, or early onset of, fatigue.

Peripheral sites – Anatomical features

There is limited information regarding the structure and function of the sites in the peripheral neuromuscular system that directly relate to fatigue in individuals with CP. The neuromuscular junction is the link between the central and peripheral aspects of the neuromuscular system. Some research has suggested that individuals with CP have extrajunctional acetylcholine receptors and other structural differences that can affect the depolarization and re-polarization of the muscle membrane following a signal from the descending motor pathways [23, 24]. A relationship has been demonstrated between increased severity of impairment in motor function and increased abnormality of the neuromuscular junction [23]. The implications of these differences are not fully understood, and increased fatigue during functional tasks in individuals with more severe motor impairments may be a result of decreased function of the neuromuscular junction in communicating the signal from the descending motor pathway.

Reports on muscle size and the resulting strength of individuals with CP has produced conflicting results and hypotheses related to fatigue in CP. Some authors attribute the lower mean torque values (and less relative fatigue) observed in individuals with CP to differences in muscle size because greater strength or muscle mass may contribute to higher levels of fatigue. Leg volumes, cross-sectional area, muscle thickness, fascicle length and pennation angle all have been shown to be reduced in people with CP [21, 25] a summary can be found in Table II. Thus because smaller muscles generate less force and less force creates less fatigue, these features have the potential to contribute to the observed increased fatigue resistance in the laboratory

testing of individuals with CP. It is not clear whether these observed anatomical changes are secondary to the damage in the central nervous system or a tertiary condition as a result of decreased activity.

[Insert Table II about here]

An alternative hypothesis suggests that weakness as a result of lower muscle mass can increase levels of fatigue as a result of the need to recruit more motor units to achieve a given force level and due to a greater frequency of excitation required to perform a given task at an absolute force requirement [26]. This is supported by reports of relatively more fatigue during functional tasks, such as ambulation, and warrants further investigation using test parameters that are not confounded by differences in skeletal muscle function. Reports that individuals with CP are more functionally fatigable may be related to a lower force-generating capacity that can lead to a lower force reserve in order to maintain constant activity as discussed earlier [3]. Similar to older adults, activities of daily living require individuals with CP to use a greater percentage of their maximal strength. Literature on aging has suggested that the rate of recovery from fatigue may also be impaired following these tasks, but this has not been tested in CP [27].

A potential contributor to the fatigue resistance observed in laboratory studies of individuals with CP may be a predominance of a specific fiber type [2]. Indeed the few available reports indicate evidence of increased area of type I muscle fibers, or atrophy of type II fibers in CP [28-30]. Muscle biopsies provide evidence of variability in fiber size with reduced diameters of type I and II fibers, that is significantly more frequent in individuals with CP over 10 years of age, but no evidence of degeneration [28-30]. Greater variation in fiber size was detected in the more severely affected side; indicating

that the severity of CP may be a contributing factor to alterations in muscle composition [28]. In addition, studies have shown varying degrees of disorganization or disorientation of myofibrils in individuals with CP [29, 30]. Together these reports indicate that changes in the motor cortex and the descending pathways influence the organization of motor units at the spinal level. A predominance of fatigue resistant muscle fibers in CP may explain the observation of reduced fatigue during laboratory testing, such that the muscle fiber composition is different between individuals with CP and their peers. This supports the concern about comparisons that are based only on normalized peak force rather than on absolute capacity. The disorganization of the myofibrils could also impair excitation-contraction coupling, further reducing the strength of each muscle contraction. A predominance of type I fibers could contribute to decreased strength in individuals with CP; having the potential to increase their fatigue during functional tasks requiring high forces or prolonged activity.

Peripheral sites – Physiological features

Sufficient blood flow is essential to maintain muscle force production in terms of oxygen delivery and removal of metabolic by-products created during contractions. Some have suggested that spastic muscles do not properly support venous return as a result of increased muscle tone associated with CP, resulting in inhibited muscle lactate and metabolite clearance during activity [31, 32]. Decreased clearance of metabolic byproducts may contribute to lower maximal oxygen consumption and increased or earlier onset of fatigue in individuals with CP.

Many studies have documented increased energy expenditure in individuals with CP compared to their peers without disabilities, a summary can be found in Table III [11, 12, 33-37]. Youth with CP have higher energy expenditure during locomotion than their peers at similar speeds, and the rate of energy expenditure increases as children with CP age [33]. An increase in body weight and size as a child matures increases the demand for energy during locomotion and other activities, and requires greater physical exertion [33]. During gait, adolescents with CP work at a higher percentage of their maximal oxygen consumption compared to the youth developing typically (one study reported values of 53.5% and 22.5% respectively) [12]. Children with CP are both working at a higher percentage of their maximal aerobic power, and working harder than their peers at a given speed (or submaximal load). This may cause them to fatigue more easily during prolonged exercise [11, 37]. Interestingly, at a given submaximal level there appears to be no differences in the respiratory exchange ratio between individuals with CP and their peers without disabilities [37]. This indicates similar cardiorespiratory responses to submaximal exercise in both groups demonstrating that the cardiorespiratory response is not a contributing factor to fatigue in CP [37]. The type and severity of CP can also influence the energy expenditure during walking. Van den Hecke et al., [38] investigated energy cost in individuals with hemiplegic CP and determined that the increase in energy cost of ambulation was due to an increased mechanical work and that the efficiency of work was similar between individuals with CP and controls when walking at the same speed [38].

[Insert Table III about here]

Summary and future directions

Controversy exists as to which factors contribute to fatigue in individuals with CP compared to peers without disability, largely dependent on how fatigue is defined and measured. Figure 1 is a graphic summary of the factors that may explain the resistance to fatigue demonstrated in isolated laboratory studies compared with the factors that may contribute to increased fatigue during functional tasks. It appears that in laboratory settings when strength is normalized, individuals with CP fatigue less than their non-disabled peers; however, comparing fatigue in an isolated manner instead of using a functional task that depends on an absolute load (i.e. body weight) does not reflect the chronicity or impact of fatigue for individuals with CP and can be confounded by several structural and functional differences in the muscles of individuals with CP. Laboratory studies are useful to understand specific sites of differences or potential limitations in the neuromuscular system of individuals with CP, but therapists must recognize how to interpret these findings for functional tasks that require a certain level of absolute ability to be performed successfully.

[Insert Figure 1 about here]

It is clear from this critical review that neuromuscular fatigue is an important challenge of individuals with CP, but there is little consensus regarding the underlying mechanisms, and the functional impact. Part of this limitation is due to the few research studies and inconsistencies among these studies in how fatigue is defined and compared. Thus, one important direction is to understand the process of fatigue in individuals with CP, with a focus on functional tasks as they relate especially to locomotion and the use of absolute loads such as body weight. Specifically, a better understanding of the rate of the

development and recovery from fatigue is also needed as this may help elucidate important factors underlying the chronic experience of fatigue in CP. Also studies designed to assess the fatigability of individuals with CP compared to a control population, need to account for differences in absolute strength and altered muscle function potentially highlighting the effect of a lower force reserve. Finally, it should be noted that the levels of fatigue experienced by individuals with CP may be related to the severity of the disability as measured by the GMFCS, therefore, fatigue should be examined across all GMFCS levels, and potentially, each level independently.

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References

1. Hilberink SR, Roebroeck ME, Nieuwstraten W, Jalink L, Verheijden JMA, Stam HJ. Health issues in young adults with cerebral palsy: Towards a life-span perspective. Journal of Rehabilitation Medicine 2007;39:605-11.
2. Moreau NG, Li L, Geaghan JP, Damiano DL. Fatigue resistance during a voluntary performance task is associated with lower levels of mobility in cerebral palsy. Archives of Physical Medicine and Rehabilitation 2008;89:2011-6.
3. Stackhouse SK, Binder-Macleod SA, Lee SCK. Voluntary muscle activation, contractile properties, and fatigability in children with and without cerebral palsy. Muscle and Nerve 2005;31:594-601.
4. van der Slot W, Nieuwenhuijsen C, van den Berg-Emons RJ, Bergen M, Hilberink S, Stam HJ, Roebroeck M. High prevalence and co-occurrence of chronic pain, fatigue and depressive symptoms in adults with spastic cerebral palsy. Developmental Medicine and Child Neurology 2010;52(suppl 5):21.
5. Opheim A, Jahnsen R, Olsson E, Stanghelle JK. Walking function, pain, and fatigue in adults with cerebral palsy: a 7-year follow-up study. Developmental Medicine and Child Neurology 2009;51:381-88.
6. Tosi LL, Maher N, Moore DW, Goldstein M, Aisen ML. Adults with cerebral palsy: A workshop to define the challenges of treating and preventing secondary musculoskeletal and neuromuscular complications in this rapidly growing population. Developmental Medicine and Child Neurology 2009;51(suppl 4):2-11.
7. Bigland-Ritchie B, Johansson R, Lippold OCJ, Woods JJ. Contractile speed and EMG changes during fatigue of sustained maximal voluntary contractions. Journal of Neurophysiology 1983;50:313-24.
8. McComas AJ, Miller RG, Gandevia SC. Fatigue brought on by malfunction of the central and peripheral nervous systems. Advances in Experimental Medicine and Biology 1995;384:495-512.
9. Palisano RJ, Rosenbaum PL, Bartlett DJ, Livingston MH. Content validity of the expanded and revised gross motor function classification system. Developmental Medicine and Child Neurology 2008;50:744-50.
10. Leunkeu AN, Keefer DJ, Imed M, Ahmaidi S. Electromyographic (EMG) analysis of quadriceps muscle fatigue in children with cerebral palsy during a sustained isometric contraction. Journal of Child Neurology 2010;25(3):287-93.
11. Leunkeu AN, Gayda M, Nigam A, Lecoutre N, Ahmaidi S. Cardiopulmonary exercise data during quadriceps isometric contraction sustained to fatigue in children with cerebral palsy. Isokinetics and Exercise Science 2009;17:27-33.
12. Unnithan VB, Dowling JJ, Frost G, Bar-Or O. Role of cocontraction in the O2 cost of walking in children with cerebral palsy. Medicine and Science in Sports and Exercise 1996;28:1498-504.
13. Burtner PA, Qualls C, Woollacott MH. Muscle activation characteristics of stance balance control in children with spastic cerebral palsy. Gait and Posture 1998;8:163-74.
14. Feltham MG, Ledebt A, Deconinck FJA, Savelsbergh GJP. Assessment of neuromuscular activation of the upper limbs in children with spastic hemiparetic

cerebral palsy during a dynamical task. Journal of Electromyography and Kinesiology 2010;20:448-56.

15. Moreau NG, Li L, Geaghan JP, Damiano DL. Contributors to fatigue resistance of the hamstrings and quadriceps in cerebral palsy. Clinical Biomechanics 2009;24:355-60.

16. Cheney PD. Pathophysiology of the corticospinal system and basal ganglia in cerebral palsy. Mental Retardation and Developmental Disabilities Research Reviews 1997;3:153-67.

17. Rose J, McGill KC. Neuromuscular activation and motor-unit firing characteristics in cerebral palsy. Developmental Medicine and Child Neurology 2005;47:329-36.

18. Brouwer B, Ashby P. Do injuries to the developing human brain alter corticospinal projections? Neuroscience Letters 1990;108:225-230.

19. Heinen F, Kirschner J, Fietzek U, Glocker F-X, Mall V, Korinthenberg R. Absence of transcallosal inhibition in adolescents with diplegic cerebral palsy. Muscle Nerve 1999;22:255–7.

20. Hodapp M, Klisch C, Mall V, Vry J, Berger W, Faist M. Modulation of soleus H-reflexes during gait in children with cerebral palsy. Journal of Neurophysiology 2007;98:3263-8.

21. Elder GCB, Stewart G, Cook K, Weir D, Marshall A, Leahey L. Contributing factors to muscle weakness in children with cerebral palsy. Developmental Medicine and Child Neurology 2003;45:542-50.

22. Robertson DW, Lee WA, Jacobs M. Single motor-unit control by normal and cerebral-palsied males. Developmental Medicine and Child Neurology 1984;26:323-7.

23. Theroux MC, Oberman KG, Lahaye J, Boyce BA, DuHadaway D, Miller F, et al. Dysmorphic neuromuscular junctions associated with motor ability in cerebral palsy. Muscle and Nerve 2005; 32:626-32.

24. Theroux MC, Akins RE, Barone C, Boyce B, Miller F, Dabney KW. Neuromuscular junctions in cerebral palsy: Presence of extrajunctional acetylcholine receptors. Anesthesiology 2002;96:330-5.

25. Moreau NG, Teefey SA, Damiano DL. In vivo muscle architecture and size of the rectus femoris and vastus lateralis in children and adolescents with cerebral palsy. Developmental Medicine and Child Neurology 2009;51:800-6.

26. Lindstrom B, Lexell J, Gerdle B, Downham D. Skeletal muscle fatigue and endurance in young and old men and women. The Journal of Gerontology: Series A Biological Sciences and Medical Sciences. 1997;52:B59-66.

27. Allman BL, Rice CL. Neuromuscular fatigue and aging: Central and peripheral factors. Muscle and Nerve 2002;25:785-96.

28. Ito J, Araki A, Tanaka H, Tasaki T, Cho K, Yamazaki R. Muscle histopathology in spastic cerebral palsy. Brain and Development 1996;18:299-303.

29. Marbini A, Ferrari A, Cioni G, Bellanova MF, Fusco C, Gemignani F. Immunohistochemical study of muscle biopsy in children with cerebral palsy. Brain and Development 2002;24:63-6.

30. Rose J, Haskell WL, Gamble JG, Hamilton RL, Brown DA, Rinsky L. Muscle pathology and clinical measures of disability in children with cerebral palsy. Journal of Orthopaedic Research 1994;12:758-68.
31. Hoofwijk M, Unnithan V, Bar-Or O. Maximal treadmill performance of children with cerebral palsy. Pediatric Exercise Science 1995;7:305-13.
32. Lundberg A. Maximal aerobic capacity of young people with spastic cerebral palsy. Developmental Medicine and Child Neurology 1978;20:205-10.
33. Campbell J, Ball J. Energetics of walking in cerebral palsy. Orthopedic Clinics of North America 1978;9:374-7.
34. Duffy CM, Hill AE, Cosgrove AP, Corry IS, Graham HK. Energy consumption in children with spina bifida and cerebral palsy: A comparative study. Developmental Medicine and Child Neurology 1996;38:238-43.
35. Johnston TE, Moore SE, Quinn LT, Smith BT. Energy cost of walking in children with cerebral palsy: Relation to the gross motor function classification system. Developmental Medicine and Child Neurology 2004;46:34-8.
36. Bell KL, Davies PS. Energy expenditure and physical activity of ambulatory children with cerebral palsy and of typically developing children. American Journal of Clinical Nutrition 2010;92:313-9.
37. Rose J, Haskell WL, Gamble JG. A comparison of oxygen pulse and respiratory exchange ratio in cerebral palsied and nondisabled children. Archives of Physical Medicine and Rehabilitation 1993;74:702-705.
38. Van Den Hecke A, Malghem C, Renders A, Detrembleur C, Palumbo S, Lejeune TM. Mechanical work, energetic cost, and gait efficiency in children with cerebral palsy. Journal of Pediatric Orthopaedics 2007;27:643-7.
39. Keefer DJ, Tseh W, Caputo JL, Apperson K, McGreal S, Vint P, Morgan DW. Interrelationships among thigh muscle co-contraction, quadriceps muscle strength and the aerobic demand of walking in children with cerebral palsy. Electromyographic Clinical Neurophyisology 2004;44:103-10.

Table 1 – Motor unit activation in individuals with cerebral palsy

Study	Muscle(s) examined	Parameter measured	Difference between CP and controls
Robertson et al. 1984[22]	Tibialis anterior	Silencing motor unit activation	Children with CP had difficulty silencing motor units at both the gross and single motor unit level after activation.
Stackhouse et al. 2005[3]	Quadriceps femoris	Voluntary muscle activation ratios†	Children with CP had 33% less voluntary activation than control children
		Knee extension force	Lower voluntary activation corresponded with 56% less force production in the children with CP
Stackhouse et al. 2005[3]	Triceps surae	Voluntary muscle activation ratios	Children with CP had 49% less voluntary activation than control children
		Plantar flexion force	Lower voluntary activation corresponded with 73% less force production in the children with CP
Rose et al. 2005[17]	Tibialis anterior	Projected maximal firing fate	Children with CP had a projected maximal firing rate of 16Hz compared to 31Hz for the control group
	Gastrocnemius	Projected maximal firing fate	Children with CP had a projected maximal firing rate of 13Hz compared to 25Hz for the control group

†Voluntary activation ratios are calculated by stimulating the muscle during a maximal voluntary contraction and dividing the augmentation of force by the force of stimulation at baseline.
Cerebral palsy (CP)

Table 2 – Muscle parameters in individuals with cerebral palsy

Study	Muscle(s) examined	Parameter measured	Difference between CP and controls
Elder et al. 2003[21]	Anterior compartment: tibialis anterior, extensor digitorium longus, extensor hallucis and peroneus tertius	Muscle volume (MRI)	27% less for individuals with CP
Elder et al. 2003[21]	Posterior compartment: soleus, gastrocnemius, plantaris, popliteus, tibialis posterior, flexors digitorum longus and hallucis longus	Muscle volume (MRI)	28% less for individuals with CP
Moreau et al. 2009[25]	Rectus femoris	Cross-sectional area (Ultrasound)	48.5% lower in individuals with CP
Moreau et al. 2009[25]	Rectus femoris Vastus lateralis	Muscle thickness	32% lower in individuals with CP 31% lower in individuals with CP
Moreau et al. 2009[25]	Rectus femoris	Fascicle length	27% shorter in individuals with CP
Moreau et al. 2009[25]	Vastus lateralis	Pennation angle	3 degrees less in individuals with CP

Magnetic resonance imaging (MRI)
Cerebral palsy (CP)

Table 3 – Energy expenditure during walking in individuals with cerebral palsy

Study	Task	Measure of energy expenditure	Differences observed
Campbell & Ball 1978[33]	Free walking at comfortable, self-selected pace	Energy cost (oxygen consumption VO_2)	Energy expenditure was greater in children with CP compared to controls at the same walking speed.
			Energy expenditure increased as children with CP aged.
Rose et al. 1993[37]	Treadmill walking at various speeds	Oxygen Uptake	Children with CP had higher oxygen uptake than controls while walking the speeds of 21.5m/min and 37.6m/min.
			Children with diplegia had higher oxygen uptake than children with hemiplegia while walking at the speeds of 21.5m/min and 37.6m/min.
Rose et al. 1993[37]	Treadmill walking at various speeds	Oxygen Pulse	Children with CP had higher oxygen pulse values compared to controls while walking at the speeds of 21.5m/min and 37.6m/min.
			Children with diplegia had higher oxygen pulse than children with hemiplegia while walking at the speed of 37.6m/min.

Rose et al. 1993[37]	Treadmill walking	Most economical walking speed	Most economical walking speed was slower for children with CP compared to controls.
			Oxygen uptake and oxygen pulse at most economical walking speed was higher for children with CP than controls
			Oxygen uptake at most economical walking speed was higher for children with diplegia compared to children with hemiplegia
Duffy et al. 1996[34]	Free walking at comfortable, self-selected pace	Oxygen uptake	Children with diplegia had a higher rate of oxygen consumption per minute than a group with spina bifidia, a group with hemiplegia and controls.
			Children with CP (both hemiplegia and diplegia) had a higher energy cost for walking than the control group.
Unnithan et al. 1996[12]	Treadmill walking	Energy cost (use of metabolic cart)	Children with CP had higher values for absolute oxygen consumption, mass-relative oxygen consumption, net mass-relative oxygen consumption, percentage of maximal oxygen

|			consumption, ventilation, heart rate, and net heart rate compared to controls while walking at the speed of 3km/h.
			When a relative intensity of 90% of the individuals fastest walking speed was used, differences between individuals with CP and controls were only observed in percentage of maximal oxygen consumption
			In individuals with CP co-contraction of the lower leg and thigh explained 42.8% and 51.4% of the variance in oxygen consumption respectively.
Keefer et al. 2004[39]	Treadmill walking	Energy expenditure (Oxygen consumption, VO_2)	No relationship was demonstrated between energy expenditure and thigh muscle co-contraction or quadriceps muscle strength in individuals with hemiplegia.
Johnston et al. 2004[35]	Walking at self-selected pace	Energy consumption (Volume of oxygen consumed per kilogram of body weight)	Increasing energy cost of walking with increasing GMFCS level.
			Significant differences between each adjacent GMFCS level.

			Children with CP demonstrated a higher energy cost of walking than children with typical development.
van den Hecke et al. 2007[38]	Walking on a motor-driven treadmill	Energy cost (oxygen consumption VO_2)	Mean energy cost value was 1.3 times greater for individuals with CP than control values.
Bell & Davies 2010[36]	Free walking	Activity-related energy expenditure (indirect calorimetry)	Children with CP expended more energy than controls. Children with diplegia expended more energy than children with hemiplegia.

Cerebral palsy (CP)
Gross Motor Function Classification System (GMFCS)
Volume of oxygen per time (VO2)

Figure 1. Factors Contributing to Conflicting Reports of Fatigability in Individuals with Cerebral Palsy.
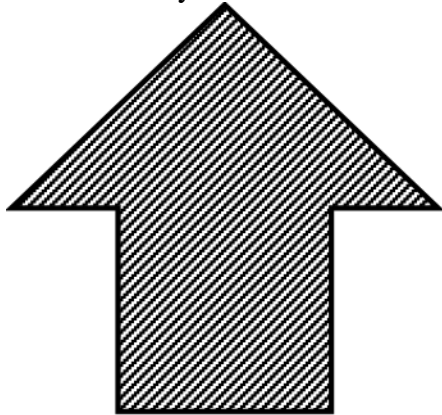
Factors Contributing to Increased/Earlier Onset of Fatigue

1. Increased energy expenditure during locomotion
2. Decreased overall force production capacity
3. Work at a higher percentage of maximal aerobic power
4. Limited removal of muscle metabolites
5. Measurement of fatigue based on a fixed or absolute resistance such as body weight
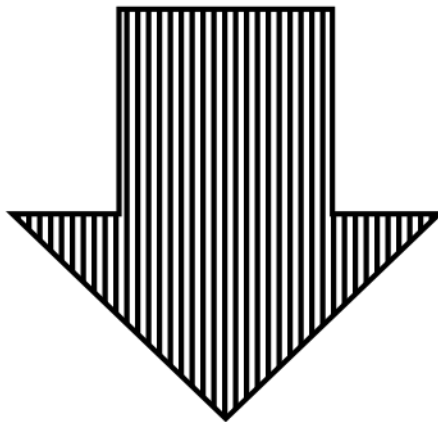
Factors Contributing to Appearance of Fatigue Resistance

1. Decreased/abnormal corticospinal projections
   a. Altered patterns of motor-unit activation
   b. Altered patterns of motor-unit recruitment
2. Dysmorphic neuromuscular junctions
3. Differences in muscle fiber composition
4. Alterations in muscle size and structure
5. Differences in muscle fiber diameter
6. Disorganization of myofibrils
7. Measurement of fatigue in relative terms