Designing Exercise to Improve Bone Health Among Individuals With Cerebral Palsy

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Purpose: Individuals with cerebral palsy (CP), ambulatory or not, have less bone strength and density than their peers. Aging individuals with CP are at a higher risk for nontraumatic fractures, progressive deformity, pain, and spinal stenosis. Critical periods for skeletal formation are during prepuberty and adolescence. Applying mechanostat theory to exercise design for individuals with CP may be beneficial.

Methods: Principles of mechanostat theory, particularly the osteogenic index, is applied to guide the design of exercise programs based on varying levels of physical capacity.

Results: Recommendations are made for optimizing dosing of a variety of interventions for improving bone health among individuals with CP based on mechanostat theory with specific type, number of repetitions, and frequency.

Conclusions: Researchers and clinicians are called to action to consider the role of exercise throughout the lifespan for all individuals with CP, regardless of level of severity. (Pediatr Phys Ther 2021;33:50–56)

Key words: bone health, cerebral palsy, exercise, mechanostat principles

INTRODUCTION

Individuals with cerebral palsy (CP), whether or not they walk or have spasticity or dystonia, have risk for decreased bone mineral density and strength compared with their peers developing typically.[1-4] Increased risk may be related to physiological processes among the endocrine system and interactions with other body functions,[5] coupled with lack of appropriate mechanical forces on the skeleton during development and adulthood.[6,7] Repetitive abnormal forces deteriorate bone and joint health with age.[8] Poor bone health places individuals with CP at greater risk than their peers for fractures, deformity, osteoporosis, spinal stenosis, and pain with aging.[5,8-11]

Physical therapy practice for individuals with CP does not have clear guidelines or recommendations for addressing poor skeletal health. Many interventions (immobilization of the limb, pharmacological agents to paralyze muscles, and bone realignment procedures) used to manage skeletal deformities may further weaken the skeleton.[12] Given the importance of the skeleton to overall health, quality of life, and function,[12] it is critical for physical therapists working with individuals with CP to thoughtfully design exercise programs to optimize bone health throughout the life span.

Factors associated with poor bone health include premature birth/low birth weight, low body mass, poor nutritional intake, long-term use of anticonvulsive or gastrointestinal reflux drugs, hormonal imbalances, physical activity and other lifestyle factors, medical interventions, physiological processes, arthritis/inflammatory diseases, and genetics/epigenetics.[9,12-16] Individuals with CP may have varying degrees of risk (high or low) depending on their specific medical history, genetics, and clinical presentation. Henderson et al[17] have suggested that adolescents with severe CP do not gain bone mass relative to gains in height, resulting in a net bone loss rather than gain during adolescence. Children with mild forms of motor impairment from CP have poorly developed bone microarchitecture and increased fatty infiltrates.[5] The small amount of work that has been done with bone health and adults with CP suggests that nutrition and lean body mass are related to bone health,[18] and there is room to improve interventions across the life span.[19]

The American Academy for Cerebral Palsy and Developmental Medicine Care Pathways for the management of osteoporosis among individuals with CP[20] indicates that the evidence to support the efficacy of weight-bearing activities to promote bone mineral density is unclear among individuals with CP. Systematic reviews of interventions to improve bone health, including standing programs,[21-23] demonstrate positive

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responses to a wide variety of interventions to improve bone health. Yet, dosing parameters are not clear for age of intervention, type, intensity, time spent doing the activity, and duration to create structural change that is sustainable.

A part of the reason that many interventions have not yielded strong treatment effects may be the dose of the intervention and a lack of rationale for the dose. Interventions designed for individuals with CP should consider basic physiological principles for designing exercise to improve bone adaptation.[7,13,15,24-31] A rationale and framework for designing and implementing exercise to improve bone health for individuals with CP are described later.

GUIDING PRINCIPLES FOR DESIGNING EXERCISE INTERVENTIONS FOR THE SKELETON

Guiding principles for designing exercise to promote bone health take into consideration exogenous and endogenous factors that impact bone adaptation[7,13,15,24-31] (Table 1). Bone responses to external stimuli are called laws or rules because they are extremely predictable.[13,15,24,28,31-33]

Age at the Time of Interventions

Responses to external stimuli can be augmented by endogenous factors, such as growth hormones or other biological agents during critical periods, such as the last trimester of gestation, prepuberty,[14] and during late life.[10,11] Timing of exercise prescription to improve the skeleton is synchronous with times of increased biological or hormonal presence within the body. Infants born preterm require targeted intervention when medically stable; 5 minutes of passive or active assist exercise daily improves bone in premature infants.[34,35] Prepuberty children should be targeted for exercise to improve bone health overall with special attention to femoral neck, spine, and distal femurs.[17,36,37] Adolescence is another time to target bone health as after children meet their maximal height, they accrue up to 25% of their total bone mass.[38] Osteogenic activities should continue throughout the life span, especially when endogenous hormones decline later in life, and may be supplemented.

Type

Bone responds to dynamic loads.[13,24,28,31-33] For reasons that are probably related to the way that bone cells receive mechanical signals,[13,24,28,31-33] it is now clear that bone *does not adapt* to loads unless they are applied in short bursts of repeated loading and unloading.[27] This means that if a load is applied and then not removed (standing still), bone does not form. Osteogenesis responds only to loads that are applied briefly and then removed and repeated (eg, jumping rope).

Bone formation on the periosteal surface in rats loaded statically at 8.5 N and 17 N showed the same amount of bone formation, which was not different to formation on the nonloaded contralateral limb.[13] Thus, *even with increasing loads, a static load does not generate a response*. However, when a dynamic load was

TABLE 1

Guiding Principles for Designing Exercise for Bone Health

Principles	Implications for Dose for Individuals at Risk for or With Cerebral Palsy
Age at intervention	
Critical periods	Age at intervention
Intervention during the life span can yield meaningful gains	Infants born preterm—when medically stable
	Prepuberty—in conjunction with endocrinologist
	Adolescence—in 3 y after reaching maximal height
	Pre-/postmenopause—in conjunction with endocrinologist
Type of activity	
Type of loading	Type of activities
Novel, dynamic, multidirectional forces produce greatest gains	Include activities that provide variability in movement
Specificity	Pick an activity that will target the desired structure
Bone remodeling occurs, specifically the loaded site, and does not generalize to the entire long bone or axial skeleton	Spine Femoral neck Distal femur Distal radius
Intensity	
Strain magnitude	Dynamic activities, either seated, supported standing or standing that provides high ground reaction force or muscle pull on bone relative to normal
The more strain, the more deformation, the greater gain in bone	
Strain rate	Movements that are at the highest rate without being unsafe for the individual
The faster the rate of strain, the greater the gain in bone	
Time spent doing activity	
Loading cycles	Short bursts of activity—100-300 repetitions; 10 min; target heart rate, or as fast as possible for short bursts 30 s to 10 min
After about 100 loading cycles, cells lose mechanosensitivity	
Duration	
Rest	One set; rest for 4-8 h
It takes about 4-8 h for the cells to restore their mechanosensitivity.	Can do multiple loading cycles a day Goal is to achieve specific osteogenic index per week
Adaptation	Will take 6-mo duration for change to occur
It takes 6 mo to impact skeletal adaptation	

TABLE 2

Hierarchy of Osteogenic Activities

Examples
Highly
Squash
Tennis
Soccer
Ice hockey
Badminton/volleyball
Volleyball
Weight lifting
Moderately
Long distance running
Stair stepping
Rowing machines
Least
Walking
Swimming
Cycling
Yoga
Calisthenics

applied at 17 N for an equivalent length of time, there was a large increase in periosteal bone formation. A load of equivalent magnitude can have very different effects, depending on whether it is applied statically or cyclically (dynamically).[13,15] Examples of dynamic loading activities, ranked from highly to least osteogenic, are shown in Table 2.

Type of loading also refers to where the load is applied to the skeleton. Bone responses are site specific.[13,24,28,31-33] Exercise must target a specific skeletal site and be of sufficient strain magnitude or at a high enough rate to allow adaptation.[15,27-29,31] From a clinical perspective, it is essential to target skeletal regions most prone to fracture such as the hip, spine, and distal femur or radius.[3,13,36,39] For example, activities such as box jumps or hip-hop dancing improve bone in the femoral neck and lumbar spine and recumbent biking targets the distal femur (Table 3). Table 3 provides examples of activities physical therapists do with individuals with CP, information about how osteogenic the activity is, the amount of loading occurring, and the skeletal structures targeted.

Intensity

The first rule of bone adaptation is that bone responds only above or below a threshold of strain or strain rate.[13,24,28,31-33]

TABLE 3

Types of Activities, Osteogenic Characteristics, Ground Reaction Force, and Site Specificity

Osteogenic Characteristic	Type	Ground Reaction Force in Terms of BW	Site Specificity	OI
Highly	Box jumps	2-8× BW depending on height of box	Femoral neck Spine	8× BW 100 loading cycles OI = 36.92
Moderately	Overground Walking	Walking 1.1 BW Running 2.7 BW	Femoral neck Spine	1.1× BW 100 loading cycles OI =5.08
Moderately	Treadmill training	Running 2.7 BW	Femoral neck Spine	2.7× BW 100 loading cycles OI =12.6
Highly	Lower-extremity plyometrics	3.5-8× BW	Femoral neck Spine	3.5× BW 100 loading cycles OI = 16.15
Moderately	Dance—hip-hop	2× BW	Femoral neck Spine	2× BW 100 loading cycles OI = 9.23
Moderately to least	Seated or standing plyometrics	65-85% of 1 repetition maximum	Upper extremities Spine	Unable to calculate
Least	Seated vibration	Not clear	Spine	Unable to calculate
Least	Punching heavy bag	As fast as possible for 10 min	Upper extremities Spine	Unable to calculate
Moderately to least	Recumbent cycling	At high resistance 3 N	Distal femur	3 N 100 loading cycles OI = 13.85
Moderately to least	Leg press	65-85% 1 repetition maximum	Distal femur	Unable to calculate
Moderately to least	Tricycle or bicycle riding	At high resistance 3 N	Distal femur	3× BW 100 loading cycles OI = 13.85
Moderately to least	Whole body vibration standing	~1-1.2× BW	Tibial plateau	1.2× BW 100 loading cycles OI =5.54
Least	Robotic gait training	0.5-0.9 of BW depending on individual	Femoral neck Spine	0.5-0.9× BW 100 cycles OI =2.31-4.15
Least	Aquatics	Exercising at target heart rate	Whole body	Unable to calculate

Abbreviations: BW, body weight; OI, osteogenic index.

If the mechanical signal is too low, then bone will be lost, but if the mechanical signal is high enough, then bone will respond by adding new bone in locations that effectively reduce the strain to within the usual range.[13,24,28,31-33] Animal studies have demonstrated that bone has a threshold for strain, below this it resorbs, before it responds, and then, adaptation occurs in a linear fashion.[13] It is likely that this is similar in humans. Intensity is usually measured in terms of loading, ground reaction force (GRF), or Newtons (N). Intensity may also be "as fast as possible" for short bursts of time or obtaining target heart rate for a specified time. It is not possible to measure the pull of the muscle on bone during rapid muscle force development, but it is a component of loading the skeleton.[13,24,28,31-33]

Activities that provide a variety of novel multidirectional impact forces, such as soccer and volleyball, are more osteogenic (Table 2).[13,24,28,31-33] Non–weight-bearing sports, such as swimming and cycling, are less osteogenic. For individuals with CP, the hierarchy of activities to promote osteogenesis should be considered in relation to the individual's usual activities. For example, for an individual at Gross Motor Function Classification System (GMFCS) level V, swimming may be a highly osteogenic activity if dosed appropriately. For individuals at GMFCS levels I-III, high-intensity cycling, leg presses, and fast walking for short burst if dosed appropriately may be highly osteogenic. As the individuals who do not walk may have greater difficultly producing high-intensity movements, more frequent bouts per day or week may be warranted.

Time Spent Doing the Activity

The loading duration can be short. Animal studies have demonstrated that bone response to loading can be of short duration, and at a certain point, the bone gets saturated and does not respond to loading.[13,24,28,31-33] Between 100 and 300 loading cycles, there is very little difference in bone response.[13,29] Bone is exceedingly sensitive to small amounts of mechanical stimuli of sufficient magnitude. Bone needs to rest for about 4 to 8 hours between bouts of loading to regain mechanosensitivity.[13,29] This means that loading activities can be done in short burst throughout the day.

The requirement that dynamic loads are required for bone's mechanical adaptation implies that the rate of application of a load may be an important component of the response.[13,29] Exercises involving loads applied at higher rates, such as running or jumping, may be more osteogenic than other forms of exercise.[13] Even short periods of impact loading can stimulate increased bone accrual or prevent decreased bone loss in immobilized animals.[13,24,29] Loading time may be short, but the rate of loading should be as high as is safe, so something as simple as 100 box jumps or 10 minutes punching a heavy bag may be sufficient for one bout of loading.

Osteogenic responses by bone to loading can be mathematically modeled using intensity (GRF or loading), frequency (number of loading cycles), and number of times a week the activity is performed.[29] The osteogenic index (OI) of an exercise can be calculated by the following formula: (intensity $\times$ ln [frequency $+1$] $\times$ times per week).[29] Given that the OI of an exercise is governed by mathematical properties, lower-intensity loading may be done more often to obtain the same effect as more intense loading. For example, to obtain an OI of 110, box jumps could be done 100 repetitions at 8 times the body weight, 3 times a week. Alternatively, box jumps could be done 100 repetitions at 2 times the body weight, 12 times a week.

Fuchs et al[40] designed an exercise intervention with prepubertal children, which demonstrated improved bone density at the femoral neck and lumbar spine in the short and long terms.[41] The intervention consisted of jumping 100× (10 minutes) off a 60-cm box, 3 times a week, producing a force 8 times the body weight, for 7 months, yielding an OI of 37 per session, or 110 per week. It is the randomized controlled trial with the largest effect size (1.38) for changes in the femoral neck,[29,42] sustainable across 8 years.[41] Of note, age at the time of intervention was approximately 9 years, a time of high endogenous hormones. Given the mathematical principles that govern bone, for individuals who tolerate less than 8 times their body weight for jumping, jumping more frequently, for example, 12 times a week at 2 times body weight could result in the same OI.

Duration

The entire process of bone adaptation in response to exercise takes about 6 months to complete.[13] Hence, measurement of the effect of exercise on bone structure and function is most reliable with 6 months or more between bone scans.[43] In addition, the cumulative OI achieved by the participants in the study by Fuchs et al[40] was achieved over 7 months of activity 3 times a week. For physical therapists working with individuals with CP, it seems possible that there are a variety of 10-minute activities that could be built into the day to promote bone health and be performed on a daily basis.

Innovations in Designing Exercise for Individuals With CP

How can physical therapists use the guiding principles of exercise and bone adaption to design more effective programs? For the first principle, age, physical therapists should target specific age ranges to enhance bone health: the last trimester of pregnancy for premature infants, prepuberty, and when hormones drop with aging, such as postmenopause. Individual preferences, capabilities, and available resources govern type, the next principle. In addition, clinical needs will also govern type. Bone response is site specific, and activities should be chosen, given the structure desired to improve: femoral neck, spine, upper extremities, distal femur, tibial plateau, or whole body.

Intensity, frequency, and time spent doing the activity are variables that can be determined once the activity is selected. For sustainable change in bone to occur, a duration of 6 months is recommended, given the physiology of bone adapatation.[7,13,28,29,43,44] The best evidence suggests that a weekly OI of 110 promotes sustainable changes in bone health for children who are without disability.[13,29,40,41,45,46]

Evidence to support how much loading the skeletons of individuals with CP require does not exist. However, similar in adapting the physical activities guidelines for typically developing children and adults with individuals with disabilities, the same or more amount of activity is recommended.

Calculating the OI of activities performed over the week with individuals with CP, especially those who are in the critical periods for optimizing bone health, can guide treatment decisions for loading.

The OI for each activity in Table 4 was calculated using the GRF, number of loading cycles, and a frequency of 3 times of week. Increasing the frequency of times per week each activity is performed could increase the OI of the overall intervention. Again, between 100 and 300 loading cycles are optimal, with rests of 4 to 8 hours between bouts.[2,13,15,28,29,47] Performing multiple skeletal loading activities for various skeletal sites within 1 exercise session is also a possibility.

Walking, whether over ground or on a treadmill, provides skeletal loading (Table 3) slightly greater than body weight.[48] Increased speeds of walking are associated with increased GRFs.[48] Walking, fast walking, or running on a treadmill or over ground can be performed with individuals at GMFCS levels I-III (with adaptations to treadmill), and with use of gait trainers for GMFCS level IV. Gait trainers, robotic gait training, and other forms of unweighting reduce the overall GRF experienced by the individual. However, this skeletal loading may be greater than usual and still be osteogenic for the individual. Adaptations and equipment used for optimizing loading with walking are shown in Table 4.

Plyometric exercises, whether seated or standing, have been shown to be safe for children with and without CP.[49-51] Plyometrics have the potential to impact bone either through skeletal loading or muscle pull on bone.[52] Standing plyometrics that focus on lower-extremity movement (jumping, box jumps, sit to stands, hopping) can provide a GRF of 2 to 8 times body weight.[44,45] Dance, particularly hip-hop moves, increases GRF up to 2 times body weight.[53] Dance can provide a fun way to improve coordination, balance, and skeletal loading. Standing lower-extremity plyometrics can be performed with individuals at GMFCS levels I-IV. Use of upper-extremity weight-bearing, gait trainers, or other devices to allow for the upright position for individuals I, II, III will decrease overall GRF but still allow for activity more osteogenic than usual (Tables 3 and 4).

Seated plyometrics and exercises—medicine ball throws, pitch back throw, overhead arm exercises, and punching the heavy bag—can provide individuals at GMFCS levels I-IV with skeletal forces through the upper extremity and trunk. There are no clinically available tools that calculate the osteogenic capacity of these activities (Table 3). However, it is most likely that these activities at high intensity and for short duration provide osteogenic activity.[52]

Standing on a vibration platform has been shown to be specific to increasing bone at the tibial plateau among those at GMFCS levels I-III. It is estimated that standing on the vibrating platform could provide 1× body weight and depending on the rate and amplitude possibly slightly more, 1.2×. Vibration platforms are also available on the bottom of tilt tables and provide

TABLE 4

Implementing Exercise

Activity	Special Equipment	Variations/Modifications
Box jumps	Boxes of various heights Parallel bars, gait trainers, walkers, crutches, and braces	Start with 2-4" box hold hands or use parallel bars Progress box as able If in gait trainer, running and jumping over box may be more effective in providing ~2× BW Evaluate ankle motion in brace and adjust if able
Overground walking	Possibly gait trainer, walker, crutches, braces	Running shuttle runs for 10-20 m may be more feasible for running If in gait trainer, running will be more effective than walking Evaluate ankle motion in brace and adjust if able
Treadmill training	Treadmill	Use of walker guide on treadmill allows use of walker or gait trainer on treadmill
Lower-extremity plyometrics	Mats, mirror, parallel bars, mini trampoline	Use of hand-held assistance as needed or parallel bars
Dance—hip-hop	Mirror, parallel bars, music	Hand-held guidance may be needed, or parallel bars
Seated or standing plyometrics	Bench, medicine ball, Theraband	Use of guidance, seat supports, manual assistance
Seated vibration	Vibrating pad on a bench	Considerations for head control with GMFCS level V
Punching heavy bag	Heavy bag; gloves	Chair with swivel seat and low back, person to guard for standing or to stabilize bag
Recumbent cycling	Recumbent bike	Can use settings for maximal speed in short bursts starting with 10 s
Leg press	Leg press machine	Calculate the 1 repetition maximum and dose at 65-85%, 6 repetitions, 6 sets
Tricycle or bicycle riding	Adapted tricycle or bike as needed	Provide opportunities for short, fast, high-resistance riding increase duration as tolerated
Whole body vibration standing	Whole body vibration platform	Can use handle for those who need assistance to stand
Robotic gait training	Exoskeletal gait trainer	For those who cannot otherwise locomote, the movement and weight-bearing are greater than usual
Aquatics	Pool, floatation devices	A variety of adaptive floatation devices exist to allow individuals to acquire the supports that allow them to be safe and have maximal movement against resistance of water, dosed at maximal aquatic heart rate

Abbreviations: BW, body weight; GMFCS, Gross Motor Function Classification System.

support for individuals at GMFCS levels IV-V. Seated vibration can be obtained using a vibration bench. There is no published evidence to support its use to change bone mineral density in the lumbar spine. Seated vibration benches hold promise for innovations in seated exercise to improve trunk musculoskeletal health.

As a non–weight-bearing activity, cycling practice is frequently associated with lower levels of bone mass. Two-thirds of the professional and master adult road cyclists could be classified as osteopenic.[54] Ground reaction force was calculated to be about 0.5× body weight for seated cycling,[55] which is less than walking. For children who are nonwalkers or walking with assistive devices for very short distances, recumbent bike cycling could provide an osteogenic stimulus, if dosed appropriately. By increasing resistance and changing the inclination of the recumbent bike, it is expected to provide larger shear forces (up to 3 N) on the distal femur to improve bone mineral density (BMD) compared with upright cycling.[56] This intervention can be implemented to improve low BMD at the distal femur.[57] Low-magnitude, high-frequency mechanical stimuli are anabolic for trabecular bone, especially in children with CP, and can stimulate high-magnitude loading (Tables 3 and 4).[58]

For individuals with little to no voluntary movement, aquatic exercise provides opportunity for supported, active assistive movement.[59] Although it is not possible to calculate the OI of the muscle pull on bone during movement in the water,[52] preliminary evidence supports the efficacy of a swim program for adults at GMFCS levels I-V to improve bone health.[60] Aquatics, dosed to target aquatic heart rate, performed 3 times a week demonstrated evidence for improving BMD in a 24-year-old individual with CP who walked with no assistive device (see Case Study in Supplemental Digital Content, available at: http://links.lww.com/PPT/A312).

DISCUSSION/CONCLUSION

Physical therapists have not aggressively addressed interventions for bone health for individuals with CP. Consumers and clinicians need to be aware of the critical importance of skeletal health and the high risk for poor bone health among individuals with CP, young as well as old, walking or not walking. Bone health should be a priority, and innovations are needed to address poor outcomes in this area.

Both researchers and clinicians should be mindful of the guiding principles for exercise and bone adaptation.[7,15,24,27,31] Researchers can identify loading thresholds for therapeutic benefit for those with different levels of impairment or osteoporosis, quantify loading of bone through muscle contraction, and create mathematical modeling for movement that provides information on osteogenic effect. Clinicians can use guiding principles of exercise for bone adaptation to individualize interventions, given person-specific needs. The description of the osteogenic characteristics of specific activities and how to implement them described previously are designed to assist with innovations in practice.

Using short, intense, frequent bouts of movement throughout the day that safely load the skeleton is a challenge for clinicians, ancillary staff, and the individuals with CP who have severe motor impairment. Physical therapists need to continue to advocate for increased opportunities for movement throughout the day for all individuals, especially individuals with difficulty moving. Working with community programs, schools, and hospitals, integrated care can better serve needs for health, wellness, and optimizing function.

Bone health can be impacted across the life span. It is important to focus on prepubescence as it is a critical period for bone growth and gains during this period are sustainable.[29,44,47,61] Duration of activities should be at least 6 months with 100 to 300 cycles of loading multiple times a day of a variety of activities.[13,29,31] Bone responses are site specific; therefore, multiple forms of activity and skeletal loading are recommended.[13,29,31] Skeletal health is foundational to health and function. Bone interventions can provide sustainable results that last a lifetime and are foundational to health.

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