Hyperbaric Oxygen Therapy Combined with Robotic Exoskeleton Assisted Walking for Cerebral Palsy

Malcolm R. Hooper
Clinical Director
OXYMED Australia ©
‘The final frontier is focussed on repair and functional restoration’
MRI pre treatment (13-03-07)

'Comparison is made with the last examination dated 10-10-05. Again demonstrating the enhancing intraspinal lesion posteriorly in the spinal canal at the level of T4-T6. It is again seen to measure 2.8cm cranio caudal and 1cm AP. The T2 imaging again shows cord atrophy with hydromyelia from T1 to at least the inferior border of the lesion'.
Classification: T4 complete
Cerebral palsy is the most common cause of pediatric neurodevelopmental and physical disability in the United States. [https://www.cdc.gov/ncbddd/cp/data.html](https://www.cdc.gov/ncbddd/cp/data.html)

There are **750,000 individuals afflicted by CP** and **11,000 children born with CP each year** in the USA (2008 census).

**Risk Factors**
1. **Low Birthweight and Premature Birth**
2. **Disruption of Blood and Oxygen Supply** to the Developing Brain.
   - Birth hypoxia has been estimated to account for less than 10% of CP cases.
3. **Infection Among Mothers**
   - Infection of the placental membranes or other signs of infection.
4. **Other Factors**
   - Birth defects of the central nervous system (brain) were found to be more common among children with CP than among those without CP.
   - Data from Metropolitan Atlanta showed that about **10% to 15% of CP was acquired** in the early years of a child’s life.
   - The most frequent causes were brain injuries from motor vehicle crashes or falls, and infections (such as meningitis).
White matter
Ventricles
Terminal branches
Middle cerebral a.

The watershed zone is the area most vulnerable when a hypoxic ischemic condition arises.

Multicystic areas
Brain cells die

Diminished blood flow and fluctuations in blood pressure lead to a state of ischemia in the watershed zone. Brain cells die without adequate blood flow.

Reduced white matter volume

Ultimately, the ischemia results in white matter that is decreased in volume due to death of brain cells.
The cost burden of Cerebral Palsy to a family

https://www.cdc.gov/ncbddd/cp/data.html

- Approximately 60% of 8-year-old children with CP had other developmental disability. More than 40% of children with CP had intellectual disability, 35% had epilepsy, and more than 15% had vision impairment.
- Nearly 1 in 4 children with CP had both intellectual disability and epilepsy.
- Nearly 50% of children with cerebral palsy also have some form of coexisting intellectual disability, such as autism or ADHD.
- Expenses related to caring for a child with CP and an intellectual disability exceeds $50,000 per year and in excess of $1M over the lifetime of the individual.
- The combined lifetime costs for all people with CP who were born in 2000 will total $11.5 billion in direct and indirect costs.

- Gross Motor Function Classification System (GMFCS Levels I – V). Individuals classified as GMFCS IV & V have the highest level of burden. Children are unable to walk with hand-held walkers due to lack of trunk, postural control, strength, range of motion and balance. These children require more supportive walkers and use of a gait trainer.
- “Increasing activity and improving participation in meaningful life activities is the major focus in current paediatric rehabilitation”. 
What about Adults?
Mobility in Ambulant Adults with Cerebral Palsy — Challenges for the Future.

March 19, 2014

Adults suffering with Lifetime Brain Injury including Cerebral Palsy suffer Multiple Co-Morbidities.

The Victorian Neurotrauma Initiative (VNI) - ‘The economic cost of persons with brain injury in Australia’ (2009)

• The lifetime cost of brain injury in 2008 alone is $10.5 billion in Australia. The largest cost is attributed to the burden of disease.

• The burden of disease includes following medical complications. 
  urinary tract infections, bacterial infections and pressure ulcers. Other complications include bladder and bowel dysfunction, circulation problems, inability to control temperature, autonomic dysreflexia, respiration difficulties, sexual dysfunction, spasms, contracture and pain (musculoskeletal and neuropathic).

• Approximately 70% of patients admitted to a hospital with a brain related injury had multiple comorbidities - more than one complication.
Robot Lokomat helps teach seven-year-old girl with cerebral palsy to walk

ABC Radio Adelaide  By Brett Williamson
Updated 10 Nov 2015, 3:53pm

PHOTO: By using a robotic physiotherapy aid, Annie Goldsmith has been able reverse some of the symptoms of cerebral palsy and learn how to walk. Physiotherapist Rosemary Nelson monitors her progress. (Supplied: Kathryn Goldsmith)
Effects of whole body vibration on muscle spasticity for people with central nervous system disorders: a systematic review.

Huang M¹, Liao LR¹,², Pang MY¹.

Abstract

OBJECTIVES: To examine the effects of whole-body vibration on spasticity among people with central nervous system disorders.

METHODS: Electronic searches were conducted using CINAHL, Cochrane Library, MEDLINE, Physiotherapy Evidence Database, PubMed, PsycINFO, SPORTDiscus and Scopus to identify randomized controlled trials that investigated the effect of whole-body vibration on spasticity among people with central nervous system disorders (last search in August 2015). The methodological quality and level of evidence were rated using the PEDro scale and guidelines set by the Oxford Centre for Evidence-Based Medicine.

RESULTS: Nine trials with totally 266 subjects (three in cerebral palsy, one in multiple sclerosis, one in spinocerebellar ataxia, and four in stroke) fulfilled all selection criteria. One study was level 1b (PEDro>6 and sample size>50) and eight were level 2b (PEDro<6 or sample size <50). All three cerebral palsy trials (level 2b) reported some beneficial effects of whole-body vibration on reducing leg muscle spasticity. Otherwise, the results revealed no consistent benefits on spasticity in other neurological conditions studied. There is little evidence that change in spasticity was related to change in functional performance. The optimal protocol could not be identified. Many reviewed studies were limited by weak methodological and reporting quality. Adverse events were minor and rare.

CONCLUSION: Whole-body vibration may be useful in reducing leg muscle spasticity in cerebral palsy but this needs to be verified by future high quality trials. There is insufficient evidence to support or refute the notion that whole-body vibration can reduce spasticity in stroke, spinocerebellar ataxia or multiple sclerosis.
Effects of Three Weeks of Whole-Body Vibration Training on Joint-Position Sense, Balance, and Gait in Children with Cerebral Palsy: A Randomized Controlled Study.

Ko MS\textsuperscript{1}, Sim YJ\textsuperscript{2}, Kim DH\textsuperscript{3}, Jeon HS\textsuperscript{4}.

\textbf{Abstract} in English, French

\textbf{Purpose}: To observe the effects of whole-body vibration (WBV) training in conjunction with conventional physical therapy (PT) on joint-position sense (JPS), balance, and gait in children with cerebral palsy (CP). \textbf{Methods}: In this randomized controlled study, 24 children with CP were randomly selected either to continue their conventional PT or to receive WBV in conjunction with their conventional PT programme. Exposure to the intervention was intermittent (3 min WBV, 3 min rest) for 20 minutes, twice weekly for 3 weeks. JPS, balance, and gait were evaluated before and after treatment. \textbf{Results}: Ankle JPS was improved after 3 weeks of WBV training ($p=0.014$). Participants in the WBV group showed greater improvements in speed ($F_{1,21}=5.221$, $p=0.035$) and step width ($F_{1,21}=4.487$, $p=0.039$) than participants in the conventional PT group. \textbf{Conclusion}: Three weeks of WBV training was effective in improving ankle JPS and gait variables in children with cerebral palsy.


Effects of whole-body vibration training on physical function, bone and muscle mass in adolescents and young adults with cerebral palsy.

Gusso S\textsuperscript{1}, Munns CF\textsuperscript{2}, Colle P\textsuperscript{3}, Derraik JC\textsuperscript{3}, Biggs JR\textsuperscript{1}, Cutfield WS\textsuperscript{1}, Hofman PL\textsuperscript{1}.

\textbf{Abstract}

We performed a clinical trial on the effects of whole-body vibration training (WBVT) on muscle function and bone health of adolescents and young adults with cerebral palsy. Forty participants (11.3-20.8 years) with mild to moderate cerebral palsy (GMFCS II-III) underwent 20-week WBVT on a vibration plate for 9 minutes/day 4 times/week at 20 Hz (without controls). Assessments included 6-minute walk test, whole-body DXA, lower leg pQCT scans, and muscle function (force plate). Twenty weeks of WBVT were associated with increased lean mass in the total body (+770 g; $p=0.0003$), trunk (+410 g; $p=0.004$), and lower limbs (+240 g; $p=0.012$). Bone mineral content increased in total body (+48 g; $p=0.0001$), lumbar spine (+2.7 g; $p=0.0003$), and lower limbs (+13 g; $p<0.0001$). Similarly, bone mineral density increased in total body (+0.008 g/cm\textsuperscript{2}; $p=0.013$), lumbar spine (+0.014 g/cm\textsuperscript{2}; $p=0.003$), and lower limbs (+0.023 g/cm\textsuperscript{2}; $p<0.0001$). Participants reduced the time taken to perform the chair test, and improved the distance walked in the 6-minute walk test by 11% and 35% for those with GMFCS II and III, respectively. WBVT was associated with increases in muscle mass and bone mass and density, and improved mobility of adolescents and young adults with cerebral palsy.
The effect of a whole-body vibration therapy on the sitting balance of subacute stroke patients: a randomized controlled trial.

Lee JH\(^1\), Kim SB\(^1\), Lee KW\(^1\), Lee SJ\(^1\), Park H\(^2\), Kim DW\(^1\).

Author information

Abstract

**BACKGROUND:** The use of a whole-body vibration (WBV) therapy has recently been applied and investigated as a rehabilitation method for subacute stroke patients.

**OBJECTIVE:** To evaluate the effects of a WBV therapy on recovery of balance in subacute stroke patients who were unable to gain sitting balance.

**METHODS:** The conventional rehabilitation group (CG) received conventional physical therapy, including sitting balance training by a physical therapist, for 30 min a one session, for twice a day for five days a week for two weeks. The whole-body vibration group (VG) received one session of conventional physical therapy, and received WBV therapy instead of conventional physical therapy for 30 min a day for five days a week for two weeks.

**RESULTS:** There were 15 patients in the CG and 15 patients in the VG who completed the two-week therapy. After the two-week therapy, both groups showed functional improvement. Patients in the VG improved functional ambulation categories, Berg balance scale, trunk impairment scale scores. But, no statistically significant correlations between the therapeutic methods and outcomes were observed in either group.

**CONCLUSION:** Our results suggest that WBV therapy led to improvement of recovery in balance recovery for subacute stroke patients. Because the WBV therapy was as effective as conventional physical therapy, we can consider a WBV therapy as a clinical method to improve the sitting balance of subacute stroke patients.
Whole Body Vibration Training Improves Walking Performance of Stroke Patients with Knee Hyperextension: A Randomized Controlled Pilot Study.


Abstract

OBJECTIVE: To investigate the effect of 8-week whole body vibration training on gait performance and lower extremity function in stroke patients with knee hyperextension.

METHODS: Total 30 subjects with stroke were randomized into the control group (n=15) or the intervention group (n=15). The patients of intervention group were treated with whole body vibration while the control group was treated with placebo. The walking function, lower limb function and knee hyperextension times were assessed in this study. Gait performances were evaluated by 10-meter walk test. The knee hyperextension times was visually observed and counted. The lower limb function was evaluated by Fugl-Meyer motor assessment.

RESULTS: The times of the knee hyperextension of the intervention group was significantly decreased compared with control groups (P=0.000, d=1.749, 95%CI[2.915,7.285]). The walking function assessed by 10-meter test of intervention group was significantly improved compared with control group (P=0.001, d=1.345, 95%CI[1.896,6.704]). The performances of all the three tests were improved after training in both groups (P=0.000/P=0.000, d=1.500/d=1.952, 95%CI[3.309,9.891]/ 95%CI[5.549,12.45]; P=0.000/P=0.000, d=2.015/d=2.952, 95%CI[5.214,11.39]/95%CI[9.423, 15.98]; P=0.000/P=0.000, d=3.537/d=5.108, 95%CI[19.05,12.35]/95%CI[16.52,22.28]).

CONCLUSION: The results suggest that 8 weeks whole body vibration training can reduce knee hyperextension and increase ambulatory speed in stroke patients.
Children with cerebral palsy suffer impaired **muscular growth and contractures**.

- **Satellite cells** are muscle stem cells critical for post-natal growth, regeneration and repair of skeletal muscles.

- Study Aim: Role of satellite cells in the development and severity of muscle contractures and its association with ability outcomes in children with CP.

- Conclusion: Loss of satellite stem cells results in increase in collagen deposition causing muscle stiffness - a result of non-use.

- Children with spastic CP have a **reduced number** of satellite stem cells.

- **Reduced satellite stem cells** results in impaired muscle growth and a decreased responsiveness of CP muscle to exercise.
Abstract

• Reduced oxygen (O₂) levels (hypoxia) are present during embryogenesis and exposure to altitude and in pathologic conditions.
• During embryogenesis, myogenic progenitor cells reside in a hypoxic microenvironment, which may regulate their activity.

Conclusion

• Satellite cells are myogenic progenitor cells suggesting that the O₂ level could affect their activity during muscle regeneration.
• Oxygen levels regulate myogenesis and muscle regeneration.
• Hypoxia impairs the regenerative capacity of injured muscles.

• Hypoxia affects satellite cell activity and myogenesis through mechanisms associated with (HIF) hypoxia-inducible factor-1α.

Horie M, Enomoto M, Shimoda M, Okawa A, Miyakawa S, Yagishita K.

Abstract

- The use of hyperbaric oxygen (HBO) treatments by elite athletes to accelerate recovery from muscle injuries has become increasingly popular.

- Study: Rats were placed in an animal chamber with 100% oxygen under 2.5 atmospheres absolute for 2 h/day, 5 days/wk for 2 wk.

- Results: The cross-sectional areas and maximum force-producing capacity of the regenerating muscle fibers were increased by HBO treatment after injury. The mRNA expression of MyoD, myogenin, and IGF-1 increased significantly in the HBO group at 3 and 5 days after injury. The number of Pax7(+)/MyoD(+), Pax7(-)/MyoD(+), and Pax7(+)/BrdU(+) positive nuclei was increased by HBO treatment.

- Conclusion: In this study, we demonstrated that HBO treatment accelerated satellite cell proliferation and myofiber maturation in rat muscle. These results suggest that HBO treatment accelerates healing and functional recovery after muscle injury.
11 CP patients were enrolled in this study, of which 4 patients underwent oxygen therapy. Before oxygen therapy and at the end of 40 sessions of oxygen treatment, SPECT was performed, and the results were compared.

RESULTS:
- 11 CP patients; 7 females and 4 males age range of 5-27 years participated in the study. In SPECT studies, all the patients showed perfusion impairments.
- The region most significantly involved was frontal lobe (54.54%), followed by temporal lobe (27.27%), occipital lobe (18.18%), visual cortex (18.18%), basal ganglia (9.09%), parietal lobe (9.09%), and the cerebellum (9.09%).
- Frontal-lobe hypoperfusion was seen in all types of cerebral palsy. Two out of 4 patients (2 males and 2 females) who underwent oxygen therapy revealed certain degree of brain perfusion improvement.

CONCLUSION:
- Study demonstrated decreased cerebral perfusion in CP patients.
- HBOT improved cerebral perfusion.
- Larger study is required to strengthen a link with other areas of neurology in which this approach may have some value.
OBJECTIVE:
- To observe the effects of hyperbaric oxygen (HBO$_2$) therapy on the treatment of sleep disorders and its safety in children with cerebral palsy (CP).

METHODS:
- A total of 71 recruited children were divided into two groups based on age: group 1, aged between 2 and 4 years; and group 2, aged between 4 and 6 years. The effects of HBO$_2$ therapy on sleep quality were observed.

DISCUSSION:
- These results indicate that HBO$_2$ therapy is beneficial to improve sleep and is safe for children with cerebral palsy, however, further studies are necessary to explore the mechanisms of HBO$_2$ on sleep.
Robotic Exoskeleton Assistive Technologies

• The patient is suspended in a harness over a treadmill and the exoskeleton frame of the robot, attached to the outside of the legs, moves the legs in a natural walking pattern.

• **Neuroplasticity mechanisms** work on the basis that by controlling the repetitive walking pattern we can help the brain and spinal cord work together to re-route signals that were interrupted by injury or illness.
• Robotics assisted walking helps to strengthen muscles and improve circulation.
• The weight bearing nature of the exercise may help strengthen bones at risk for osteoporosis due to lack of use.

Old Rehabilitation Model

• Two or more physical therapists manually move the patient’s legs in a walking pattern. However, the labor-intensive, strenuous nature and variability of the manual method can limit the frequency, quality and duration of the therapy.

• **The robotic device does the heavy work** - pattern and pace are consistent and the exercise can be sustained over longer training time.
• The effectiveness of robot-assisted walking therapy varies from person to person – typically patients undertake 3-5 sessions per week for 30-60 minutes durations over 8-12 weeks initially.

Is it an effective and financially feasible treatment?


Abstract: Growing number of adult and pediatric spinal cord injury (SCI) and traumatic brain injury (TBI) cases each year indicates an increasing need for treatment modalities, like Body Weight-Supported Treadmill Training (BWSTT) to assist functional recovery. In addition to treatment of SCI cases, BWSTT has been used for managing other various neurological diseases such as stroke and multiple sclerosis (MS), cerebral palsy and other neurodegenerative states. Robotically Gait Assisted BWSTT (Lokomat) has been shown to be more accurate and financially feasible, compared to the other BWSTT modalities. In this article, we intend to review related articles and evidence to explain the medical and financial feasibility of using this treatment modality for neurological diseases.

Keywords: locomotion, exoskeleton, locomotor training, bodyweight support, robotics

Corresponding author: Malcolm R. Hooper Director Rehabilitation HyperMED NeuroRecovery Australia 13th floor 15 Collins St Melbourne 3001. Email info@hypermed.com.au T: +61 3 9650 3136 F: +61 3 9650 3150.
Children with cerebral palsy have an acquired dysfunction which their central nervous system function deems normal. This is evident when CP children undertake an intensive Lokomat Gait Training protocol. Many of these children demonstrate a ‘normal gait’ whilst on the Lokomat which raises question of acquired neural pathways and motor function wrongly developed and reinforced over time. When these same children come off the Lokomat they immediately return back to the acquired gait. Intensity and repetition enables the CP child to generate a new functionality which resembles a ‘normal gait’. It is a frequent finding to observe the bewilderment of both parents and CP child when the child sees themselves ‘walking normal’ on the Lokomat. Visualization whilst on the Lokomat is an important paradigm shift for not only the CP child and parent but also the therapist.
Lokomat® Pro

AGRIAT'S THERAPY PLAN
3 items, 15 minutes

- Curve Pursuit
  - Duration: 5 min
- Balloon Chase
  - Duration: 5 min
- Body Weight Support
  - Duration: 5 min

Challenge Patient

Duration [min]
- 5

Orthosis Speed
- AUTO

Real Body Weight Support
- 34 kg
  - 50 %

Distance: 125 m
End Session
### END SESSION

#### REPORT SUMMARY

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**NEXT ACTIONS WITH AGRIAT:**

- LOKOMAT TRAINING
- MANUAL TRAINING
- ASSESSMENT
- REPORT

**SELECT NEXT PATIENT**

*We move you*
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The Brain That Changes Itself

Norman Doidge, MD

Stories of personal triumph from the frontiers of brain science

'A remarkable and hopeful portrait of the endless adaptability of the human brain.' OLIVER SACKS

The Brain's Way of Healing

Remarkable discoveries and recoveries from the frontiers of neuroplasticity

NORMAN DOIDGE, MD

'A lively, anecdotal account of potential new directions that may point the way to major therapeutic breakthroughs.'
— Kirkus Reviews
Neuroplasticity Activity Based Rehabilitation

Three KEY principles of motor learning.

• **Practice** is the first principle. More functional learning will occur with more 'accurate practice'.

• **Specificity** is the second principle. The best way to improve performance of a motor task is to 'execute that specific motor task repeated many times.'

• **Effort** is the third principle. Individuals need to maintain a high degree of 'focus, participation and involvement' to facilitate motor learning.

• These three principles are critical to promoting **activity-dependent plasticity** – by altering the excitation patterns of neural pathways by activating those pathways.

• Plasticity occurs in neural pathways that are both active and inactive – (penumbra state).
The field of **neurorehabilitation** is changing. After years of evidence the old, deep rooted rehabilitative principles of compensation and adaptation are slowly starting to change.

- **The adult injured central nervous system** is capable of **reorganization** allowing for significant improvement following injury.
- The reorganization and plasticity occurs: **cortical, subcortical, spinal cord, and in the peripheral nervous system.**
- The repair process is referred to as **synaptic plasticity** and occurs in pre-existing connections (peripheral and central) resulting in **sprouting and formation of new connections.**

- **Neuroplasticity** refers to the remyelination and new cell birth correcting, restoring, and replacing the damaged nerve cells.
- **Neurogenesis** reported in adult brain: **hippocampus and olfactory system.**
- Physical activity stimulates **neurogenesis** - proliferation of neuronal stem cells.
- **Activity reverses** decline in neurogenesis associated with aging. Exercise activates neighbouring axons and proliferates precursor cells.
• **Benefits of maintaining physical activity for those with disability:** cardiovascular, muscle and bone mass, longevity, cognition and quality of life but also reduces the risk of coronary heart disease, colon cancer, diabetes, and high blood pressure.

• Regular activity helps to control weight; strengthens bones, muscles, and joint; reduce falls among the elderly; reduce the pain of arthritis; reduce anxiety and depression; reduce the need for medication; reduce hospitalizations.

• **Robotic exercise** was found to have 2-fold increase in O2 uptake, 3-fold increase in ventilation rate and a five beats/min increase. Robotic exercise improves muscle and bone mass.

• **24 weeks resisted quadriceps strengthening utilizing electrical stimulation:** recovery of 30% proximal tibia bone mass and muscle strength gains. However, bone and muscle gains disappeared after ceasing the activity.

• Robotic - assisted training improves bone mineral density, muscle volume, stimulated quadriceps strength, and lowers the resting heart rate.

• **Activity based interventions** are not ‘the cure’ for paralysis but assist with the multitude of complications that ultimately increase morbidity and mortality. ABRTs are evidence-based rehabilitative interventions - **activity as a tool for neurological recovery.**
In contrast to convention: **neuronal plasticity occurs throughout life - neurogenesis, cellular apoptosis, synaptic-dependent activity and the reorganization of neuronal networks.**

- The **hippocampus** dentate gyrus is a ‘**highly plastic region**’
- The DG is the only hippocampal region able to **generate new neurons**; the DG can **double or triple** in size after physical exercise.
- Physical exercise induces **hippocampal plasticity – neurogenesis, cell proliferation and dendritic branching.**
- **BDNF** is one of the major modulators of the CNS and **brain plasticity.**
- In 1995, Neeper et al. physical exercise enhanced **BDNF gene expression in the hippocampus** in rodents.

**Other trophic factors up-regulated by physical exercise:**
- nerve growth factor (NGF),
- vascular endothelial growth factor (VEGF) and
- fibroblast growth factor 2 (FGF-2)
- Insulin Growth factors (IGFs)
• **Insulin Growth factors (IGFs)** are peptides that can be stimulated by growth hormone (GH) or act independent of GH. **IGF-1** promotes growth, differentiation and cellular survival.

• **IGF-1** is **upregulated** in specific regions of the adult brain and the **hippocampus**.

• **IGF-1** acts as a **neurotrophic factor** in the CNS and involved in **differentiation, proliferation, synaptic plasticity and neurogenesis**.

• **IGF-1** is involved in **spatial learning and memory**.

• Elevated blood **IGF-1** levels is reported with increased **neurogenesis & cognitive function**.

• **IGF-1** and BDNF pathways are upregulated between memory and physical exercise.

• **Physical exercise** and **task specific activity** requiring **hippocampus-dependent memory** expressed higher circulating levels of BDNF in the **hippocampus, cerebellum and spinal cord**.

• Ding et al. subjected rats to 5 days of voluntary physical exercise reported higher levels of hippocampal BDNF and IGF-1.

• In the same study, a group of rats was trained, but hippocampal **IGF-1R** was **blocked**. The authors demonstrated that **IGF-1R is critical for memory formation** because blocking it compromised performance in the Morris water maze when compared to mice that did not have their IGF-1 receptors blocked.

• **Resistance training** increases blood levels of IGF-1.
Angiogenesis and learning and memory

• Physical exercise, similarly to injury, is a compelling stimulant of new vessels (angiogenesis) and endothelial cell proliferation - VEGF.

• **Neurogenesis and plasticity** appear to be mediated by **IGF-1, BDNF and VEGF**.
• **Resistance training** and **aerobic exercise upregulates** IGF-1, BDNF and VEGF in the hippocampus and peripheral circulation.

• Using arterial spin labeling MRI in humans, an increase in the cortical hippocampal flow was verified in elderly individuals exposed to 4 months of aerobic exercise.
• Cerebral blood volume (CBV) in the DG was also increased in young subjects after 3 months of aerobic training.
• **Cognitive improvements** were also associated with aerobic training and increased cerebral blood volume.

• Physical conditioning increased the number of small blood vessels in elderly individuals indicating **angiogenesis**.
• In contrast sedentary individuals displayed increased numbers of **vessel tortuosity** in both brain hemispheres.
IGF-1 Increases with Hyperbaric Oxygen Therapy and Promotes Wound Healing in Diabetic Foot Ulcers

Figen Aydin, 1, 2, * Ahmet Kaya, 3 Levent Karapinar, 3 Mert Kumbaraci, 3 Ahmet Imerci, 3 Hasan Karapinar, 3 Cengiz Karakuş, 1 and Mustafa İncsesu 3

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This article has been cited by other articles in PMC.

Abstract

Objectives. To investigate insulin-like growth factor I (IGF-1) levels in response to hyperbaric oxygen therapy (HBOT) for diabetic foot ulcers and to determine whether IGF-1 is a predictive indicator of wound healing in patients with diabetic foot ulcers. Design and Methods. We treated 48 consecutive patients with diabetic foot ulcers with HBOT. Alterations of IGF-1 levels in patients whose wound healed with HBOT were compared with those in patients who did not benefit from HBOT. Results. There was no significant difference in initial IGF-1 levels between the two groups \( (P = 0.399) \). The mean IGF-1 level increased with HBOT \( (P < 0.05) \). In the healed group, the mean IGF-1 increase and the final values were significantly higher \( (P < 0.05) \). In the nonhealed group, the mean IGF-1 increase was minus and the final values were not significantly different \( (P < 0.05) \). The increase in IGF-1 level with HBOT was significantly higher in the healed group \( (P < 0.001) \). Conclusions. IGF-1 increased significantly in the healed group. We believe that HBOT is effective in the treatment of diabetic foot ulcers, with an elevation of IGF-1. This alteration seems to be a predictive factor for wound healing in diabetic foot ulcers treated with HBOT.
Training with robot-applied resistance in people with motor-incomplete spinal cord injury: Pilot study

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• Journal Rehabilitation Research & Development 2015: Almost half of all people with incomplete spinal cord injury (SCI) have some voluntary motor function below the level of injury. People with motor-incomplete SCI can recover basic walking with intensive, task-specific gait training.
• ‘Scientific evidence suggests’ that BWSTT is not better than overground gait training in SCI or other neurologic disorders. [There was debate as to whether the overground training used in this clinical trial was reflective of a realistic ‘conventional therapy’ ie BWSTT vs living with disability.]
• The results were consistent – intensive practice and task-oriented gait retraining (whether it is provided by BWSTT or overground practice) can result in improved walking outcomes.
• **Task-specific locomotor training** adopting alterations in the movement can mediate ‘**feedback-error learning**’.

• **Feedback-error learning** during walking can be used to elicit locomotor adaptations in individuals with neurologic injury including SCI.

• **Following short-term adaptation** to a **robot-applied resistance against hip flexion** the subject demonstrates a longer stride length that persist when subjects step overground immediately after walking against resistance.

• Individuals with **neurologic gait dysfunction** commonly present with diminished hip, knee and ankle flexion observed **during swing phase**, compromising foot clearance height – **toe stabbing**.

• In individuals with **chronic stroke** - 12 wk of BWSTT combined with leg weights around the paretic limb lead to **improved functional ambulation**, including the ability to climb stairs.

• 3-month training study using **robotic applied resistance** in individuals with chronic **motor-incomplete SCI** showed very promising results.

• Improvements were noted not only in **overground walking speed and distance** but also in skilled walking tasks, such as obstacle crossing and stair climbing, as well as the kinematic quality of the gait pattern.
• A major shift and focus is now on the potential efficacy of Robotic-applied resistance (Robotic-R) training on functional ambulation, overground walking with chronic m-iSCI and other neurologic disorders.

• Robotic-R was assessed using the Spinal Cord Injury-Functional Ambulation Profile (SCI-FAP): (1) 5 m carpet walk, (2) Timed “Up and Go” test, (3) 5 m obstacle-crossing task, (4) walking up and down a set of four stairs, (5) opening a door and walking through a doorway, (6) stepping up and off a 21 cm high block, and (7) walking 5 m while carrying a bag weighing 5 lb.

• Overall - The Robotic-R group showed a significantly greater improvement in the SCI-FAP at post training than the Control.

• **Robotic-R could feasibly be combined with BWSTT** in people with neurologic disability. **Robotic-R training is more intensive than standard Robotic Assisted training.** Higher training intensity would presumably affect overall gait function, including endurance.

• The ability to generalize is considered a hallmark of learning, as opposed to rote memorization. Musselman et al. compared BWSTT with an overground training program involving **practice of a variety of walking tasks, including negotiating obstacles, stairs, steps, and sloped surfaces.**

• While improvements in walking outcomes were observed after both types of training, subjects tended to show greater improvements in skilled walking following the **overground training program.**
The possibility of greater improvements in overground skilled walking combined with Robotic-R training could be indicative of task- and context-related generalization of locomotor gains.

Adaptations to Robotic applied velocity-dependent resistance include strategies that enhance swing phase initiation and foot clearance height, such as increased hamstrings and rectus femoris activity.

Variability during practice is seen as a key feature for facilitating learning because the nervous system is presented with repeated (and varied) opportunities to experience errors and solve motor problems.

Others have also suggested that variability or ‘noise’ during training helps to reinforce convergent synaptic connections from central and sensory inputs to the locomotor circuitry.

Robotic applied resistance would also have required greater engagement during training to avoid toe drag and stumbling.

Greater cognitive engagement during training elicited greater involvement of cortical regions associated with gait adjustments of motor output during swing.

Indeed, it has been shown that corticospinal excitability is tuned according to the level of cognitive engagement during gait.
• **Swing-phase deviations** are related to quadriceps spasticity, hip flexion weakness, ankle dorsiflexion weakness or spasticity, hamstring contracture, spasticity and quadriceps weakness, which will lead to inadequate knee joint flexion and extension as well as excessive knee joint flexion and extension.

• Clinical evidence shows that **task-oriented repetitive intensive movement swing-phase training** improved walking speeds, endurance and performance on functional tasks for individuals with neurologic gait disability.

• **Gait rehabilitation robots, which are precise** can quantitatively assess rehabilitation effectiveness with **high accuracy**, could yield better training outcomes than traditional physiotherapists.

• Optimal control strategy should comprise **task-specificity, repeatability, intensity and optimal physical and mental engagement**.

• **Robotic swing-assistance task-specific, intensive and non-fatigue training, can improve the locomotion ability** of the incomplete SCI patient and other neurologic gait dysfunction (cerebral palsy).
Effect of powered gait orthosis on walking in individuals with paraplegia

Mokhtar Arazpour¹, Monireh Ahmadi Bani¹, Reza Vahab Kashani¹, Farhad Tabatabai Ghomshe², Mohammad Ebrahim Mousavi¹ and Stephen William Hutchins³

Abstract
Background: The important purpose of a powered gait orthosis is to provide active joint movement for patients with spinal cord injury.
Objectives: The aim of this study was to clarify the effect of a powered gait orthosis on the kinematics and temporal-spatial parameters in paraplegics with spinal cord injury.
Study Design: Quasi-experimental.
Methods: Four spinal cord injury individuals experienced gait training with a powered gait orthosis for a minimum of 6 weeks prior to participating in the following walking trials: walking with an isocentric reciprocating gait orthosis and walking with both separate and synchronized movements with actuated orthotic hip and knee joints in a powered gait orthosis. Specific parameters were calculated and compared for each of the test conditions.
Results: Using separate and synchronized actuated movement of the hip and knee joints in the powered gait orthosis increased gait speed and step length and reduced lateral and vertical compensatory motions when compared to the isocentric reciprocating gait orthosis, but there were no significant differences in these parameters. Using the new powered gait orthosis improved knee and hip joint kinematics.
Conclusions: The powered gait orthosis increased speed and step length as well as hip and knee joint kinematics and reduced the vertical and lateral compensatory motions compared to an isocentric reciprocating gait orthosis in spinal cord injury patients.

Clinical relevance
This new powered gait orthosis has the potential to improve hip and knee joint kinematics, the temporal-spatial parameters of gait in spinal cord injury patients walking.
Comparison of a robotic-assisted gait training program with a program of functional gait training for children with cerebral palsy: design and methods of a two group randomized controlled cross-over trial

This is the first RCT comparing RAGT to an active gait-related PT intervention in paediatric CP - addresses gait-related gross motor, participation and individualized outcomes, and expected to provide comprehensive information as to the potential role of RAGT in clinical practice. Enhancement of functional ambulation is a key goal of rehabilitation for children with cerebral palsy (CP).

• Robotic-assisted gait training may permit longer training duration, faster and more variable gait speeds, and support walking pattern guidance more than overground/treadmill training to capitalize on motor learning principles.

• RCT: Children are randomly allocated to the RAGT or PT arm - twice weekly sessions for eight weeks then with cross-over to the other intervention arm following a six-week break.

• Assessments occur pre/post each intervention arm include: gross motor functional ability and 6-minute walk test; with secondary outcome measures assessing: (a) individualized goals; (b) gait variables and daily walking amounts; and (c) functional abilities, participation and quality of life.
Abstract

• **Robot-assisted gait training (RAGT)** can complement conventional therapies in children with cerebral palsy. We investigated changes in walking-related outcomes between children with different Gross Motor Function Classification System (GMFCS) levels and the dose-response relationship.

• Data from 67 children (3.9-19.9 years) with **GMFCS levels II-IV** were evaluated retrospectively. Every child received RAGT complementing a multidisciplinary rehabilitation program. Changes in various walking-related outcomes were assessed.

Results:

• Walking-related outcomes did not improve differently between GMFCS level groups. **Significant within-group improvements were mainly observed in children with GMFCS level IV.** A dose-response relationship was present for children with GMFCS levels III and IV.

Conclusions:

• Children with **GMFCS level IV walked less during an average RAGT session and experienced significant improvements in walking-related outcomes.**
Robot-enhanced therapies are increasingly being used to improve gross motor performance in patients with cerebral palsy.

- **Aim:** To evaluate gross motor function, activity and participation in patients with bilateral spastic cerebral palsy (BS-CP) after Robot-enhanced therapy.

- **Study:** Participants trained 30-60 min in each of 12 sessions within a 3-week period.
- **GMFM, walking distance, self-selected walking speed ‘Activity’ & ‘Participation’ were measured. Outcome measures were assessed three weeks in advance (V1), the day before (V2) as well as the day after (V3), and 8 weeks after training (V4).

- **Results:** 18-patients BS-CP; range: 5.0-21.8 years, GMFCS levels I-IV.

- **GMFM statistically improved for V3 (day after) and at V4 (8-weeks after), compared to V1 or V2.**

- **Conclusion:** Following Robotics - significant and clinically meaningful improvements of function in domains of "activity" and "participation" in patients with BS-CP.
Cerebral Palsy (CP) is a disorder of posture and movement. The use of robotic devices as alternative treatment to improve the gait function in patients with CP has increased. A new robotic platform CPWalker in children with spastic diplegia.

- CPWalker consists of a smart walker with body weight and autonomous locomotion support and an exoskeleton for joint motion support.
- CPWalker enables strategies to improve postural control during walking.
- Patient-tailored therapies were programmed in three children with spastic diplegia for 5 weeks.
- After ten sessions the children improved the mean velocity (51.94 ± 41.97 %), cadence (29.19 ± 33.36 %) and step length (26.49 ± 19.58 %) in each leg.
- The results show the potential of the novel robotic platform to serve as a rehabilitation tool. The autonomous locomotion and impedance control enhanced the children's participation during therapies.
- Moreover, participants' postural control was substantially improved, which indicates the usefulness of the approach based on promoting the patient's trunk control while the locomotion therapy is executed. Although results are promising, further studies with bigger sample size are required.
(d) Exoskeleton System

(c) System for the control of hip height

(b) PBWS system

(a) Drive System
Robotic-assisted gait training improves walking abilities in diplegic children with cerebral palsy.
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Abstract
The robotic-assisted gait training therapy (RAGT), based on intensity and repetition of movement, presents beneficial effects on recovery and improvement of postural and locomotor functions of the patient.

- Thirty children with bilateral spastic CP were evaluated assessing both the lower and upper limb kinematics. The children were divided into two groups in such a way as to obtain a randomized controlled population: i) a group of fourteen children (Treated Group) underwent 20 sessions of RAGT using the driven gait orthosis compared to ii) a group of sixteen children receiving only daily physiotherapy.

- Significant improvements were reported between the pre- and post-test values of i) the kinematic data of the full-body in the sagittal and frontal planes and ii) the Gross Motor Function Measure test (D and E).
- This study reports the usefulness of RAGT mainly in the balance control in gait.
- Further, the Treated Group demonstrated more appropriate control of the upper body associated with an improvement of the lower limbs kinematics.
Optimal rehabilitation should involve:

- **Active (patient) participation** in the training,
- Training that does not only involve **many repetitions**, but also **continues to challenge the skill** of the training person,
- **Resistance training**,
- **Feedback error learning** – changing and challenging environment
- **Motivation and reward**,
- **Intensive training** and practice over a long time,
- Combination training in relation to other **overground training activities**, and
- Incorporation of other potentially beneficial parameters such as **sleep and diet**.

- ‘Learn to walk by learning not to fall’ concept
NeuroRehab improvements in the Personal Robotic Exoskeletons

• Originally passive assist - guide the lower limbs of patients applying **pre-programmed physiological gait patterns in the hip and knee joints**.

• Today and emerging - new powered gait orthosis featuring programmable **variable assist** movements in the hip and knee joints enabling independent training and neurorehabilitation in a clinical environment and at home.
June 6, 2017 in Industry: *Interview with Fourier Intelligence at WearRAcon17 – An ExR Exclusive Report*
Soft Exosuits

- **Lightweight Exosuits** are a new class of **soft robots** that combine classical robotic design and control principles with functional apparel to increase the wearer’s strength, balance and endurance.
- **Soft Exosuits** offer a new way to assist the elderly in maintaining or restoring their gait, in **rehabilitating children and adults with movement disorders** due to Stroke, Multiple Sclerosis and Parkinson’s Disease, or to **ease the physical burden of soldiers, firefighters, paramedics, farmers and others whose jobs require them to carry extremely heavy loads.**
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Usain Bolt