Neurodisorders Congress 2018
16-17 July 2018, Melbourne, Australia

Malcolm R. Hooper

OXYMED Australia

Hyperbaric Oxygen Therapy

combined with **LOKOMAT**
(Robotic Exoskeleton Walking) assisting Neuroplasticity in Brain and Spinal Cord disabilities

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MALCOLM R. HOOPER

- OXYMED Australia (HyperMED). Over the past twenty-five years, he gained international renown for providing the wider ‘off-label’ applications of Hyperbaric Oxygenation.
- In 1983, Hooper’s humble beginnings were as a chiropractor including Masters App Sci. Hooper established the multidisciplinary clinic known as Spinal Rehabilitation Group, integrating orthodox medical and allied treatment approaches.
- Then, in 1993, tragedy struck when their 18-month old daughter fell into a smouldering ash fire and suffered third degree burns. It was during this period he became acquainted with the use of Hyperbaric Oxygen for treating burns and other neurologic disorders.
- In 1996, Hooper incorporated the use of Hyperbaric Oxygen into the multidisciplinary rehabilitation model with focus on orthopaedic and neurologic disorders. The reputation of the clinic grew, especially in 1999 when a quadriplegic patient gained significant functional changes. This was a remarkable breakthrough as this individual was 6-years post injury and classified as “C7 complete”.
- This took Hooper on the path of utilising Body Weight Support innovations to promote the evergreen concept of ‘neuroplasticity’. **In 2006, he introduced Australia’s first LOKOMAT – Adult and Paediatric Robotic Gaited Assisted Walking Machine. The pioneering applications of HBOT and Lokomat – a ‘world first’**.
- **Hyperbaric Oxygen Therapy enhances stem cell mobilisation and epigenetic modulation. The ‘penumbra state’ describes cells and neural pathways in a ‘dormant’ low metabolic state due to hypoxia. The effects of HBOT combined with LOKOMAT repetitive gait assisted movement enhances neuroplasticity and functional changes**.
- In Australia, Hyperbaric Oxygen Therapy and LOKOMAT are viewed as “novel and unique”. Hooper has not practiced as a “traditional chiropractor” for over 25 years.
- An International Executive Board Member serving both the International Hyperbaric Medical Foundation (IHMF) & International Hyperbaric Medical Association (IHMA).

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Stem Cell mobilization and HBOT (2005)

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Am J Physiol Heart Circ Physiol. 2006 Apr;290(4):H1378-86. Epub 2005 Nov 18.

Stem cell mobilization by hyperbaric oxygen.

Thom SR[1], Bhopale VM, Velazquez OC, Goldstein LJ, Thom LH, Buerk DG.

Author information

Abstract

We hypothesized that exposure to hyperbaric oxygen (HBO(2)) would mobilize stem/progenitor cells from the bone marrow by a nitric oxide (*NO) -dependent mechanism. The population of CD34(+) cells in the peripheral circulation of humans doubled in response to a single exposure to 2.0 atmospheres absolute (ATA) O(2) for 2 h. Over a course of 20 treatments, circulating CD34(+) cells increased eightfold, although the overall circulating white cell count was not significantly increased. The number of colony-forming cells (CFCs) increased from 16 +/- 2 to 26 +/- 3 CFCs/100,000 monocytes plated. Elevations in CFCs were entirely due to the CD34(+) subpopulation, but increased cell growth only occurred in samples obtained immediately posttreatment. A high proportion of progeny cells express receptors for vascular endothelial growth factor-2 and for stromal-derived growth factor. In mice, HBO(2) increased circulating stem cell factor by 50%, increased the number of circulating cells expressing stem cell antigen-1 and CD34 by 3.4-fold, and doubled the number of CFCs. Bone marrow *NO concentration increased by 1,008 +/- 255 nM in association with HBO(2). Stem cell mobilization did not occur in knockout mice lacking genes for endothelial *NO synthase. Moreover, pretreatment of wild-type mice with a *NO synthase inhibitor prevented the HBO(2)-induced elevation in stem cell factor and circulating stem cells. We conclude that HBO(2) mobilizes stem/progenitor cells by stimulating *NO synthesis.

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Case Study – T4 complete

Young Isabel has never walked.

At 8-months age Isabel, was operated on for a benign tumour resulting in her becoming a ‘T4 complete paraplegic’.

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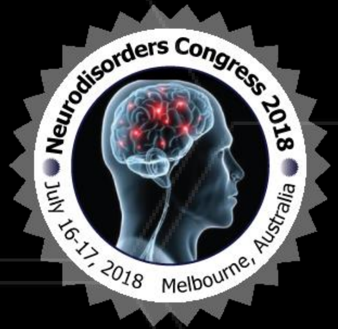
Syringomyelia, cord atrophy

MRI 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”.



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Chanel 7 News

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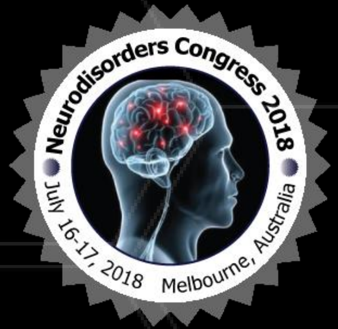
4 months after intensive HBOT & LOKOMAT



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Case Study – T12 Spinal Cord Injury

Kyle was told he would "never walk again".

Now Kyle is walking limited distance with calipers.

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Have to love his attitude

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Case Study – Stroke Victim

Marco - massive arteriovenous malformation

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Case Study – Drowning Victim

Young Chloe – near drowning victim.

Chloe on the LOKOMAT

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Case Study – Cerebral Palsy

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Case Study – C3/4 Quadriplegia

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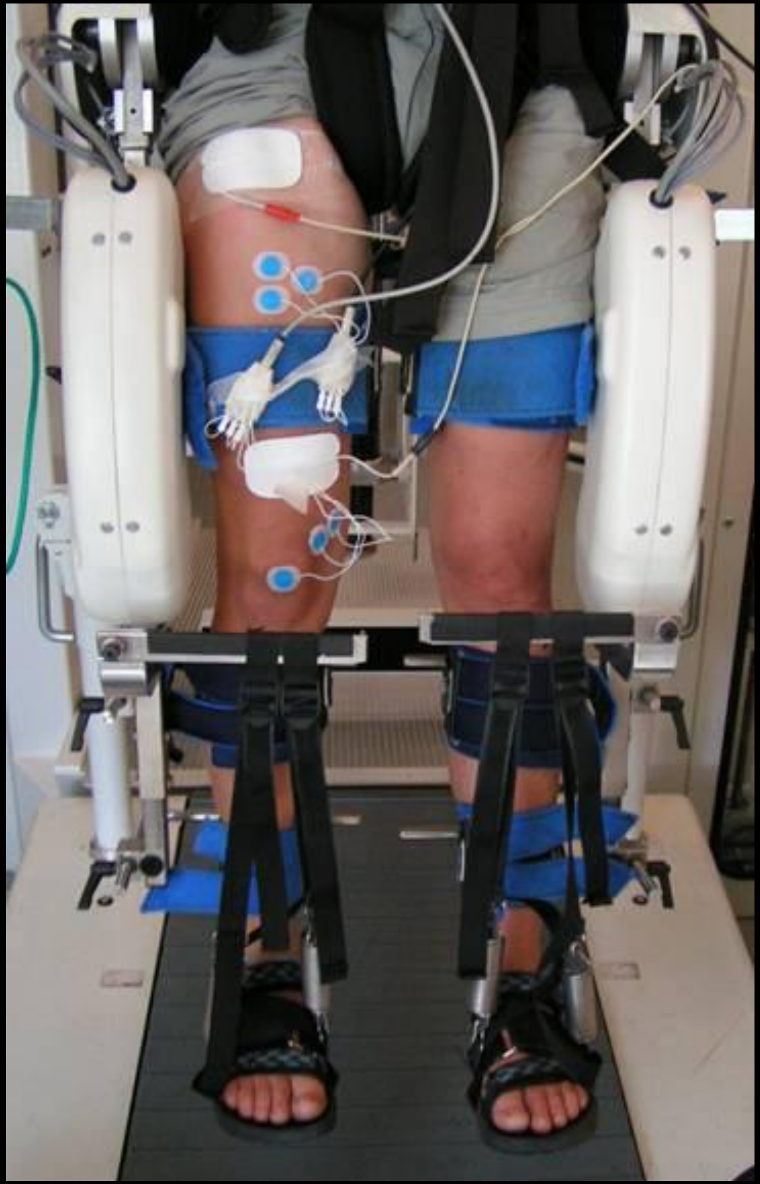
How to work with spasticity



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Old Rehabilitation Model

Robotic Exoskeleton Assisted Walking

OLD REHABILITATION MODEL - "Living and coping with disability"

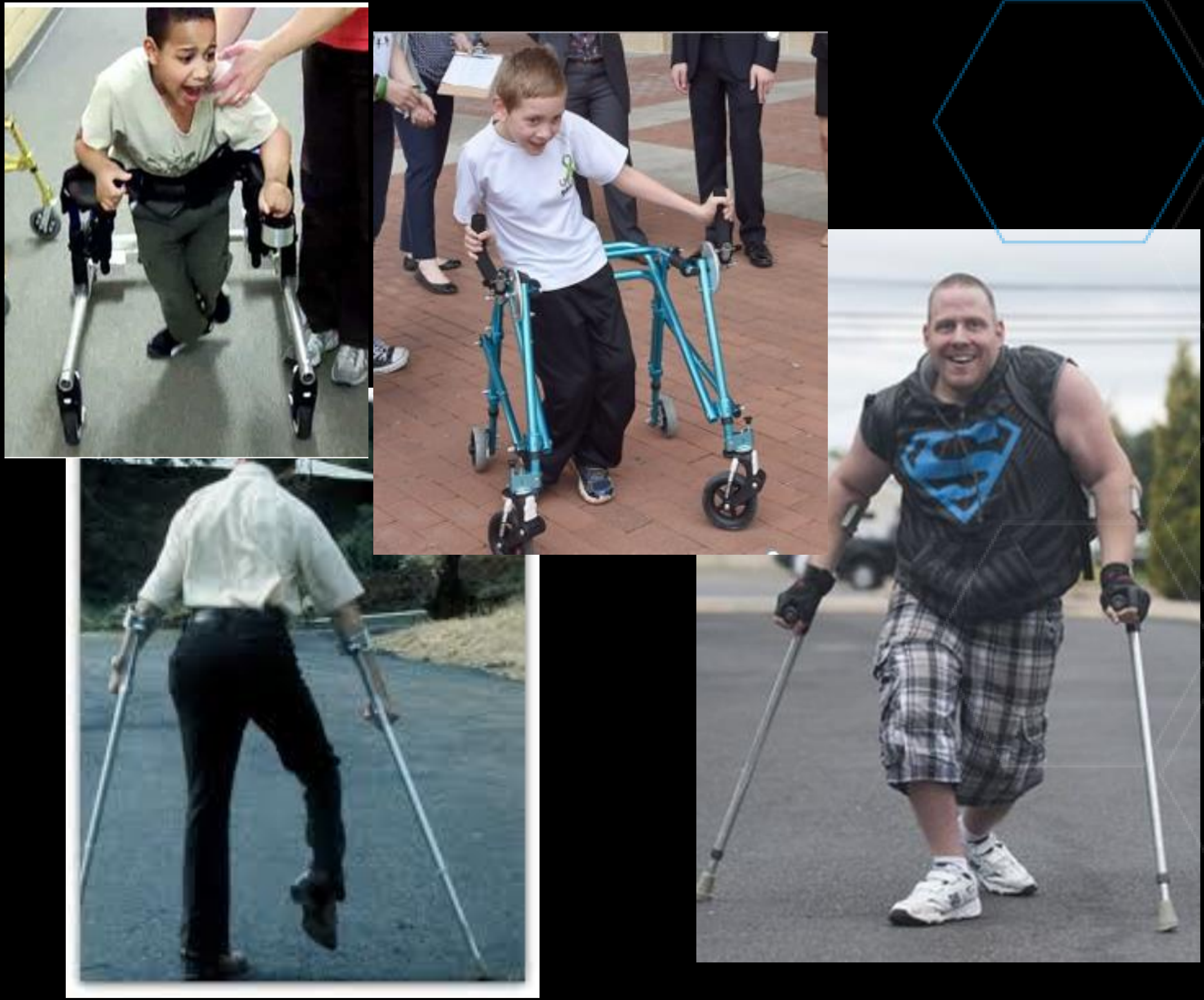
BODY WEIGHT SUPPORT TREADMILL TRAINING

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

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 robotic device does the heavy work** - pattern and pace are consistent and the exercise can be sustained over longer training time.
- Typically patients undertake 3-5 sessions per week for 30-60 minutes durations over 8-12 weeks initially.

Acquired negative neuroplasticity



Hypoxic Ischemic Encephalopathy (HIE)

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Hypoxic Ischemic Encephalopathy (HIE)

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Hypoxic Ischemic Encephalopathy (HIE)

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Hypoxic Ischemic Encephalopathy (HIE)

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Periventricular Leukomalacia (PVL)

Hypoxic Ischemic Encephalopathy (HIE)

Periventricular Leukomalacia (PVL)

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C5/6 Spinal Cord Ischemia

Whole Body Vibration

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WBV – spasticity, bone density

Clin Rehabil. 2017 Jan;31(1):23-33. doi: 10.1177/0269215515621117. Epub 2016 Jul 11.

Effects of whole body vibration on muscle spasticity for people with central nervous system disorders: a systematic review.

Huang M[1], Liao LR[1,2], Pang MY[1].

Author information

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.

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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)

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Neurodegenerative disorders

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Neurorecovery ‘gymnasiums’

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Monorail Walking

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Spasticity issues – prime with WBV

Clin Rehabil. 2017 Jan;31(1):23-33. doi: 10.1177/0269215515621117. Epub 2016 Jul 11.

Effects of whole body vibration on muscle spasticity for people with central nervous system disorders: a systematic review.

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Joint position, balance, joint sense

Physiother Can. 2016;68(2):99-105.

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[1], Sim YJ[2], Kim DH[3], Jeon HS[4].

⊕ Author information

Abstract in **English**, French

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). ***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. ***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. ***Conclusion:*** Three weeks of WBV training was effective in improving ankle JPS and gait variables in children with

Bone density, muscle mass

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Sci Rep. 2016 Mar 3;6:22518. doi: 10.1038/srep22518.

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

Gusso S[1], Munns CF[2], Colle P[1], Derraik JG[1], Biggs JB[1], Cutfield WS[1], Hofman PL[1].

⊕ Author information

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(2); $p = 0.013$), lumbar spine (+0.014 g/cm(2); $p = 0.003$), and lower limbs (+0.023 g/cm(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.

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Sitting balance & coordination

Top Stroke Rehabil. 2017 Mar 23:1-6. doi: 10.1080/10749357.2017.1305655. [Epub ahead of print]

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 the 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 stoke patients.

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Gait improvement, knee extension control

CNS Neurol Disord Drug Targets. 2015;14(9):1110-5.

Whole Body Vibration Training Improves Walking Performance of Stroke Patients with Knee Hyperextension: A Randomized Controlled Pilot Study.

Guo C, Mi X, Liu S, Yi W, Gong C, Zhu L, Machado S, Yuan TF, Shan C[1].

Author information

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.

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Contracture, spasticity - reduction of Satellite Cells

J Orthop Res. 2015 Jul;33(7):1039-45. doi: 10.1002/jor.22860. Epub 2015 Apr 10.

Reduced satellite cell number in situ in muscular contractures from children with cerebral palsy.

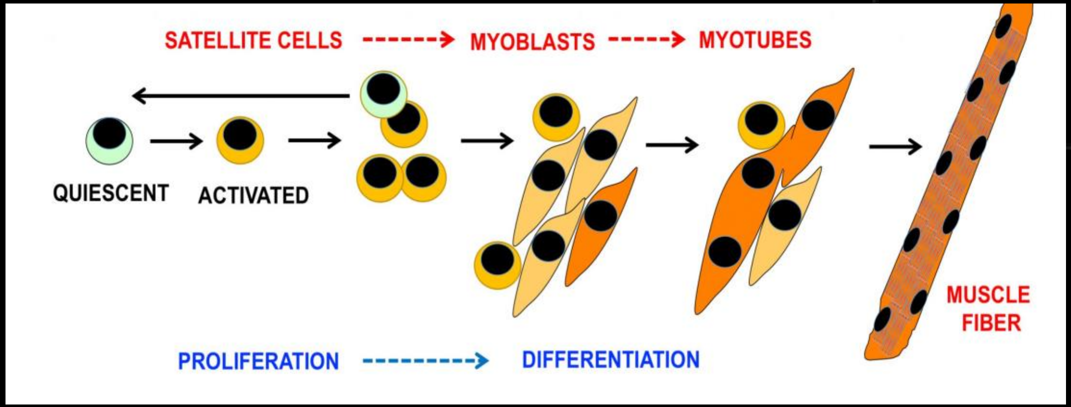
Dayanidhi S[1,2], Dykstra PB[1], Lyubasyuk V[1], McKay BR[3], Chambers HG[1,4], Lieber RL[1,2,5].

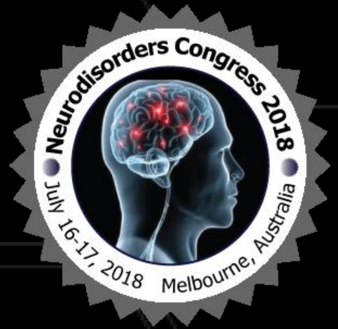
Children with cerebral palsy suffer impaired muscular growth and contractures.

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

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.





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Oxygen, Hypoxia and Satellite Cells

FASEB J. 2016 Dec;30(12):3929-3941. Epub 2016 Sep 6.

Regulation of myogenesis and skeletal muscle regeneration: effects of oxygen levels on satellite cell activity.

Conclusion:

- **Satellite cells are myogenic progenitor cells.**
- Oxygen levels regulate myogenesis and muscle regeneration.
- Hypoxia impairs the regenerative capacity of injured muscles.
- **Hypoxia impairs satellite cell activity and myogenesis through mechanisms associated with (HIF) hypoxia-inducible factor-1α.**

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HBOT increases satellite cell differentiation

J Appl Physiol (1985). 2014 Jan 15;116(2):149-55. doi: 10.1152/japplphysiol.00235.2013. Epub 2013 Dec 12.

Enhancement of satellite cell differentiation and functional recovery in injured skeletal muscle by hyperbaric oxygen treatment.

Horie M[1], 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:

- HBO treatment **accelerated satellite cell proliferation and myofiber maturation** in rat muscle.
- HBO treatment **accelerates healing and functional recovery** after muscle injury.

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SPECT Hypoperfusion Cerebral Palsy

Int J Clin Exp Med. 2015 Jan 15;8(1):1101-7. eCollection 2015.

99mTc-ECD brain perfusion SPECT imaging for the assessment of brain perfusion in cerebral palsy (CP) patients with evaluation of the effect of hyperbaric oxygen therapy.

Asl MT[1], Yousefi F[2], Nemati R[2], Assadi M[3].

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.
- 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.

CONCLUSION:

- Study demonstrated decreased cerebral perfusion in CP patients.
- Two out of 4 patients (2 males and 2 females) who underwent oxygen therapy revealed brain perfusion improvement. HBOT improved cerebral perfusion.
- Larger study is required to strengthen a link this approach may have some value.

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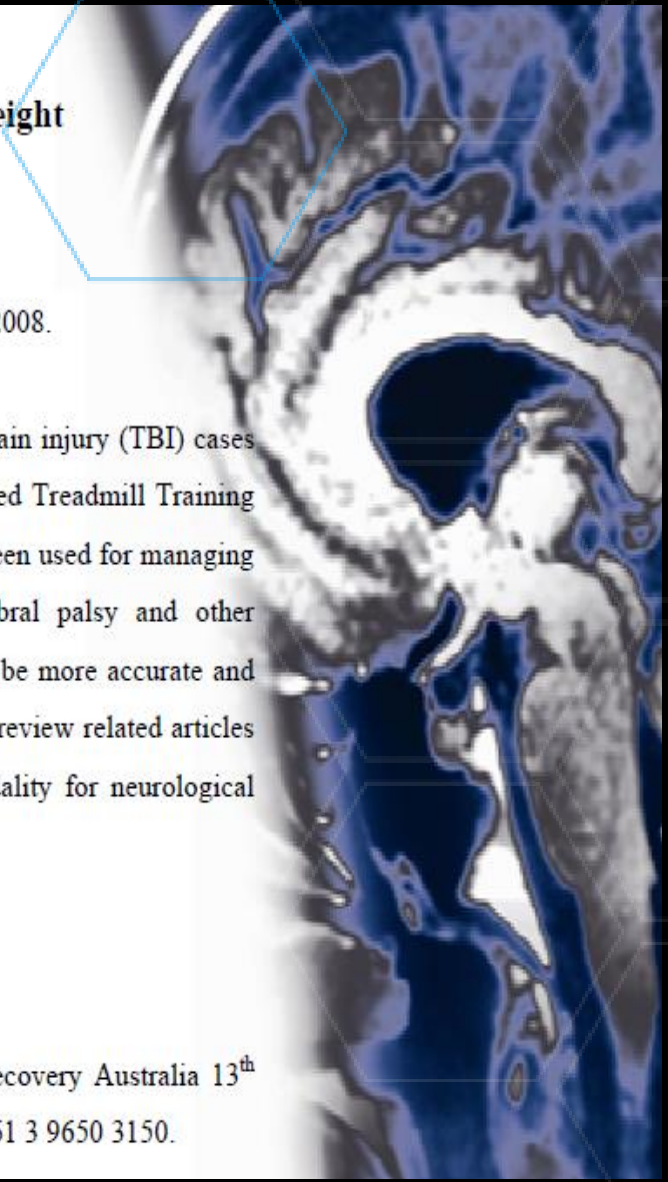
LOKOMAT - Australia experience



LOKOMAT Australian Experience: Robotically Gait Assisted Body Weight Support Treadmill Training (BWSTT) – Lokomat Gait Training.

Is it an effective and financially feasible treatment?

HyperMED NeuroRecovery Centre – Melbourne, Australia. M. R. Hooper, T. Chamacham 2008.

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.

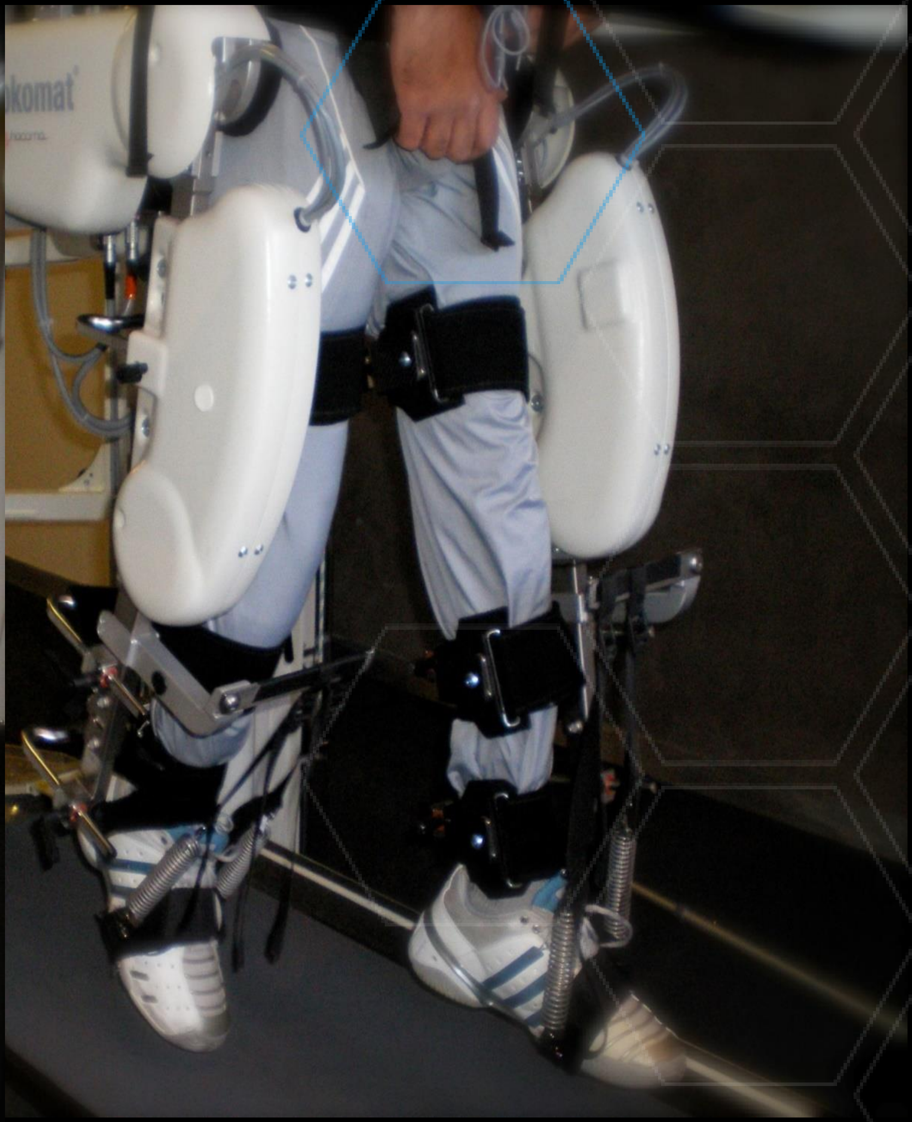
Keywords: locomotion, exoskeleton, locomotor training, bodyweight support, robotics

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.

Figure 3: HyperMED cerebral palsy patients on Pediatric Lokomat [43]

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.

Robotic assisted fluidity – matching the patient



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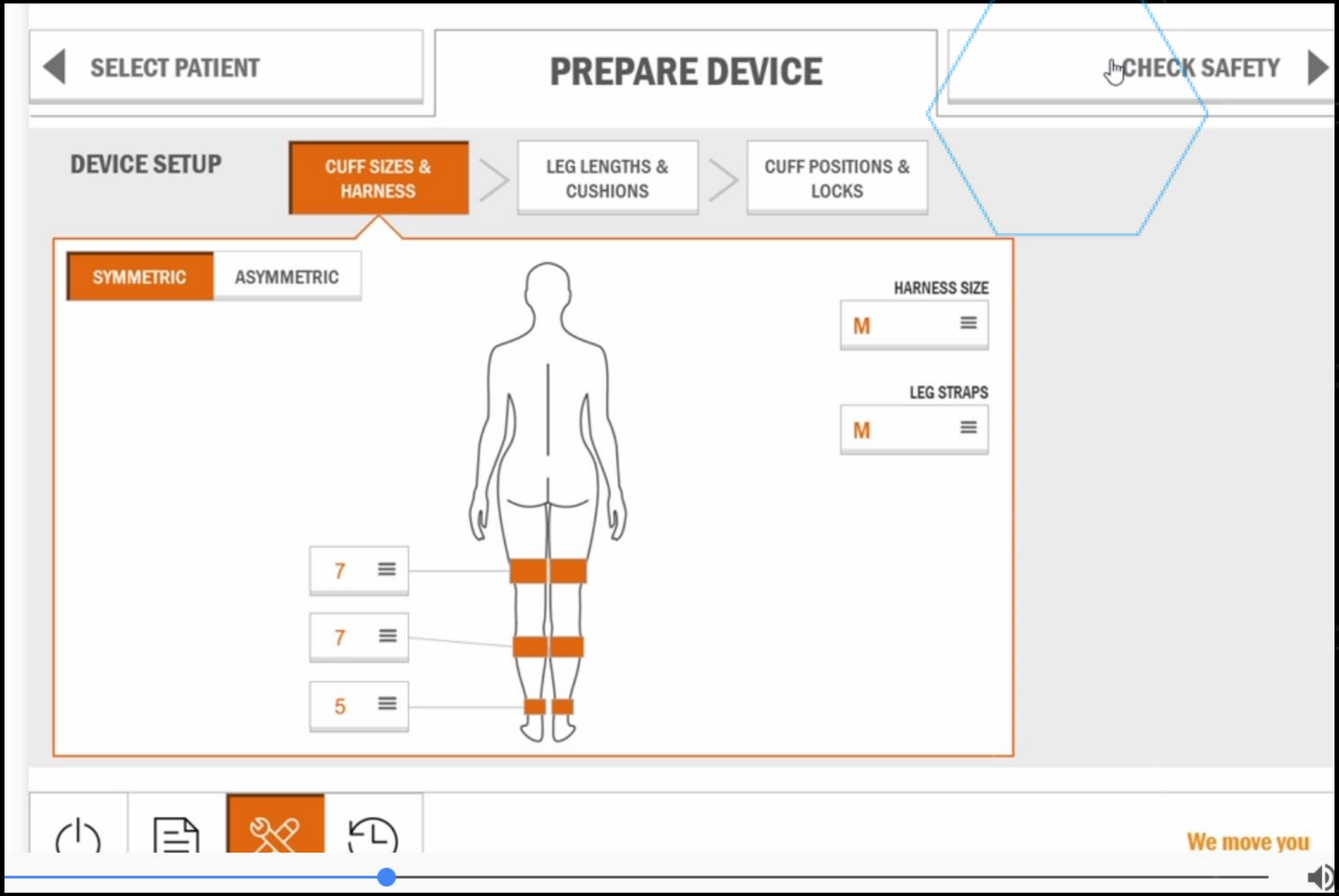
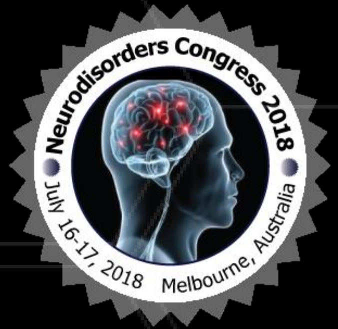
LOKOMAT settings





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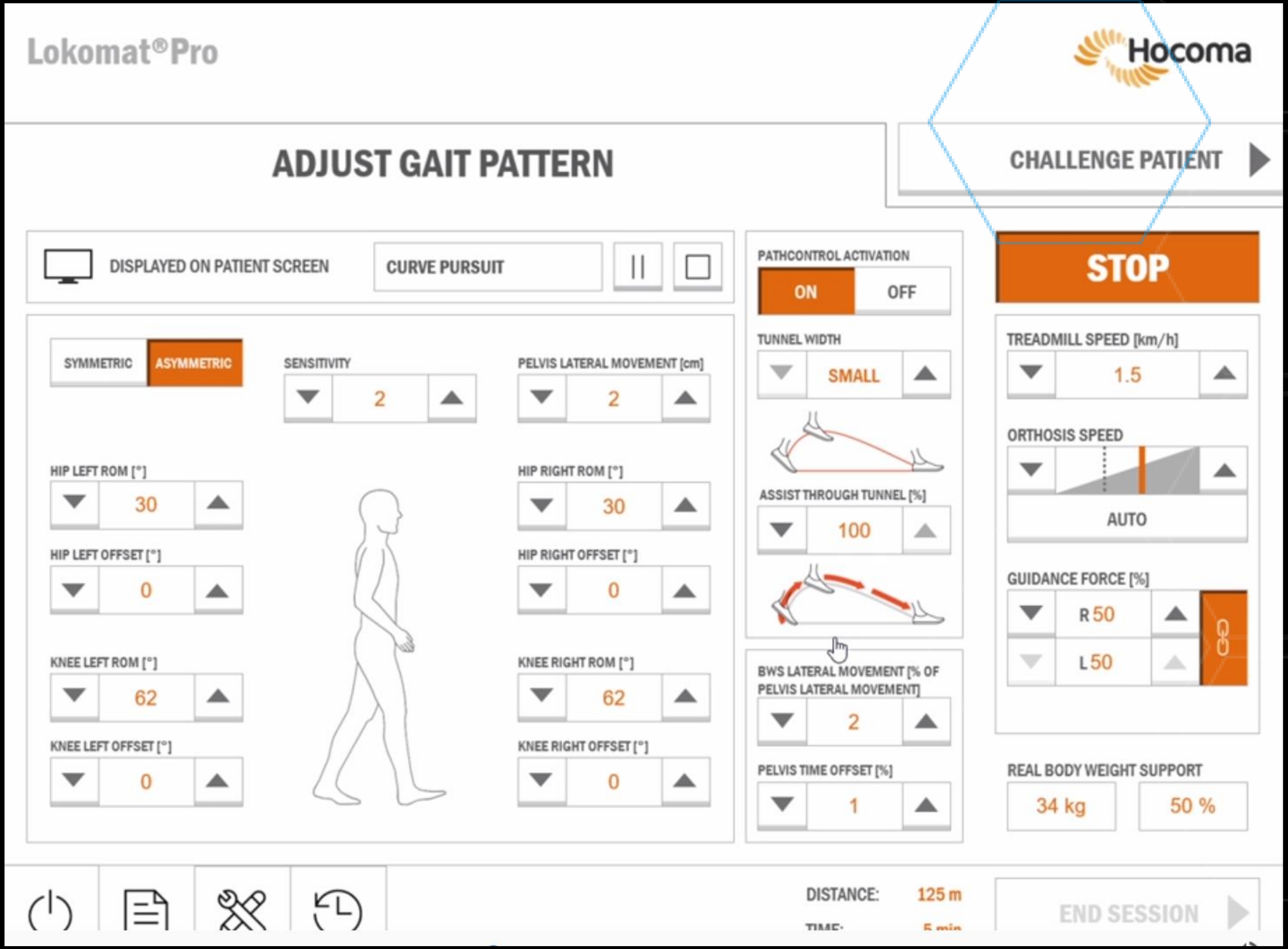
Gait Pattern



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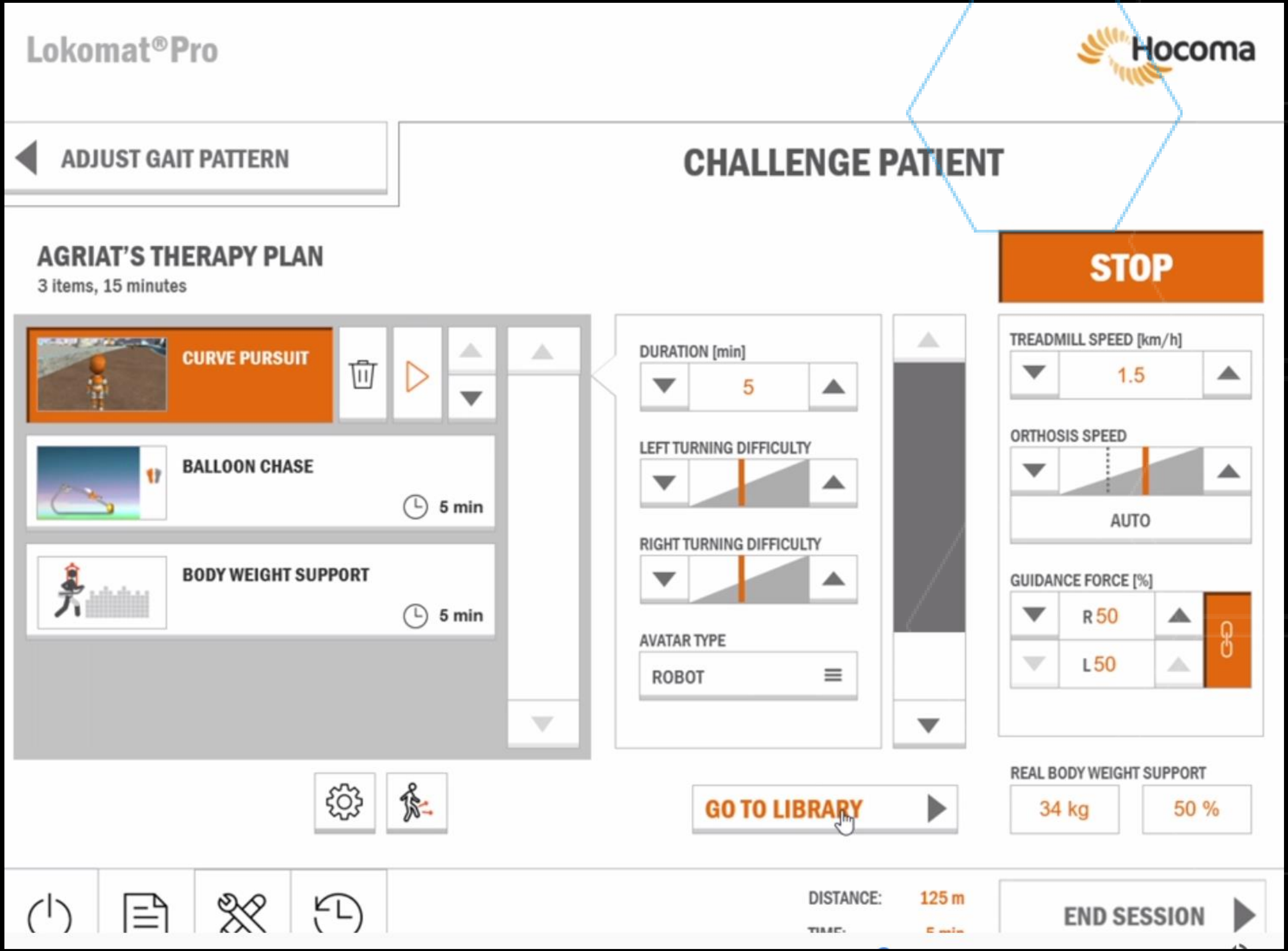
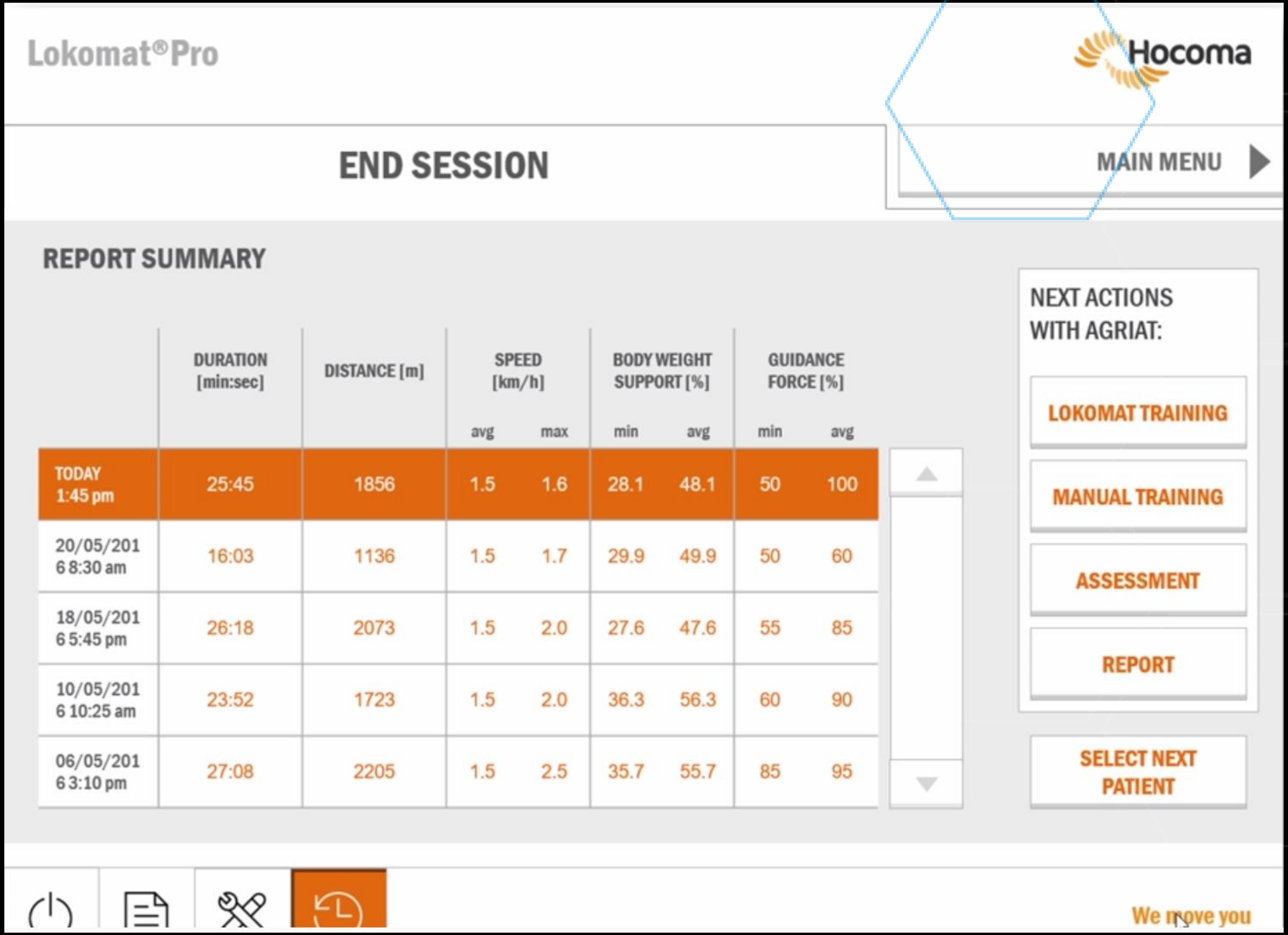
Patient challenge programs



Tracking



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Hocoma

END SESSION

MAIN MENU

REPORT SUMMARY

	DURATION [min:sec]	DISTANCE [m]	SPEED [km/h]		BODY WEIGHT SUPPORT [%]		GUIDANCE FORCE [%]	
			avg	max	min	avg	min	avg
TODAY 1:45 pm	25:45	1856	1.5	1.6	28.1	48.1	50	100
20/05/2016 8:30 am	16:03	1136	1.5	1.7	29.9	49.9	50	60
18/05/2016 5:45 pm	26:18	2073	1.5	2.0	27.6	47.6	55	85
10/05/2016 10:25 am	23:52	1723	1.5	2.0	36.3	56.3	60	90
06/05/2016 3:10 pm	27:08	2205	1.5	2.5	35.7	55.7	85	95

NEXT ACTIONS WITH AGRIAT:

LOKOMAT TRAINING

MANUAL TRAINING

ASSESSMENT

REPORT

SELECT NEXT PATIENT

We move you

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Comparison

END SESSION

	TODAY	OVERALL
	10’265 steps	49’497 steps
	1865 m	8993 m
	26 min	119 min

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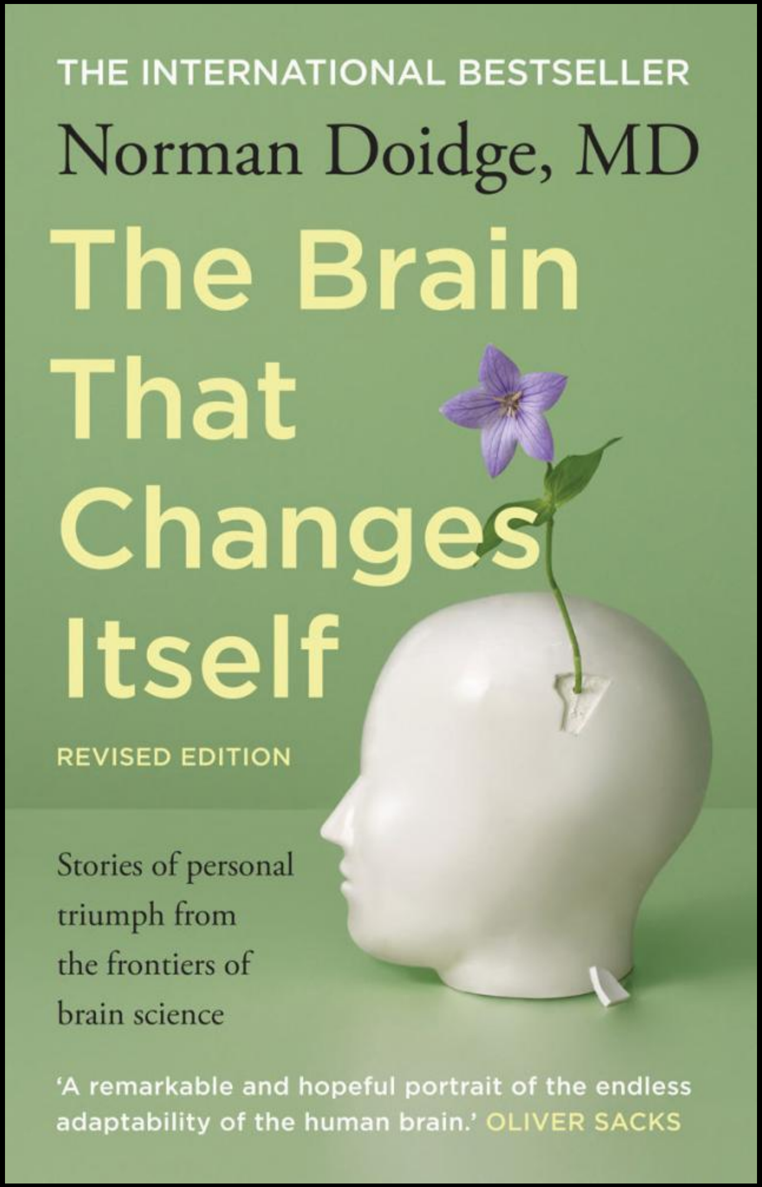
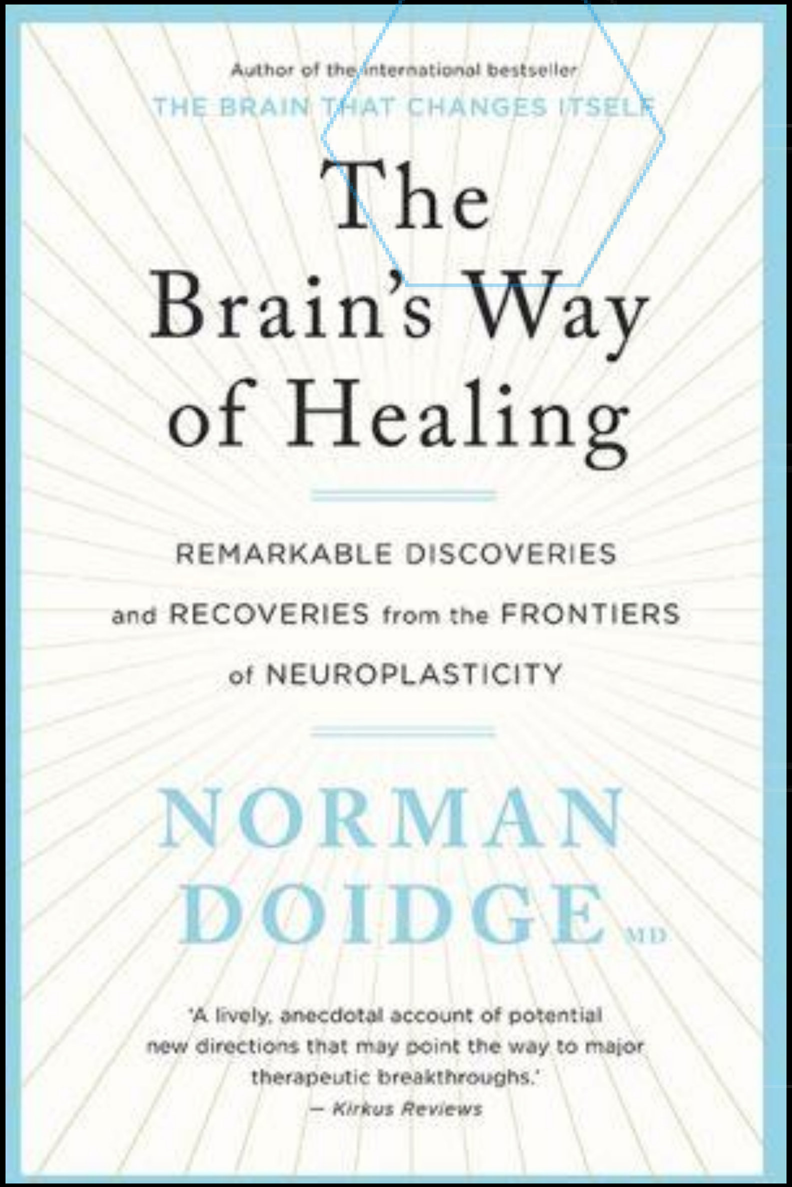
Dr Norman Doidge - neuroplasticity





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Practise makes perfect

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Work with your patient

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As opposed to working against your patient

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Neuroplasticity finds a way

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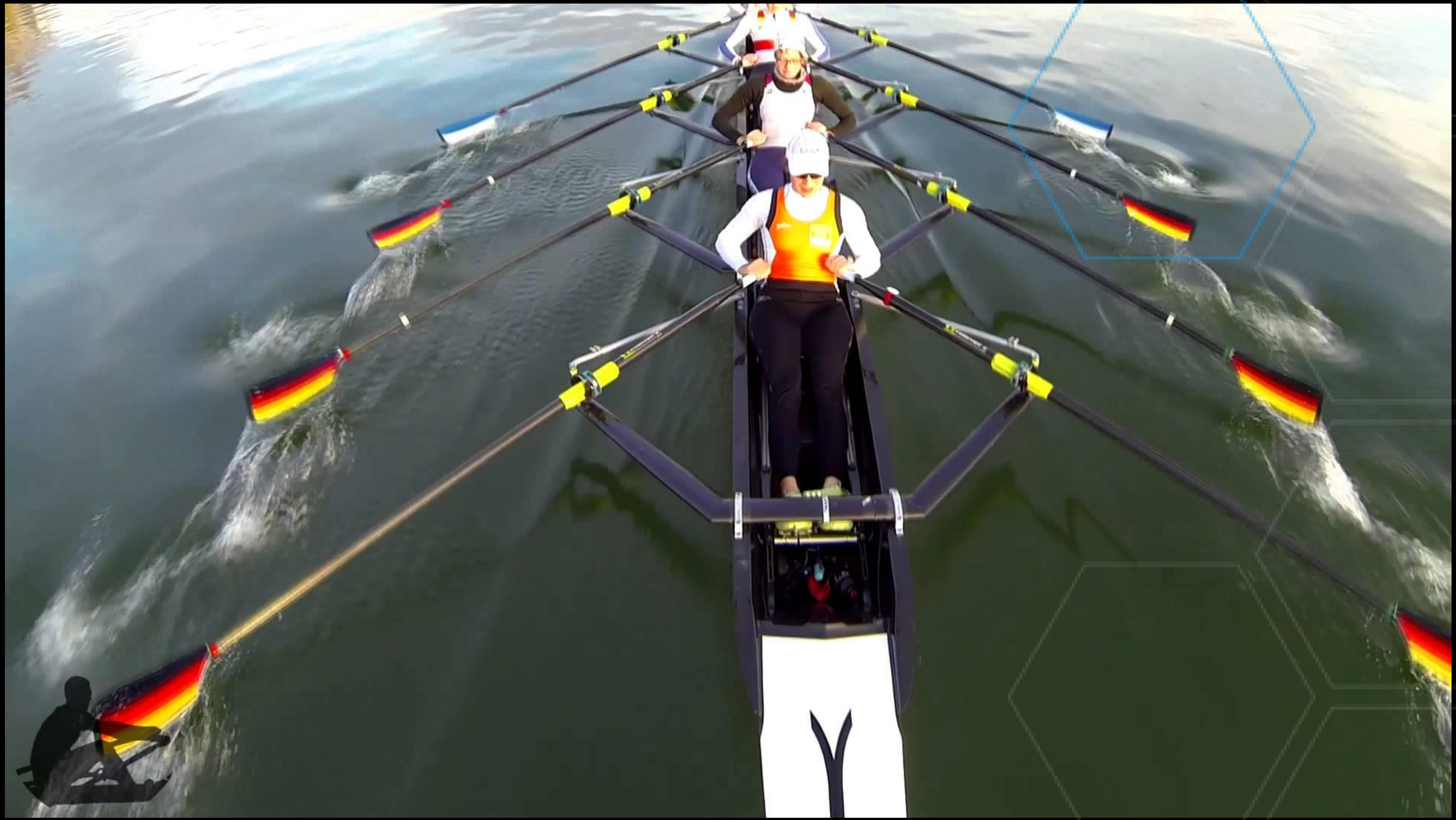
Neuroplasticity recruitment with purpose



Hard work is required by therapist and patient

Neuroplasticity - Activity Based Rehabilitation

THREE KEY PRINCIPLES OF MOTOR LEARNING -

1. Practice

- More functional learning will occur with more 'accurate practice'.

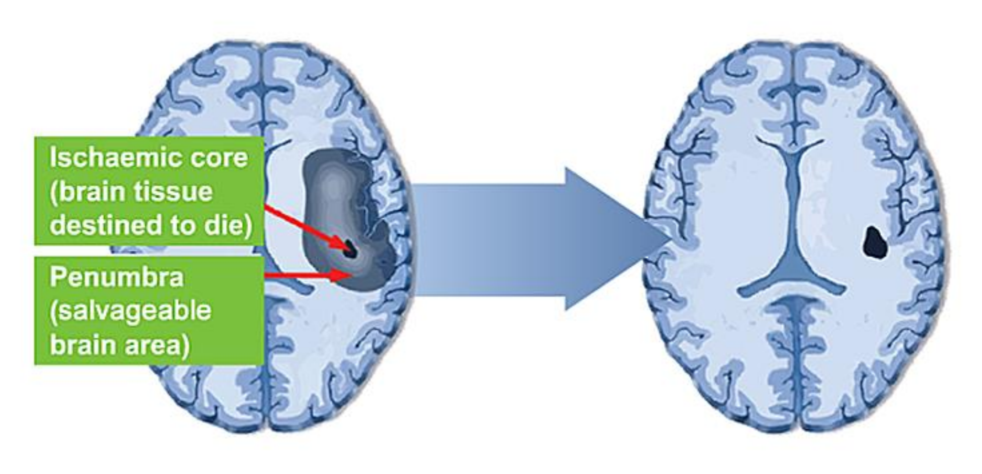
2. Specificity

- The best way to improve performance of a motor task is to 'execute that specific motor task repeated many times.'

3. Effort

- Individuals need to maintain a high degree of 'focus, participation and involvement' to facilitate motor learning – not watching "days of our lives" and taking another 'generic' tablet.

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.



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Activity stimulates plasticity, neurogenesis

Dev Disabil Res Rev. 2009;15(2):112-6. doi: 10.1002/ddrr.61.

Activity-based restorative therapies: concepts and applications in spinal cord injury-related neurorehabilitation.

Sadowsky CL[1], McDonald JW.

- 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.**
- **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.

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Neural Plasticity occurs through life

Cell Mol Life Sci. 2016 Mar;73(5):975-83. doi: 10.1007/s00018-015-2102-0. Epub 2015 Dec 8.

Physical exercise, neuroplasticity, spatial learning and memory.

Cassilhas RC[1,2], Tufik S[3], de Mello MT[4].

NEURONAL PLASTICITY OCCURS THROUGHOUT LIFE

- **neurogenesis, synaptic-dependent activity and the reorganization of neuronal networks**.

The hippocampus dentate gyrus is a '**highly plastic region**' able to **generate new neurons**, and can **double or triple in size** after physical exercise.

Physical exercise induces hippocampal plasticity – **neurogenesis, cell proliferation and dendritic branching.**

Brain Derived Neurotrophic Factor (BDNF) is one of the major modulators of the CNS and brain plasticity. In 1995, Neeper et al. demonstrated that physical exercise enhanced **BDNF gene expression in the hippocampus**.

NEUROTROPHIC FACTORS UP-REGULATED BY PHYSICAL EXERCISE

- Nerve Growth Factor (NGF), Vascular Endothelial Growth Factor (VEGF), Fibroblast Growth Factor 2 (FGF-2), BDNF and Insulin Growth Factors (IGFs)

Insulin Growth Factor (IgF1) - promotes **growth, differentiation and cellular survival**. Is upregulated in the hippocampus. Has neurotrophic effects in the CNS and involved in **differentiation, proliferation, synaptic plasticity and neurogenesis**. IgF1 is increased in **neurogenesis & cognitive function**.

- Physical exercise and task specific activity requiring **hippocampus-dependent memory expressed** higher circulating levels of **IgF1 and BDNF** in the **hippocampus, cerebellum and spinal cord**.

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Angiogenesis, learning & 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 was verified in elderly individuals exposed to 4 months of aerobic exercise. **cortical hippocampal flow**
- **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.**

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Robotic resistance vs Over ground walking

JRRD
Volume 52, Number 1, 2015
Pages 113–130

Training with robot-applied resistance in people with motor-incomplete spinal cord injury: Pilot study

Tania Lam, PhD;[1–2*] Katherine Pauhl, MSc;[1–2] Amanda Ferguson, BScPT;[3] Raza N. Malik, BKin;[1–2] Andrei Krassioukov, MD, PhD;[2,4–5] Janice J. Eng, PhD[2,5–6]
[1]School of Kinesiology and [2]International Collaboration on Repair Discoveries, University of British Columbia, Vancouver, British Columbia, Canada; [3]NeuroMotion Physical Therapy, Vancouver, British Columbia, Canada; [4]Department of Medicine, Division of Physical Medicine and Rehabilitation, University of British Columbia, Vancouver, British Columbia, Canada; [5]GF Strong Rehabilitation Centre, Vancouver, British Columbia, Canada [6]Department of Physical Therapy, University of British Columbia, Vancouver, British Columbia, Canada

- **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**.

- 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.

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Resistance & “Noise”

- 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**.
- **Short-term adaptation** to **robot-applied resistance against hip flexion** demonstrates a longer stride length that persists overground immediately after walking against resistance.
- Diminished hip, knee and ankle flexion observed **during swing phase**, compromising foot clearance height – **toe stabbing**.
- Improvements in **overground walking speed** and distance but also in **skilled walking tasks, obstacle crossing and stair climbing, as well as the kinematic quality of the gait pattern.**
- **Variability during practice** is seen as a key feature for facilitating learning - **repeated (and varied) opportunities to experience errors and solve motor problems**.
- **Variability** or **‘noise’** during training helps to reinforce **convergent synaptic connections** from central and sensory inputs to the locomotor circuitry. (Learning not to fall).
- **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 training and resistance.**

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Robotic accuracy & repetition

A patient-specific muscle force estimation model for the potential use of human-inspired swing-assist rehabilitation robots

Ye Ma, Shengquan Xie & Yanxin Zhang

Pages 948-964 | Received 13 Feb 2016, Accepted 27 Mar 2016, Published online: 22 Apr 2016

GAIT REHABILITATION ROBOTS, WHICH ARE PRECISE

- **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,** 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.**

Robotic Exoskeletons assisting neurodevelopment disorders

Eur J Paediatr Neurol. 2014 Jul;18(4):502-10. doi: 10.1016/j.ejpn.2014.04.012. Epub 2014 Apr 25.

Prospective controlled cohort study to evaluate changes of function, activity and participation in patients with bilateral spastic cerebral palsy after Robot-enhanced repetitive treadmill therapy.

Schroeder AS[1], Homburg M[2], Warken B[2], Auffermann H[2], Koerte I[3], Berweck S[4], Jahn K[5], Heinen F[2], Borggraefe I[6].

Springerplus. 2016; 5(1): 1886. PMCID: PMC5084143

Published online 2016 Oct 28. doi: 10.1186/s40064-016-3535-0

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

Dev Neurorehabil. 2016 Dec;19(6):410-415. Epub 2015 Apr 2.

Robot-assisted gait training might be beneficial for more severely affected children with cerebral palsy.

van Hedel HJ[1,2,3], Meyer-Heim A[1,2,3], Rüsch-Bohtz C[1,2].

Eur J Paediatr Neurol. 2017 May;21(3):557-564. doi: 10.1016/j.ejpn.2017.01.012. Epub 2017 Feb 2.

Robotic-assisted gait training improves walking abilities in diplegic children with cerebral palsy.

Wallard L[1], Dietrich G[2], Kerlirzin Y[2], Bredin J[3].

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Optimal rehabilitation

Journal of Motor Behavior, Vol. 47, No. 1, 2015
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REVIEW ARTICLE

Science-Based Neurorehabilitation: Recommendations for Neurorehabilitation From Basic Science

Jens Bo Nielsen[1], Maria Willerslev-Olsen[1], Lasse Christiansen[1], Jesper Lundbye-Jensen[1], Jakob Lorentzen[2]

[1]Department of Neuroscience and Pharmacology and Department of Nutrition, Exercise and Sports, University of Copenhagen, Denmark. [2]Helene Elsass Center, Charlottenlund, Copenhagen, Denmark.

Optimal rehabilitation should involve :

- **Robotic assisted devices combined with overground walking**
- **Active (patient) participation and engagement**
- Training involving **many repetitions**, but **continues to challenge the skill**
- **Resistance training**
- **Feedback error learning** – changing and challenging environment
- **Motivation and reward**
- **Intensive training** and practice over a long time
- Combination training - **overground training activities**
- “Learn to walk by learning not to fall”

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“Learning not to fall”

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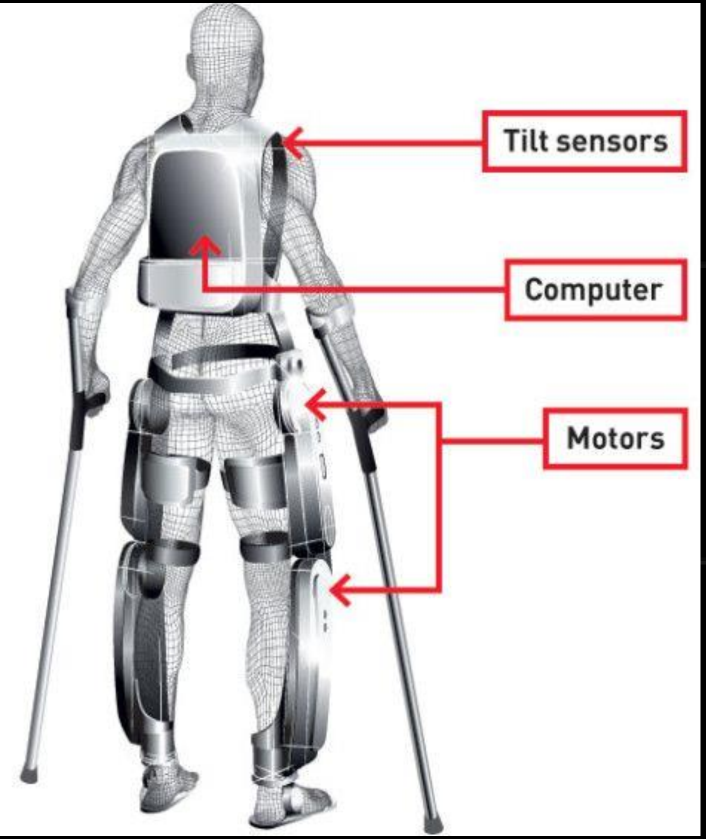
Variable Assist Exoskeletons

NEUROREHAB IMPROVEMENTS USING 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.



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Variable Assist Exoskeletons

Variable Assist Exoskeletons

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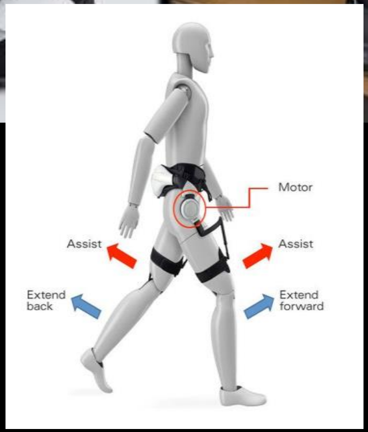
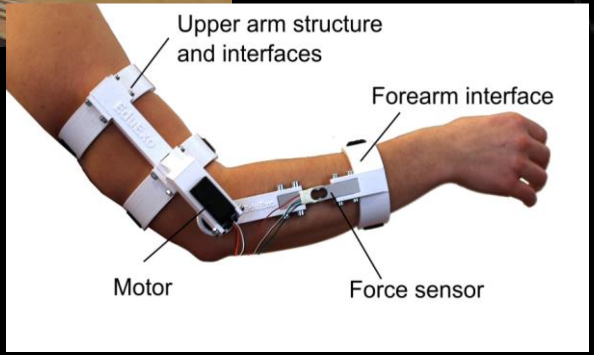
Lifestyle Assist Exoskeletons

Lifestyle Assist Exoskeletons





Industrial and Military Exoskeletons

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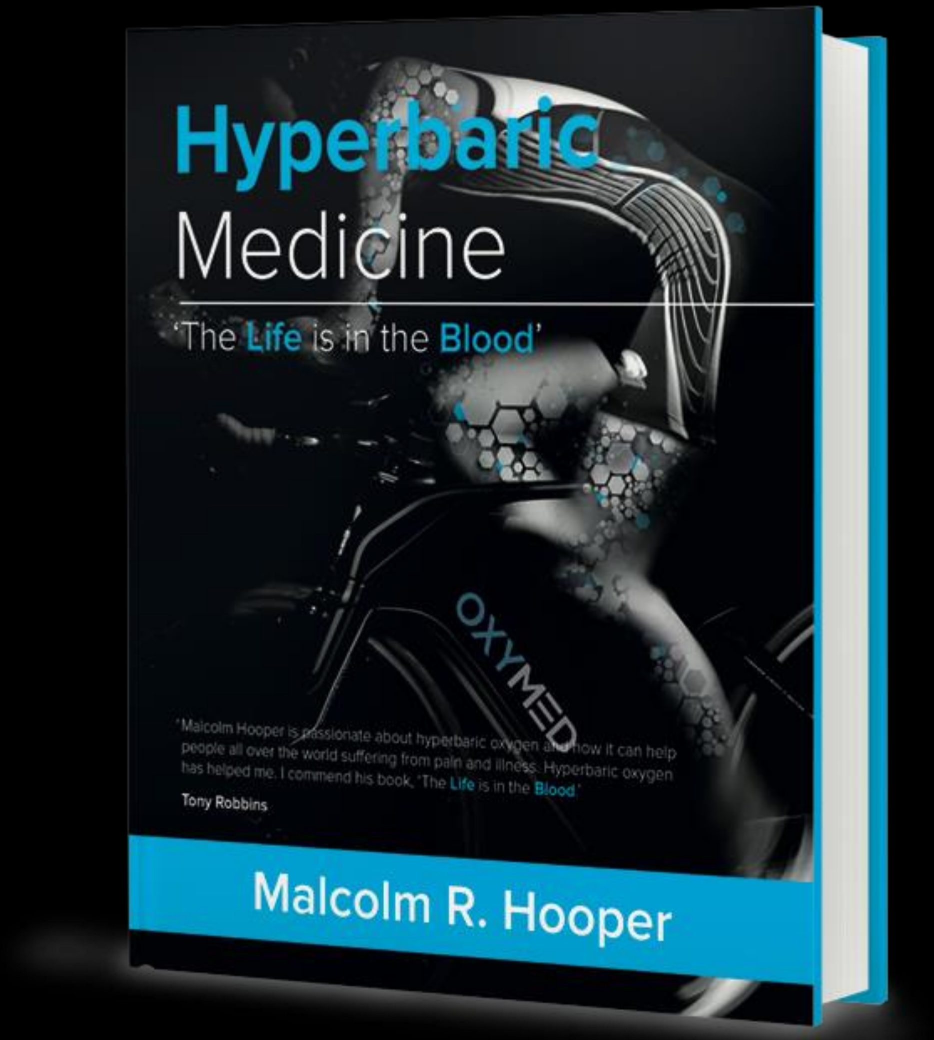
Malcolm R Hooper



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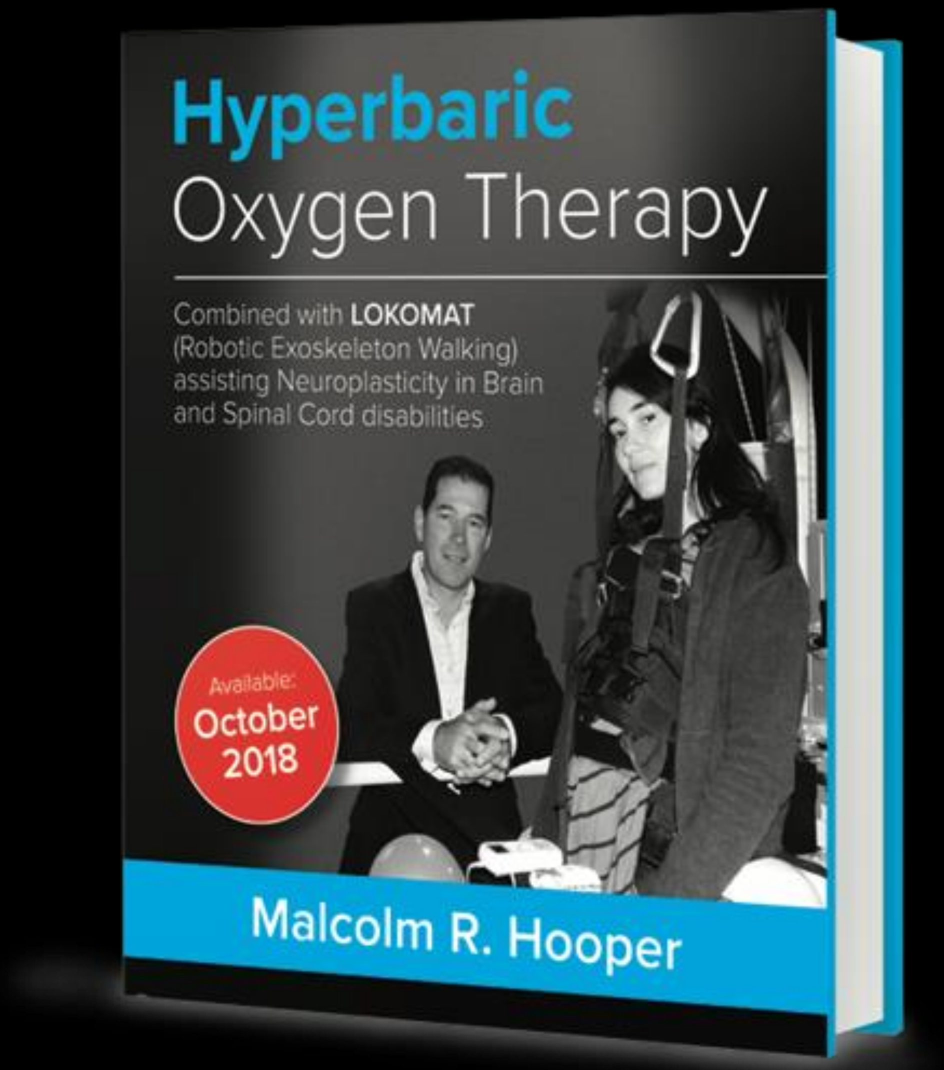

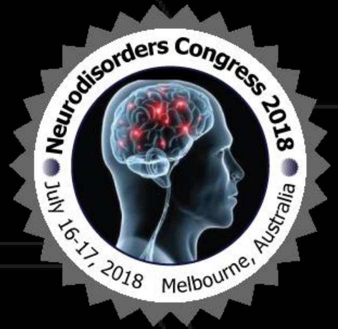

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