Muskelfysiologi och fysisk aktivitet hos barn och unga vuxna med cerebral pares

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Assistant Professor
Neuropediatrics unit, Dept of Women's and Children's health
Karolinska Institutet

This is me:

- Resident in Pediatrics
  Assistant Professor of muscle Physiology

- Education:
  - Msc human Physiology 2007
  - MD 2009
  - PhD 2015

- Postdoc Cerebral palsy & muscle 2015-2019
- University of Kentucky 2019-2020

- Interest: muscle adaptation to exercise and neuropediatrics (CP, DMD, SMA)

Agenda

- Short introduction to Cerebral palsy
- Skeletal muscle in CP
- Frame running as a tool to study exercise physiology
- Ongoing research

Cerebral palsy (CP)

- CP is the most common motor disorder in kids.
- 2 kids in a 1000 have cerebral palsy.
- Approx. at least 17 million people have CP world wide.
- Limited access to physical activity (adapted physical activity).
- At an increased risk of poor health.

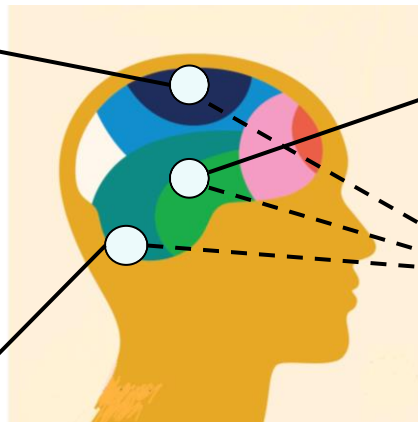
Jonsson, U., et al., Cerebral palsy prevalence, subtypes, and associated impairments: a population-based comparison study of adults and children. Dev Med Child Neurol, 2019.
Oskoui, M., et al., *An update on the prevalence of cerebral palsy: a systematic review and meta-analysis.* Dev Med Child Neurol, 2013.

What is cerebral palsy?

Cerebral Palsy (CP) is a heterogenous group

Motor types

Spastic ~80%
stiff muscles

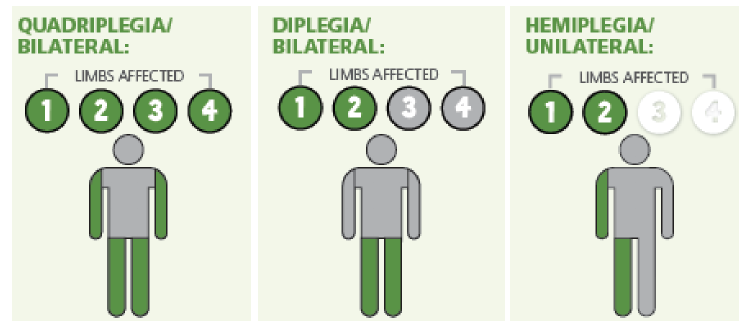


Dyskinetic: ~10%
involuntary movements

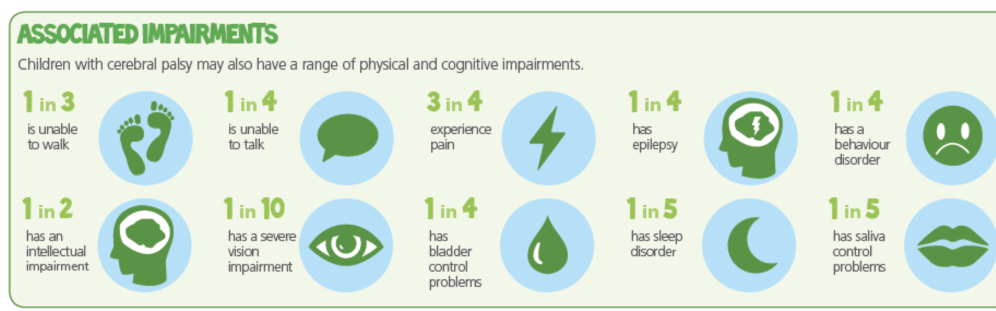
Mixed types

Ataxic: ~6%
Shaky movements
poor balance
Poor sense of positioning in space

Parts of the body



Associated impairments



Reference: https://www.ucpboston.org/world-cp-day/
Jonsson, U., et al., Cerebral palsy prevalence, subtypes, and associated impairments: a population-based comparison study of adults and children. Dev Med Child Neurol, 2019. 61(10): p. 1162-1167.

PubMed.gov

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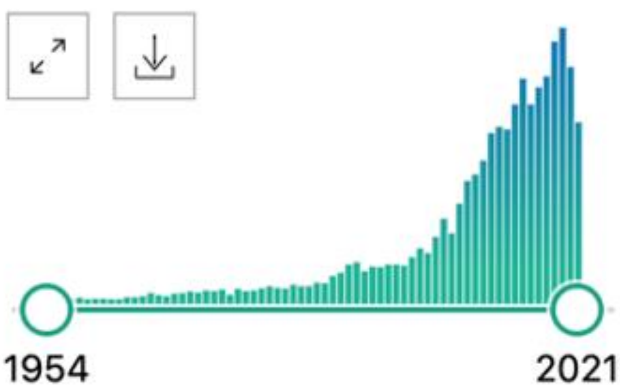
Tradition - physical activity in CP

(physical function) AND (cerebral palsy)

6489 results

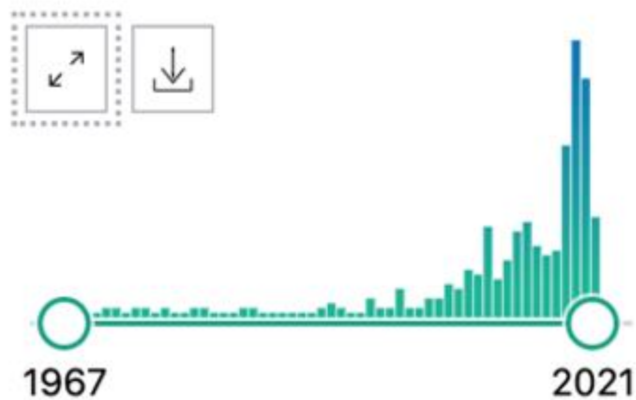
RESULTS BY YEAR



(physical fitness) AND (cerebral palsy)

257 results

RESULTS BY YEAR



The reality when having CP?

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Review > Disabil Rehabil. 2013 Apr;35(8):647-55. doi: 10.3109/09638288.2012.715721. Epub 2012 Oct 17.

Differences in habitual physical activity levels of young people with cerebral palsy and their typically developing peers: a systematic review

Stacey L Carlon [1], Nicholas F Taylor, Karen J Dodd, Nora Shields

Affiliations + expand

PMID: 23072296 DOI: 10.3109/09638288.2012.715721

CiOS Clinics in Orthopedic Surgery

Clin Orthop Surg. 2020 Mar; 12(1): 107–112. PMCID: PMC7031426
Published online 2020 Feb 13. doi: 10.4055/cios.2020.12.1.107 PMID: 32117546

Correlation between Accelerometer and Questionnaire-Based Assessment of Physical Activity in Patients with Cerebral Palsy

Ki Bum Kwon, MD, Young Choi, MD,* Ki Hyuk Sung, MD,† Chin Youb Chung, MD, Kyoung Min Lee, MD, ...ook Park, MD

...formation Disclaimer

ELSEVIER

Research in Developmental Disabilities
Volume 34, Issue 1, January 2013, Pages 157-167

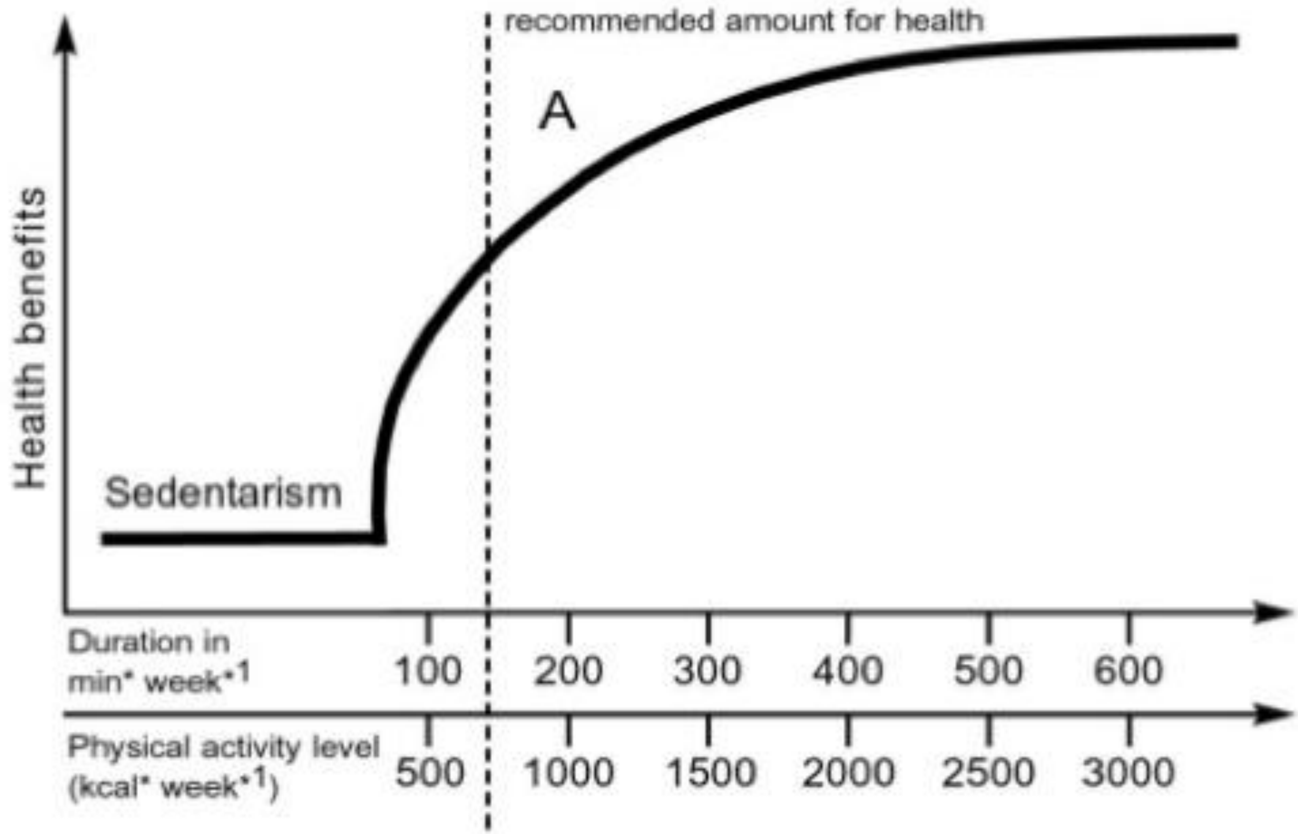
Physical activity in a total population of children and adolescents with cerebral palsy

Katarina Lauruschkus [a], Lena Westbom [b], Inger Hallström [a], Philippe Wagner [c], Eva Nordmark [a]

- 13% to 53% less habitual physical activity than their peers
- The higher GMFCS – the less active and lower degree of physical activity during leisure time.
- GMFCS IV and V were offered the least opportunities to participate in PA e.g. in school sports.

4.

Huge Health Benefits of Even Small Increases in Physical Activity



Bouchard C. Physical activity and health: introduction to the dose-response symposium. Medicine and Science in Sports and Exercise 2001; 33: S347-350

Pucher: Walking and Cycling for Health

5.

The reality when having CP?

Musculoskeletal and Endocrine Health in Adults With Cerebral Palsy: New Opportunities for Intervention

A. Trinh, P. Wong, M. C. Fahey, J. Brown, A. Churchyard, B. J. Strauss, P. R. Ebeling, P. J. Fuller, and F. Milat

Department of Endocrinology (A.T., P.W., P.R.E., P.J.F., F.M.), Monash Health, 3168 Melbourne, Australia; Hudson Institute of Medical Research (A.T., P.W., M.C.F., P.J.F., F.M.), Clayton 3168, Melbourne, Australia; Department of Medicine (A.T., J.B., A.C., B.J.S., P.R.E., P.J.F., F.M.), Monash University, 3800 Melbourne, Australia; and Department of Paediatrics (M.C.F., J.B.), Monash Health, 3168 Melbourne, Australia

J Clin Endocrinol Metab, March 2016, 101(3):1190–1197

- **50% of men and almost 80% of women have lower skeletal muscle mass**
- **38% had a previous history of fracture due to osteoporosis**

Research Letter

FREE

JAMA

December 1, 2015

Chronic Conditions in Adults With Cerebral Palsy

Mark D. Peterson, PhD, MS[1]; Jennifer M. Ryan, PhD[2]; Edward A. Hurvitz, MD[1]; et al

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	Without CP (n = 206 600)[b]	With CP (n = 1015)[b]	*P* Value[c]
Dependent Variables[e]			
Diabetes	6.3 (6.1-6.5)	9.2 (7.4-11.1)	<.001
Asthma	9.4 (9.1-9.7)	20.7 (17.3-24.2)	<.001
Hypertension	22.1 (21.8-22.4)	30.0 (26.1-33.5)	<.001
Other heart conditions	9.1 (8.9-9.3)	15.1 (12.9-17.4)	<.001
Stroke	2.3 (2.2-2.4)	4.6 (3.5-5.7)	<.001
Emphysema	1.4 (1.3-1.5)	3.8 (2.6-4.9)	<.001
Joint pain	28.0 (27.5-28.5)	43.6 (39.4-47.7)	<.001
Arthritis	17.4 (17.1-17.7)	31.4 (28.3-34.5)	<.001

Increased risk for chronic diseases in CP!

Inactivity,
↓ VO2,
↓ muscle health

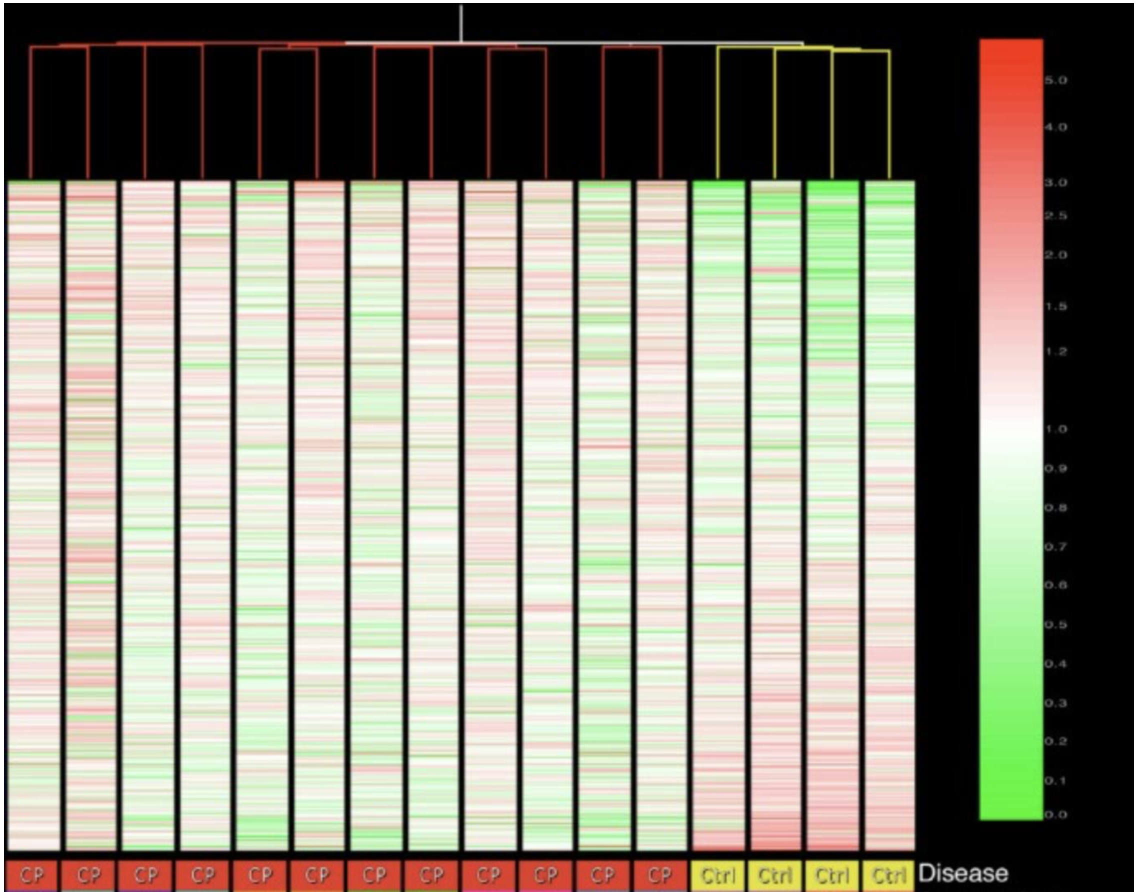
What stands out with CP muscle?

- Thin and stiff
- Contractures are common
- Why contractures develop are not clear

<u>Multiple processes altered</u>

- Extracellular matrix
- Capillaries
- Muscle stem cells
- Mitochondria
- Growth machinery (ribosomes)

Global gene expression is altered in CP skeletal muscle



Smith, Pontén et al 2009. BMC Genomics

Dysregulation of metabolism related skeletal muscle gene expression in CP

Neuromuscular Junction

Gene	FC
UTRN	0.52
CHRN	0.70
MUSK	0.70
COL4	0.76
GABP	0.81
ERBB	0.89
RAPSN	0.93
AGRN	0.94
ITGB1	1.00
LRP4	1.08
LAMA5	1.10
ACHE	1.12
LAMB2	1.17
HSPG2	1.43
NID1	1.56
COLQ	1.76
CHRNG	#N/A
YWHAG	#N/A
NRG1	#N/A

Calcium Handling

Gene	FC
ASPH	0.70
DHPR	0.78
CALM1	0.80
SLN	0.84
PLN	0.85
ATP2A	0.87
TRDN	0.87
PVALB	0.89
SCN4A	0.89
PPP3CA	0.90
S100A1	0.92
CAMK2	0.98
FKBP1A	1.01
RYR1	1.02
CAPN	1.06
CASQ	1.14
TRPC	1.22
RYR3	2.37
SYPL2	#N/A
JPH1	#N/A

Muscle Contraction

Gene	FC
TCAP	0.76
MYH	0.80
TNNT	0.84
MYBPC	0.84
TMOD	0.85
CAPZ	0.86
TNNI	0.89
TTN	0.90
TPM	0.96
MYOT	0.96
NEB	0.96
TNNC	0.97
MYL	1.00
MYOM	1.09
ACT	1.27
ACTN	1.29
MYH8	1.49
MYH3	6.14
MYPN	#N/A

Cytoskeleton

Gene	FC
UTRN	0.52
EMD	0.59
NOS1	0.73
VCL	0.85
SGC	0.87
DMD	0.88
LDB3	0.89
SYNM	0.89
DTN	0.90
SNT	0.90
SYNC	0.90
LARGE	0.95
DES	0.96
TLN1	0.99
ITGB1	1.00
ITGA7	1.00
OBSCN	1.01
DYSF	1.03
DAG1	1.05
ANK	1.08
CSRP3	1.09
LMNA	1.18
FLNC	1.31
SPT	1.34
VIM	1.37
MYOZ2	1.79
FKRP	#N/A

Extracellular Matrix

Gene	FC
MMP9	0.85
COL4	1.02
P4H	1.04
PLOD3	1.11
DCN	1.15
TGFB1	1.22
LTBP4	1.31
SDC	1.39
BGN	1.42
LAM	1.43
HSPG2	1.43
COL6	1.57
LOX	1.57
FN1	1.77
MMP2	1.90
CTGF	2.09
TIMP1	2.26
TNC	2.32
COL3A1	2.74
COL1	2.79
MMP14	#N/A
TIMP2	#N/A
MMP1	#N/A

Metabolism

Gene	FC
AMPK	0.55
TFAM	0.73
LIPE	0.77
SDH	0.80
PFKM	0.81
LDHA	0.82
CREB1	0.83
ATF2	0.85
VEGFA	0.86
MAPK14	0.87
PPARGC1A	0.87
TFB	0.88
PDH	0.89
CS	0.89
MB	0.89
CKM	0.89
CYC	0.90
COX	0.91
NDUF	0.91
PYGM	0.92
ATP5	0.94
PNPLA2	0.94
MEF2	0.95
FABP3	0.95
CAMK2	0.98
NRF1	0.99
NFE2L2	1.00
MLYCD	1.03
CD36	1.05

Inflammation

Gene	FC
HSF2	0.61
HSF1	0.79
MAPK14	0.87
NFKB1	1.08
CASP1	1.22
TGFB1	1.22
IGF1	1.37
IL1B	#N/A
TNF	#N/A
IL6	#N/A
IL10	#N/A
IL1RN	#N/A
SOCS3	#N/A
IFNG	#N/A
IL8	#N/A
PTGS2	#N/A
IKBKE	#N/A
TRIM63	#N/A
FBXO32	#N/A
SLC2A4	1.06
NFATC1	1.07
HADH	1.10
TP53	1.12
GYS1	1.12
CPT1B	1.24
HK2	1.47
LPL	1.87
CAMK4	#N/A
GPAM	#N/A

Muscle Signaling

Gene	FC
MAPK8	0.45
MSTN	0.50
ACVR2B	0.59
RPS6KB1	0.66
FOXO3	0.73
MYOG	0.73
IGF1R	0.77
CALM1	0.80
EIF4E	0.82
MAPK14	0.87
GSK3B	0.89
PPP3CA	0.90
MEF2	0.91
MYF6	0.93
PIK3R	0.93
MYOD1	0.94
MYF5	0.96
FRAP1	0.96
CAMK2	0.98
MAPK1	1.01
HDAC	1.03
EIF2B4	1.03
MAP2K1	1.04
NFATC1	1.07
EIF4EBP1	1.10
AKT1	1.18
IGF1	1.37
FST	1.62
FGF2	2.12

Gene	FC
RPTOR	#N/A
PDK1	#N/A
CDKN1A	#N/A
HGF	#N/A

Fiber Type Isoforms

Slow Isoform		*Fast Isoform*	
Gene	FC	Gene	FC
MYH7	0.97	MYH1	0.70
		MYH2	0.89
MYL2	0.94	MYL1	0.87
MYL3	1.09		
MYBPC1	0.92	MYBPC2	0.77
TNNT1	0.95	TNNT3	0.73
TNNI1	0.99	TNNI2	0.81
TNNC1	0.96	TNNC2	0.90
TPM3	1.08	TPM1	0.87
TMOD1	0.85	TMOD4	#N/A
CASQ2	1.41	CASQ1	0.92
ATP2A2	0.94	ATP2A1	0.80
PVALB	0.89		

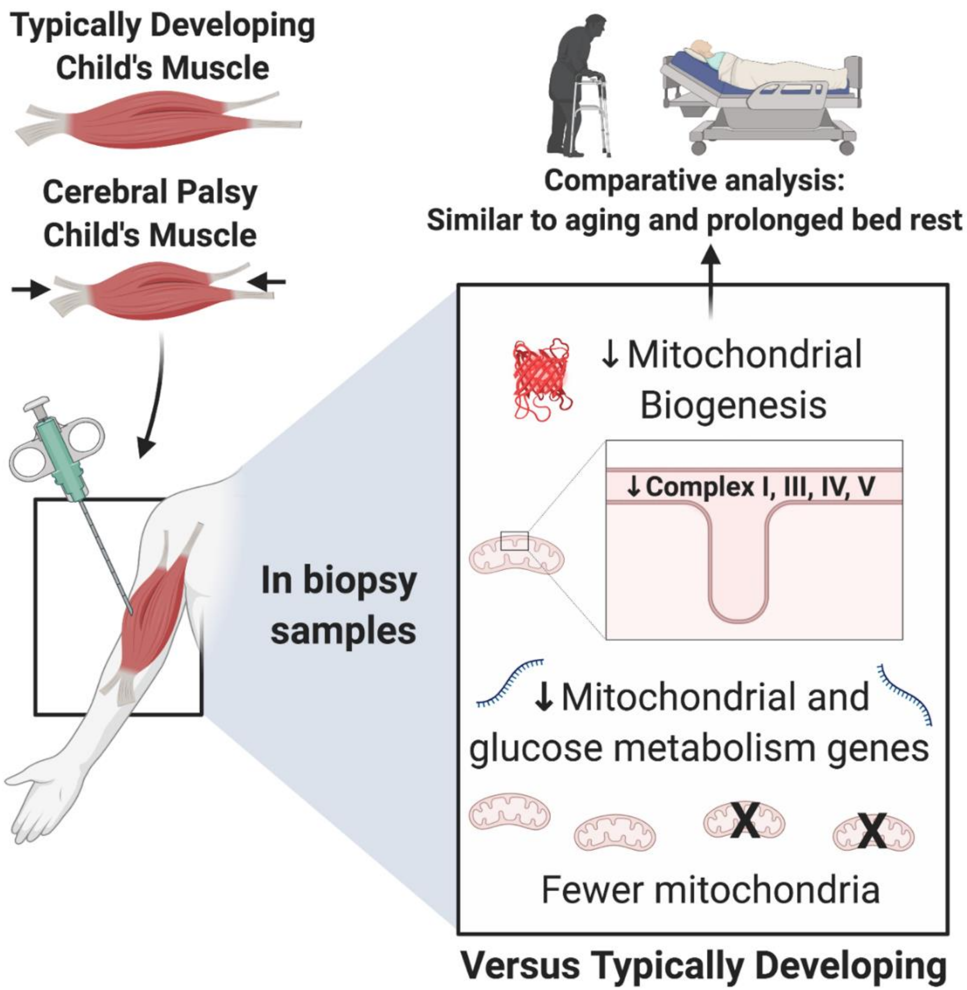
Smith et al 2012. PLOS One

DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY ORIGINAL ARTICLE

Reduced mitochondrial DNA and OXPHOS protein content in skeletal muscle of children with cerebral palsy

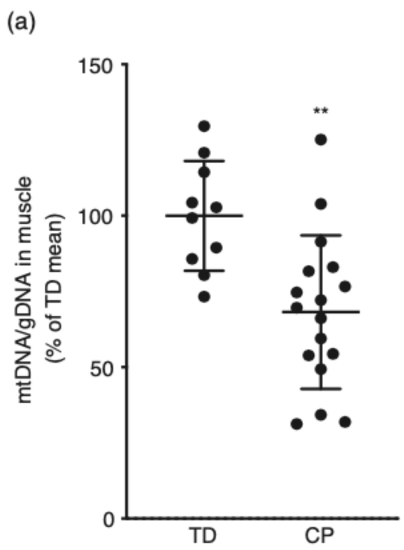
FERDINAND VON WALDEN[1,2,3,*] | IVAN J VECHETTI JR[2,3,4,*] | DAVIS ENGLUND[3,5] | VANDRÉ C FIGUEIREDO[2,3] | RODRIGO FERNANDEZ-GONZALO[6,7] | KEVIN MURACH[3,5] | JESSICA PINGEL[8] | JOHN J MCCARTHY[2,3] | PER STÅL[9] | EVA PONTÉN[1]

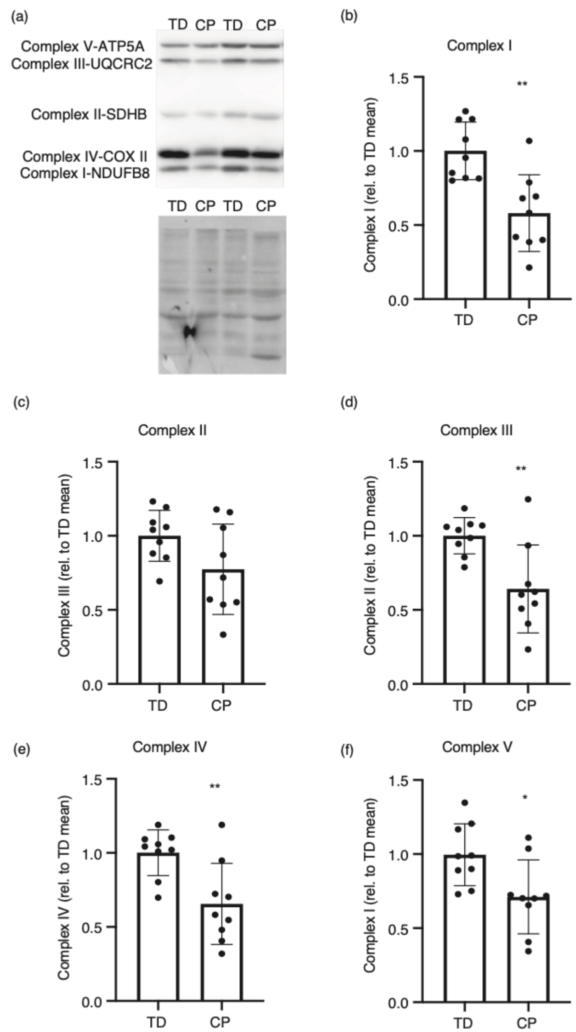
Reduced expression of key factors in mitochondrial biology



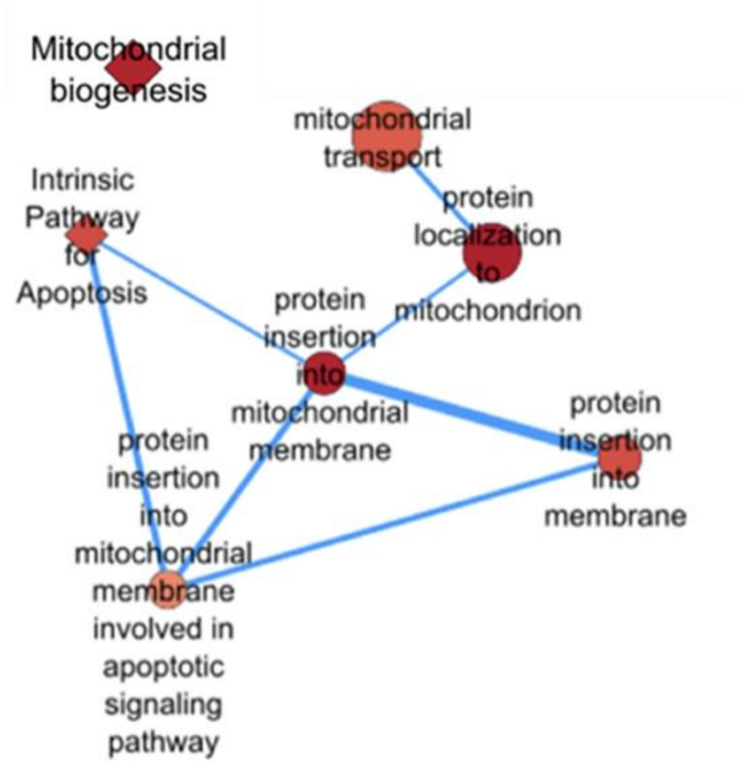
Von Walden et al 2021. DEV MED

Reduced mtDNA content and OXPHOS protein content in CP muscle



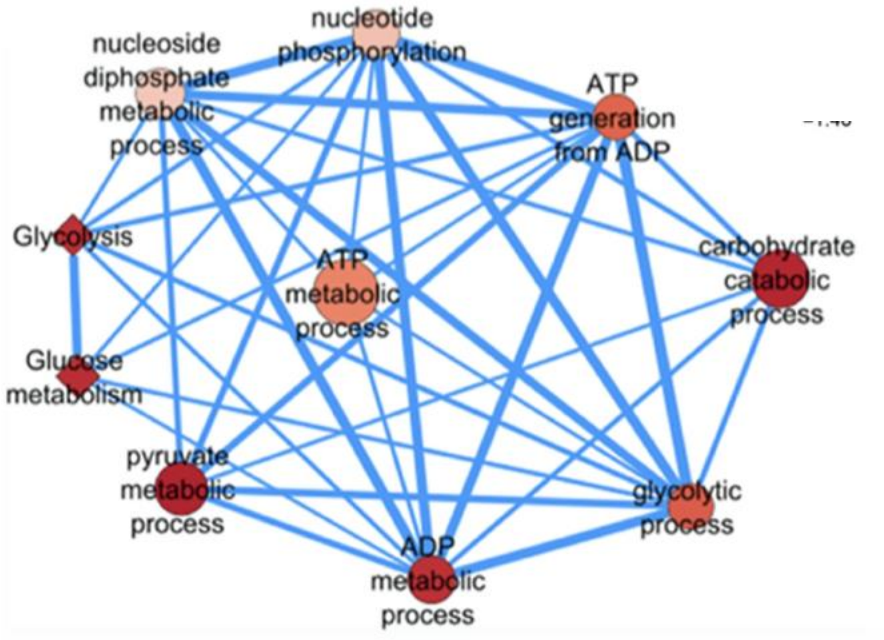


Reanalyzed data – down regulated genes



Von Walden et al 2021. DEV MED

Reanalyzed data – down regulated genes



Von Walden et al 2021. DEV MED

Aging and disuse atrophy data sets

Journals of Gerontology: BIOLOGICAL SCIENCES
Cite journal as: J Gerontol A Biol Sci Med Sci 2013 September;68(9):1035–1044
doi:10.1093/gerona/glt015

Advance Access publication February 15, 2013

Microarray Analysis Reveals Novel Features of the Muscle Aging Process in Men and Women

Dongmei Liu,[1] Maureen A. Sartor,[1] Gustavo A. Nader,[2] Emidio E. Pistilli,[3] Leah Tanton,[4] Charles Lilly,[4] Laurie Gutmann,[3] Heidi B. IglayReger,[1] Paul S. Visich,[5] Eric P. Hoffman,[6] and Paul M. Gordon[1]

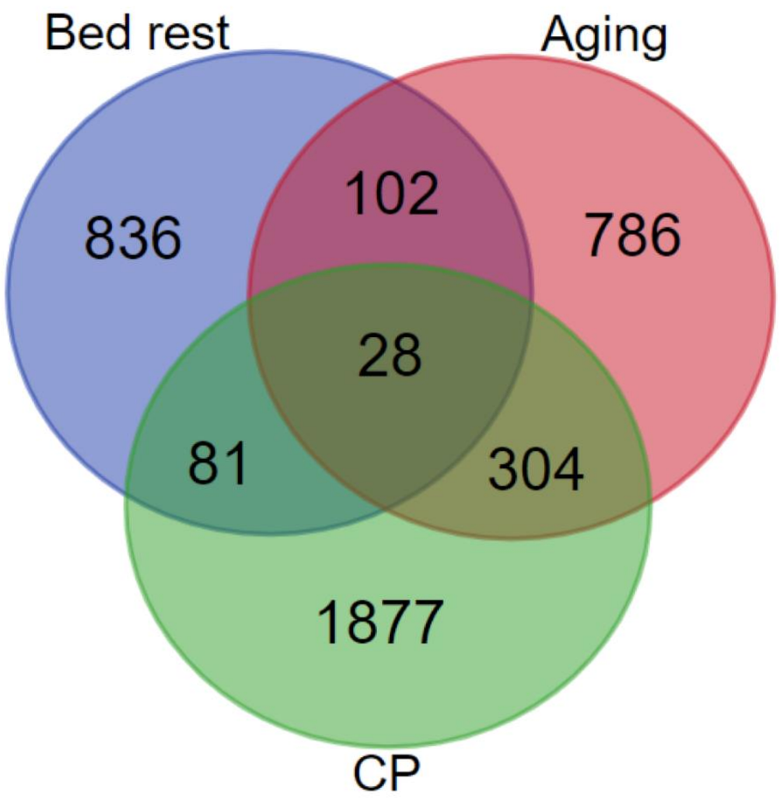
RESEARCH ARTICLE

THE FASEB JOURNAL

Three months of bed rest induce a residual transcriptomic signature resilient to resistance exercise countermeasures

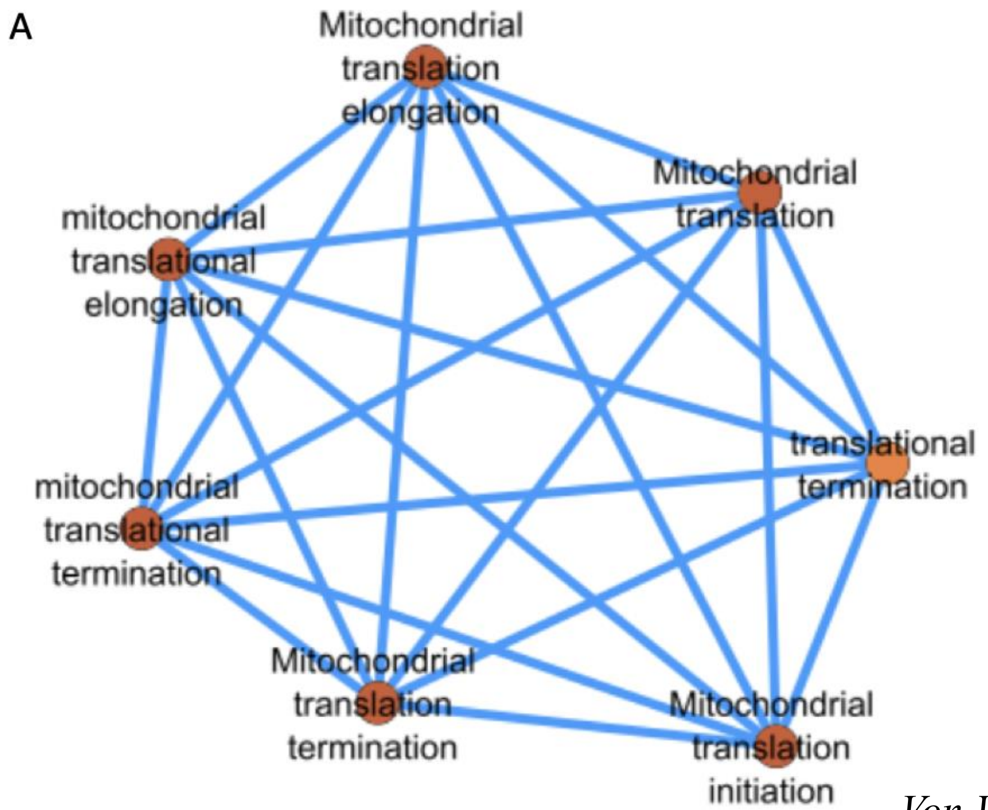
Rodrigo Fernandez-Gonzalo[1] | Per A. Tesch[2] | Tommy R. Lundberg[1] | Björn A. Alkner[3,4] | Eric Rullman[1] | Thomas Gustafsson[1]

Comparative analysis - CP vs aging vs disuse



Von Walden et al 2021. DEV MED

Downregulated mitochondria related gene expression common for all conditions

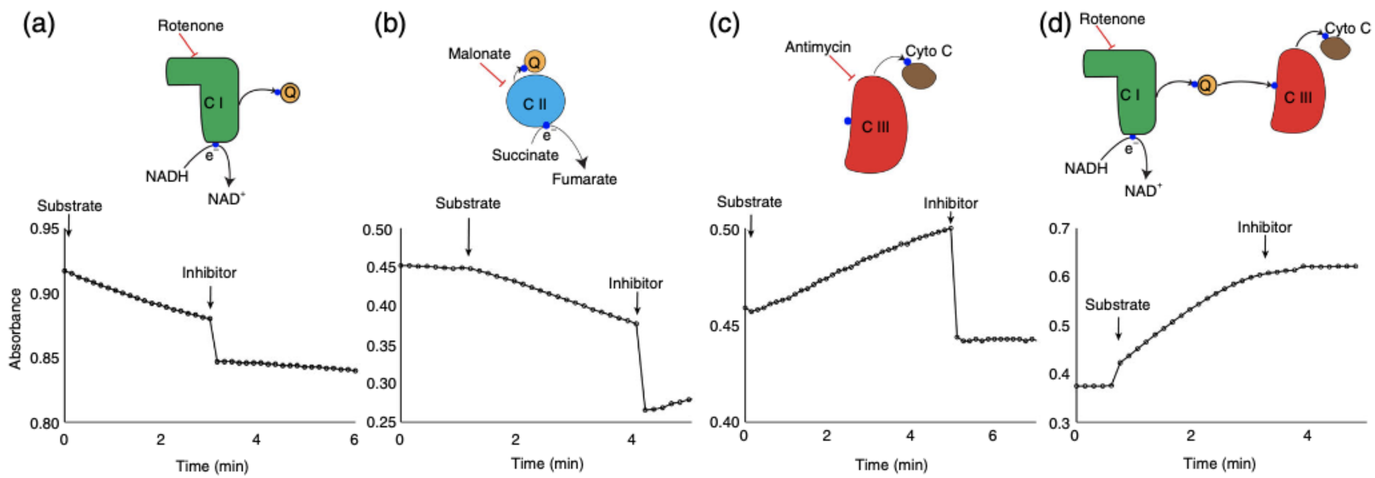


Von Walden et al 2021. DEV MED

DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY | ORIGINAL ARTICLE

Skeletal muscle maximal mitochondrial activity in ambulatory children with cerebral palsy

SUDARSHAN DAYANIDHI[1,2,3] | ELISA H BUCKNER[1,4] | ROBIN S REDMOND[3] | HENRY G CHAMBERS[1,5] | SIMON SCHENK[1,4] | RICHARD L LIEBER[1,2,3,6]



DEVELOPMENTAL MEDICINE & CHILD NEUROLOGY ORIGINAL ARTICLE

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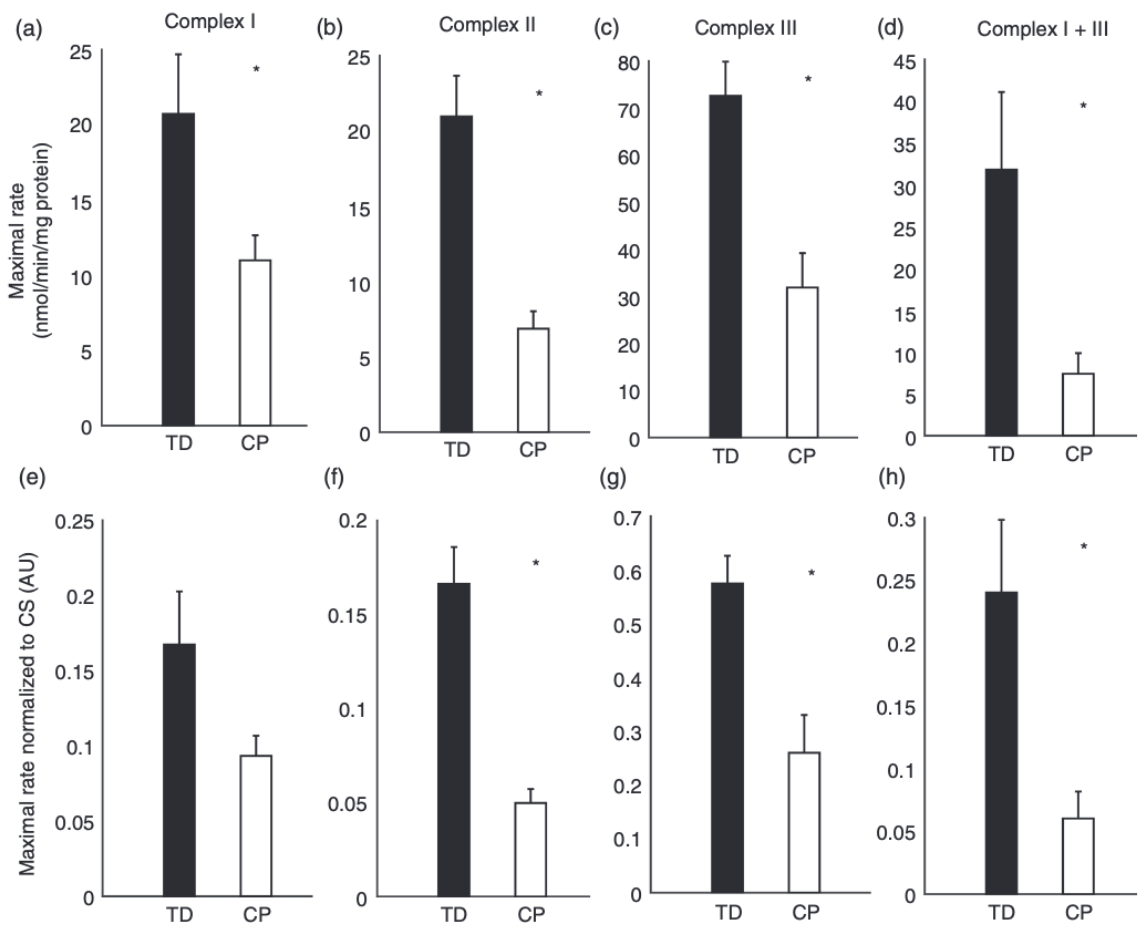
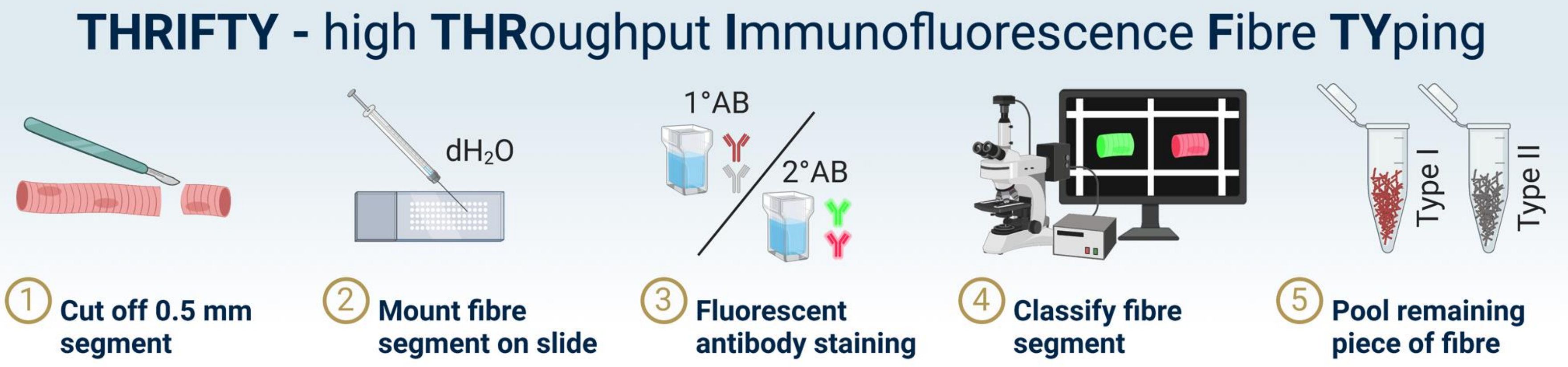
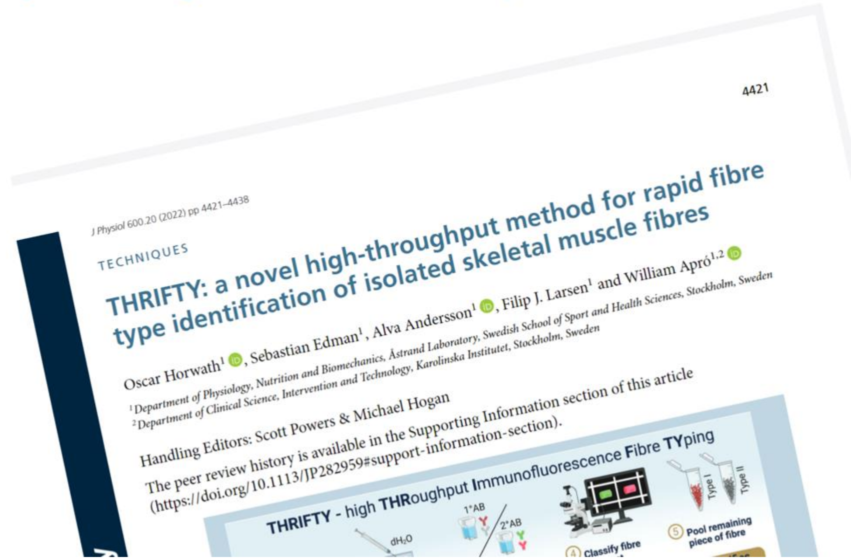
Skeletal muscle maximal mitochondrial activity in ambulatory children with cerebral palsy

SUDARSHAN DAYANIDHI[1,2,3] | ELISA H BUCKNER[1,4] | ROBIN S REDMOND[3] | HENRY G CHAMBERS[1,5] | SIMON SCHENK[1,4] | RICHARD L LIEBER[1,2,3,6]





Sebastian Edman, new postdoc


4421

J Physiol 600.20 (2022) pp 4421–4438

TECHNIQUES

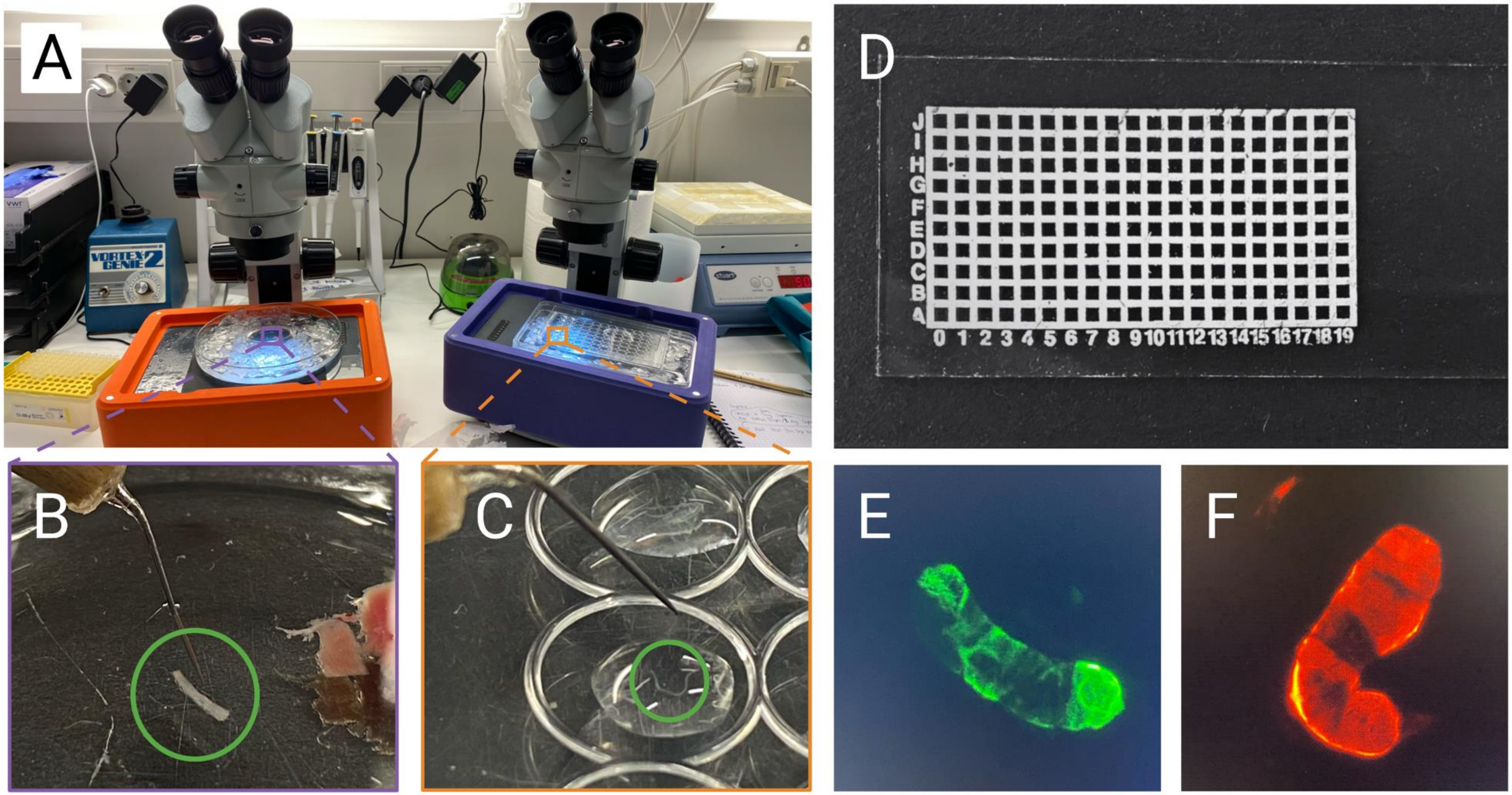
THRIFTY: a novel high-throughput method for rapid fibre type identification of isolated skeletal muscle fibres

Oscar Horwath[1], Sebastian Edman[1], Alva Andersson[1], Filip J. Larsen[1] and William Apró[1,2]

[1]Department of Physiology, Nutrition and Biomechanics, Åstrand Laboratory, Swedish School of Sport and Health Sciences, Stockholm, Sweden
[2]Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden

Handling Editors: Scott Powers & Michael Hogan

The peer review history is available in the Supporting Information section of this article (https://doi.org/10.1113/JP282959#support-information-section).


A
B
C
D
E
F
J
I
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F
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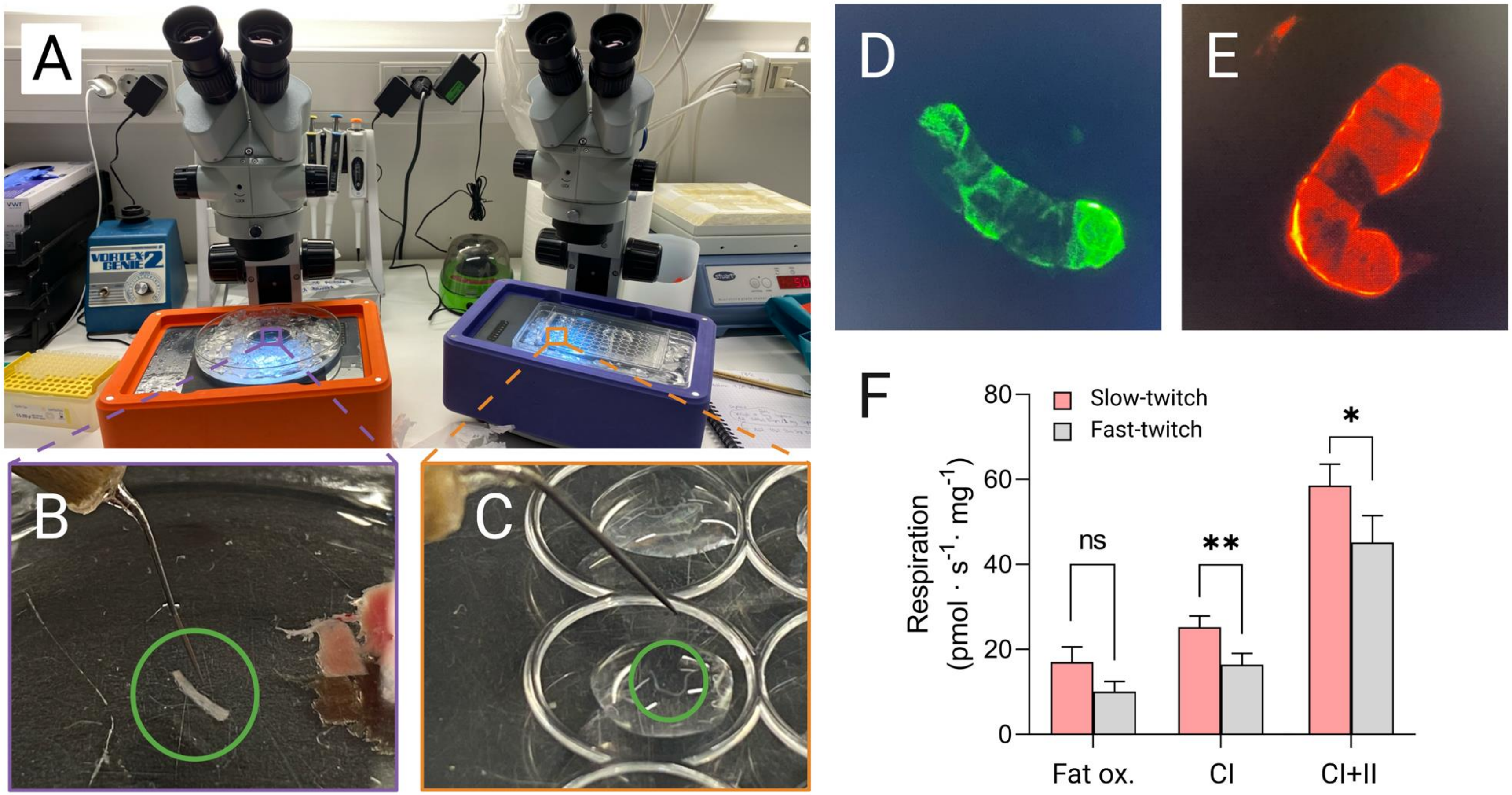
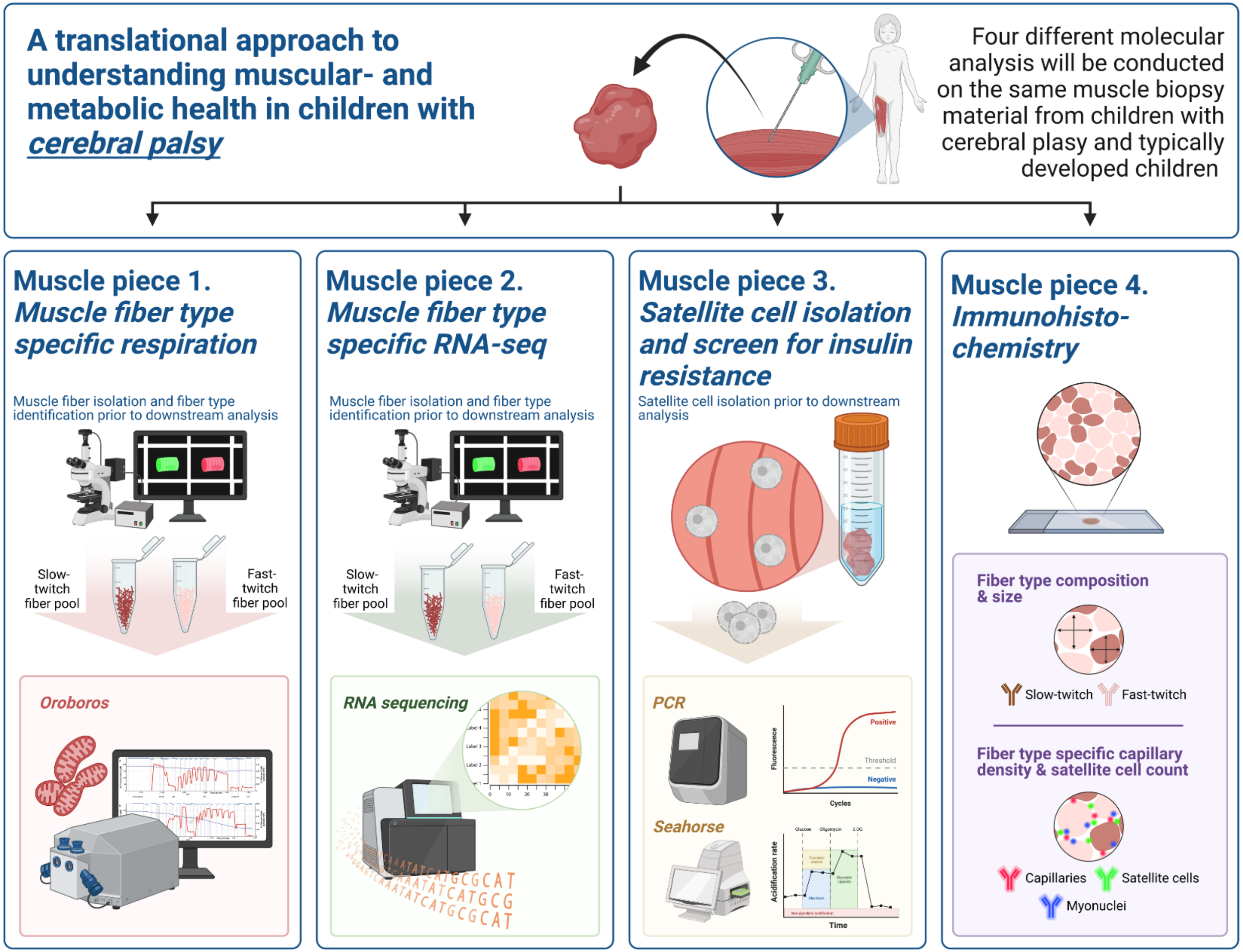
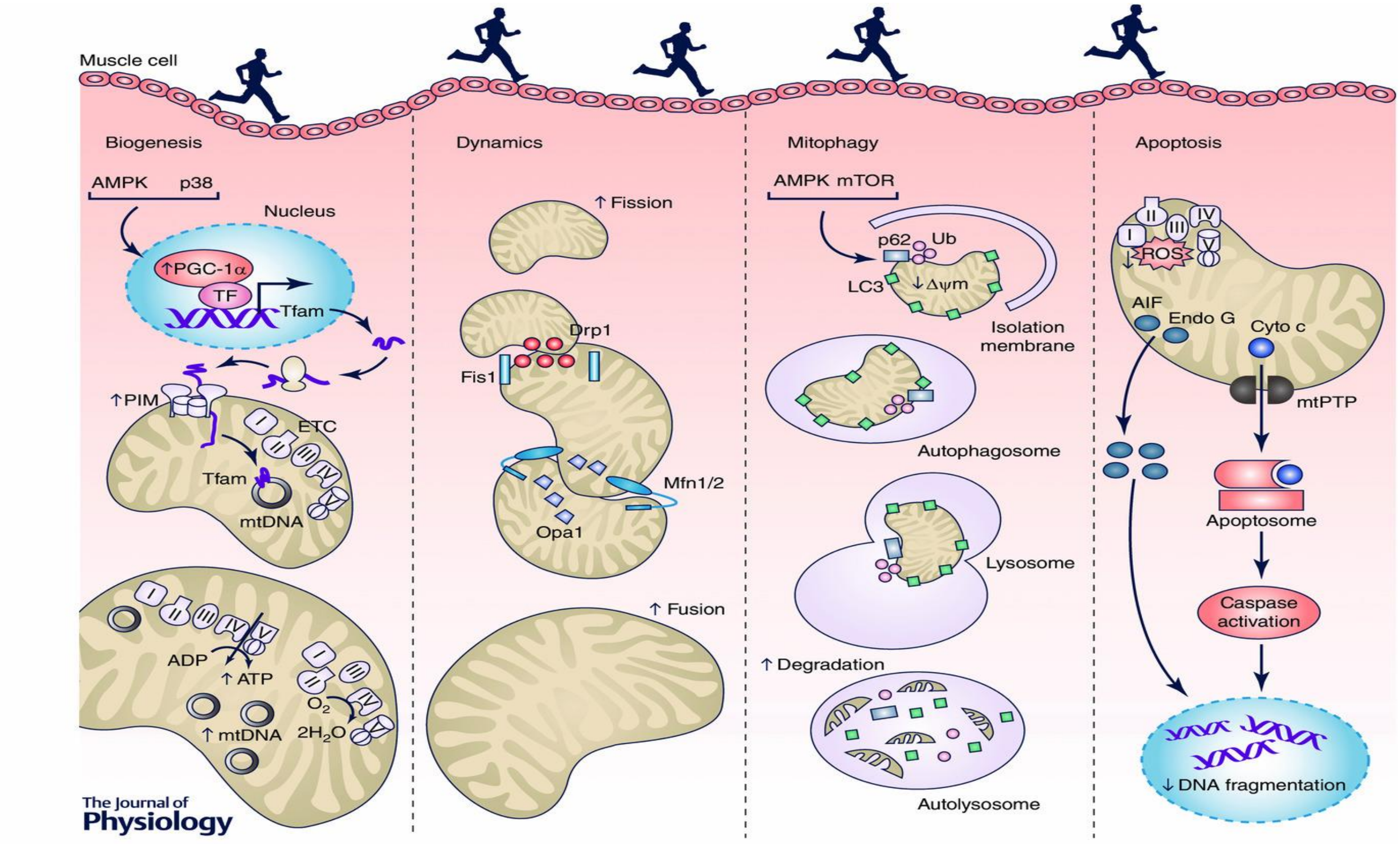
D
C
B
A
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19
VORTEX GENIE 2


A
VORTEX GENIE 2
B
C
D
E
F
Slow-twitch
Fast-twitch
Respiration
(pmol · s⁻¹ · mg⁻¹)
80
60
40
20
0
ns
**
*
Fat ox.
CI
CI+II



A translational approach to understanding muscular- and metabolic health in children with cerebral palsy
Four different molecular analysis will be conducted on the same muscle biopsy material from children with cerebral plasy and typically developed children
Muscle piece 1. Muscle fiber type specific respiration
Muscle fiber isolation and fiber type identification prior to downstream analysis
Slow-twitch fiber pool
Fast-twitch fiber pool
Oroboros
Muscle piece 2. Muscle fiber type specific RNA-seq
Muscle fiber isolation and fiber type identification prior to downstream analysis
Slow-twitch fiber pool
Fast-twitch fiber pool
RNA sequencing
Muscle piece 3. Satellite cell isolation and screen for insulin resistance
Satellite cell isolation prior to downstream analysis
PCR
Positive
Threshold
Negative
Fluorescence
Cycles
Seahorse
Acidification rate
Time
Muscle piece 4. Immunohisto-chemistry
Fiber type composition & size
Slow-twitch
Fast-twitch
Fiber type specific capillary density & satellite cell count
Capillaries
Satellite cells
Myonuclei

Exercise as a countermeasure for reduced mitochondrial content/function with aging



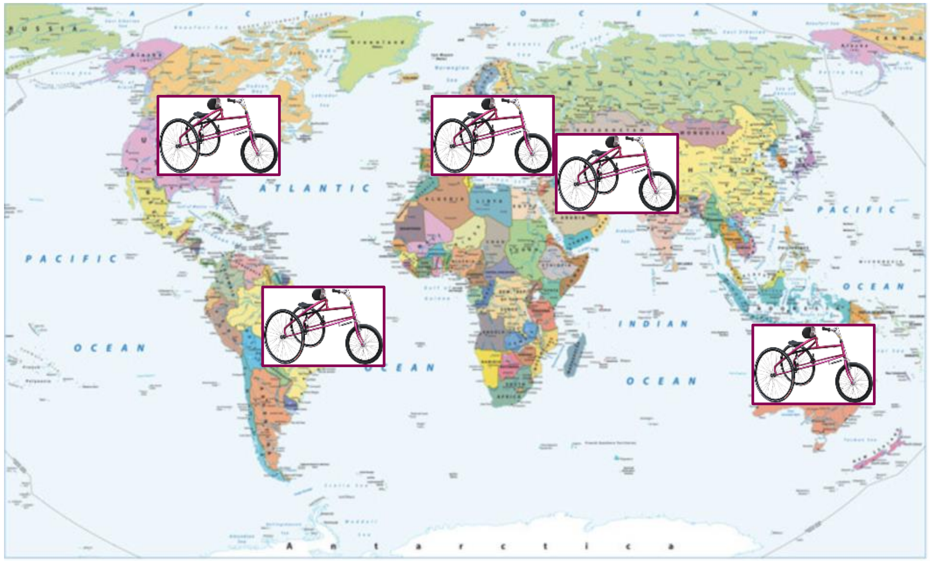
Joseph et al 2015. J Phys

Frame Running /RaceRunning

Innovative option to physical activity for motor impaired people.

Invented in Denmark 1990s

(Connie Hansen and Mansoor Siddiqi)



"RaceRunning is the fastest growing para athletics disciplines and one of only few sports for the most severely disabled and athletes with an impaired balance"

Mansoor Sadiqi, CPISRA Head of RaceRunning Development

Frame Running /RaceRunning

What?

- Locomotion in daily life
- Recreation
- Aerobic exercise
- Competitive athletic parasport: 40-5000m

Who?

- People with impaired posture, balance and motor control.
- No running ability.

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Hjalmarsson *et al. BMC Musculoskeletal Disorders* (2020) 21:193
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BMC Musculoskeletal Disorders

RESEARCH ARTICLE Open Access

RaceRunning training improves stamina and promotes skeletal muscle hypertrophy in young individuals with cerebral palsy

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Abstract

Background: Individuals with cerebral palsy (CP) are less physically active, spend more time sedentary and have lower cardiorespiratory endurance as compared to typically developed individuals. RaceRunning enables high-intensity exercise in individuals with CP with limited or no walking ability, using a three-wheeled running bike with a saddle and a chest plate for support, but no pedals. Training adaptations using this type of exercise are unknown.

Methods: Fifteen adolescents/young adults (mean age 16, range 9–29, 7 females/8 males) with CP completed 12 weeks, two sessions/week, of RaceRunning training. Measurements of cardiorespiratory endurance (6-min RaceRunning test (6-MRT), average and maximum heart rate, rate of perceived exertion using the Borg scale (Borg-RPE)), skeletal muscle thickness (ultrasound) of the thigh (vastus lateralis and intermedius muscles) and lower leg (medial gastrocnemius muscle) and passive range of motion (pROM) of hip, knee and ankle were collected before and after the training period.

Results: Cardiorespiratory endurance increased on average 34% (6-MRT distance; pre 576 ± 320 m vs. post 723 ± 368 m, $p < 0.001$). Average and maximum heart rate and Borg-RPE during the 6-MRT did not differ pre vs. post training. Thickness of the medial gastrocnemius muscle increased 9% in response to training ($p < 0.05$) on the more-affected side. Passive hip flexion increased ($p < 0.05$) on the less-affected side and ankle dorsiflexion decreased

Study I

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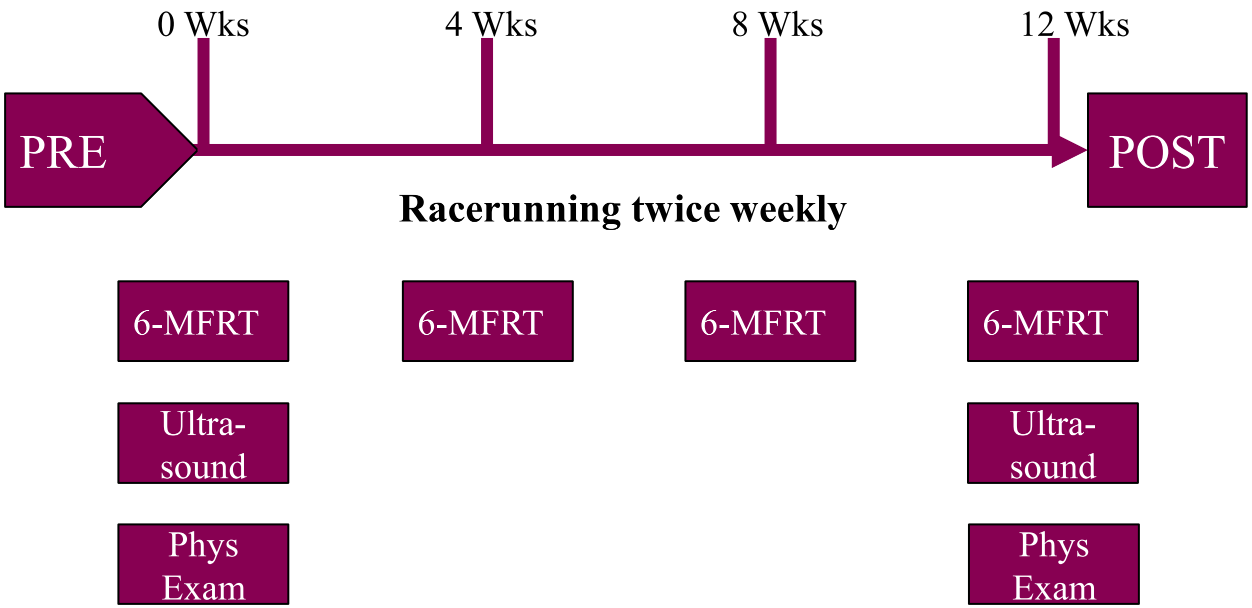
Purpose:

Determine the effect of Frame running training on:

- **Cardiovascular adaptation**
- **Skeletal muscle thickness**

Experimental study design



6-MFRT = 6 minute Frane running Test

Methods

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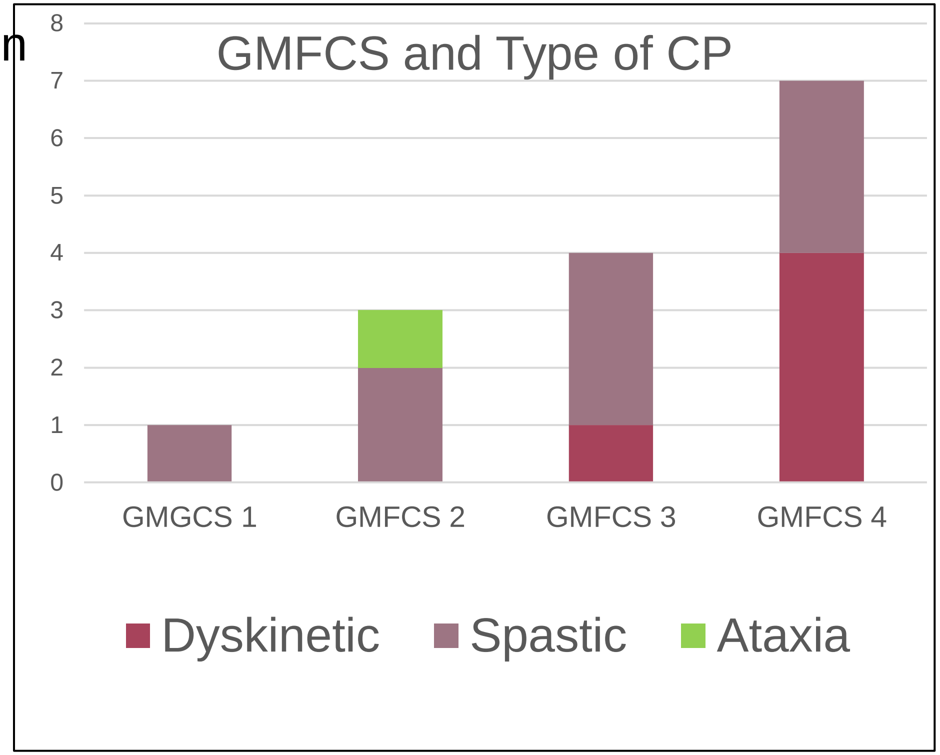
Participants

- Collaboration with Racerunning clubs in Stockholm, Västerås and Uppsala.
- 15 participants.
- Mean age 16, range 9-29,
- 8 males / 7 females
- Types Spastic 9 / Dyskinetic 5 / Ataxia 1.
- GMFCS I-IV; 1-3-4-7



Study I

Methods

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Pre- and post measurements

- **Cardiorespiratory endurance**
  6-min RaceRunning test (6-MRT) ,
  - Average and maximum heart rate measurement,
  - Borg RPE scale (rated physical exertion).
  - Trip computer with speed sensor.

- **Muscle thickness**
  Ultrasound of
  - thigh (vastus lateralis and intermedius muscles)
  - calf muscles (medial gastrocnemius muscle).

- **Physio exam and classification**
  - Passive range of motion (hip, knee and foot)
  - Spasticity (Modified Ashworth Scale) (hip, knee and foot).
  - Classification GMFCS and FMS (Functional Mobility Scale).

Intensity during training;

Average time in motion per 60 min session= **25 min**

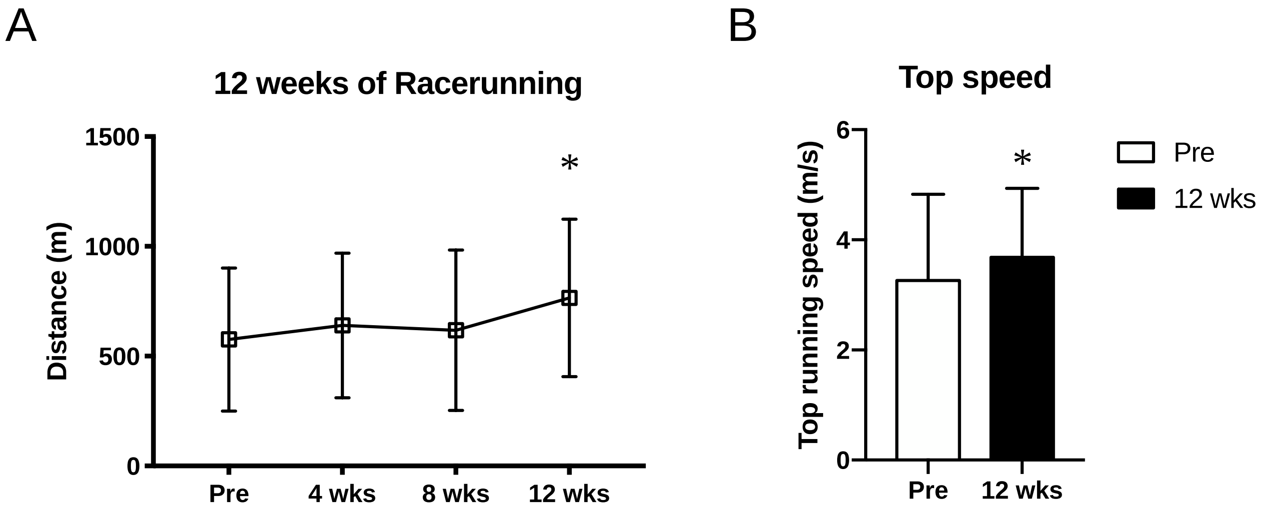
Average **HR 136 bpm** = **69%** of estimated HR max.

Average **max HR 168 bpm** = **85%** of estimated HR max

Study I

Results

Cardiorespiratory endurance
(6-MRT)



Equal effort

no change pre vs post
- heart rate
- Borg RPE

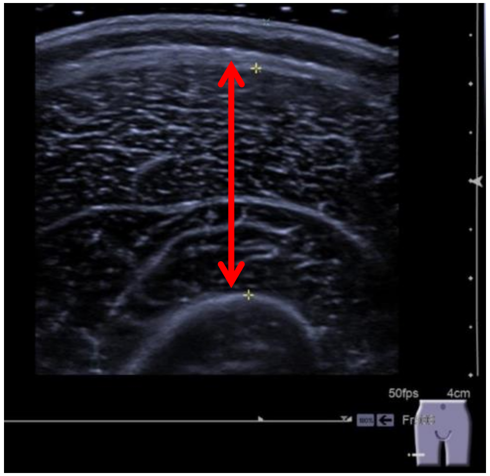
34% improvement

21% improvement

(6-MRT distance; pre 576 ± 320m vs. post 723 ± 368 m, $p < 0.001$)

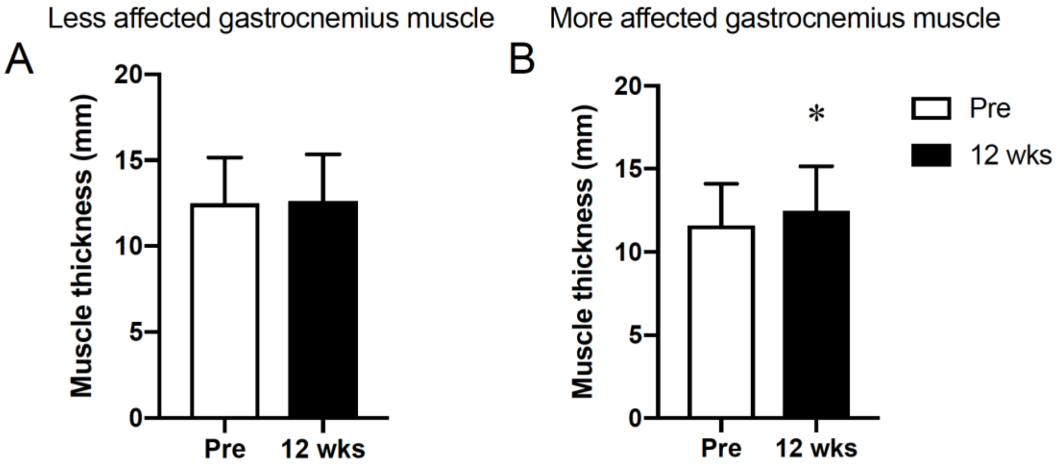
Results

Muscle thickness



Thigh: No change

Calf: + **9%** on more aff. side



(Week 0: mean 11,6 mm, SD 2,7. Week 12: mean 12,6 mm, SD 2,6. ($p < 0.05$)

Conclusion

12 weeks of Frame running training:

Clear effects of training on both central (stamina) and peripheral level (muscle).

How can we measure VO2 max in individuals with CP?

Purpose

- To determine the physiological response to the 6-Minute RaceRunning Test (6-MRT) in persons with cerebral palsy (CP)

- To investigate whether the distance covered on the 6-MRT correlates to peak oxygen uptake (VO2peak).

RESEARCH REPORT

Physiological Response to the 6-Minute Frame Running Test in Children and Adults With Cerebral Palsy

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Pediatric Physical Therapy Exercise Testing in Cerebral Palsy 529

Study II

Methods

Study-design, setting and recruitment:

Cross-sectional observational study.

- 6-MRT - total distance covered (m),

HR_{peak}

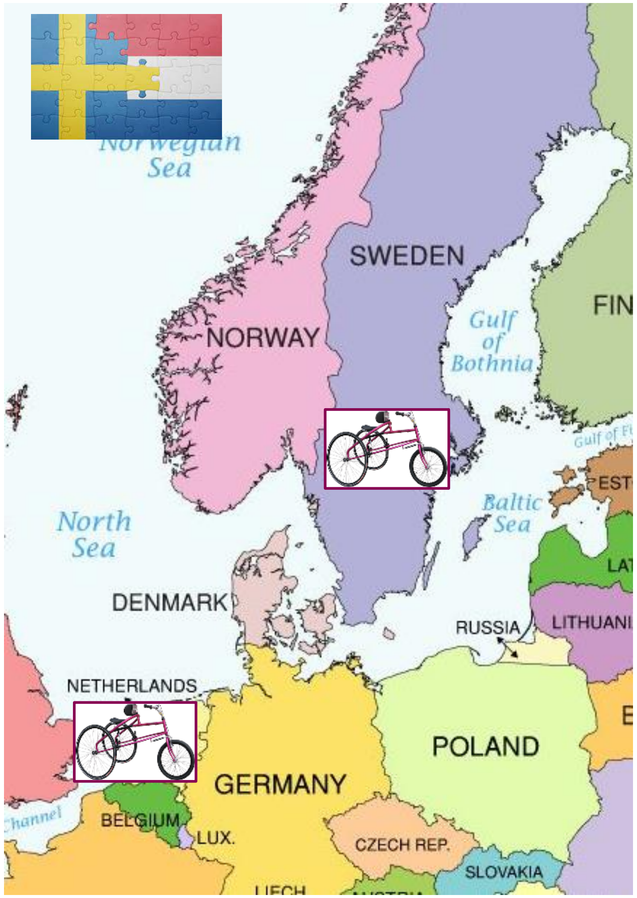
- peak heart rate

RER_{peak}

- peak Respiratory Exchange Ratio

VO_{2peak}

- peak oxygen uptake



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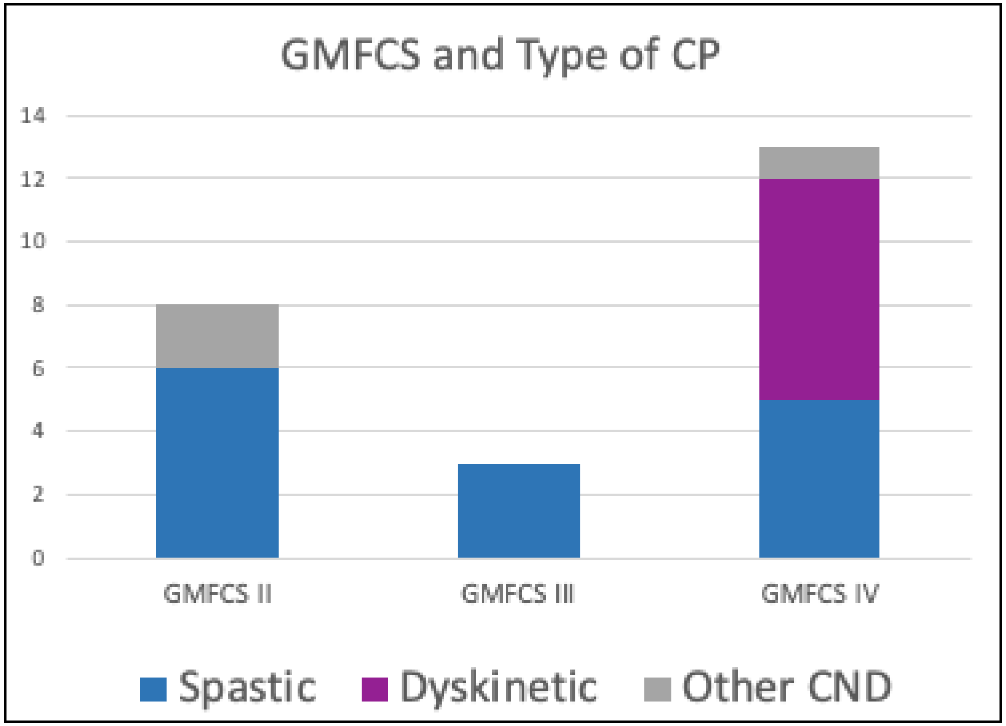
Participants

- 24 participants.
- Mean age 19y range 8-37y,
- 14 males / 10 females
- Types Spastic 14 / Dyskinetic 7 / Other CND 3.
- GMFCS II-III-IV; 8-3-13



Results

	Total (24) Mean ± SD
$\dot{V}O_{2\ peak}$ (ml/kg/min)	29.3 ± 7.3
$\dot{V}O_{2\ peak}$ (L/min)	1.40 ± 0.48
HR_{peak} (bpm)	180.7 ± 14.3
RER_{peak}	1.16 ± 0.16
6-MRT distance (m)	707 ± 244

Edelman Bos et al 2022. Ped Phys Ther

Results

Average heart rate and oxygen uptake with error bars (SD) of all participants during 6-minute RaceRunning Test

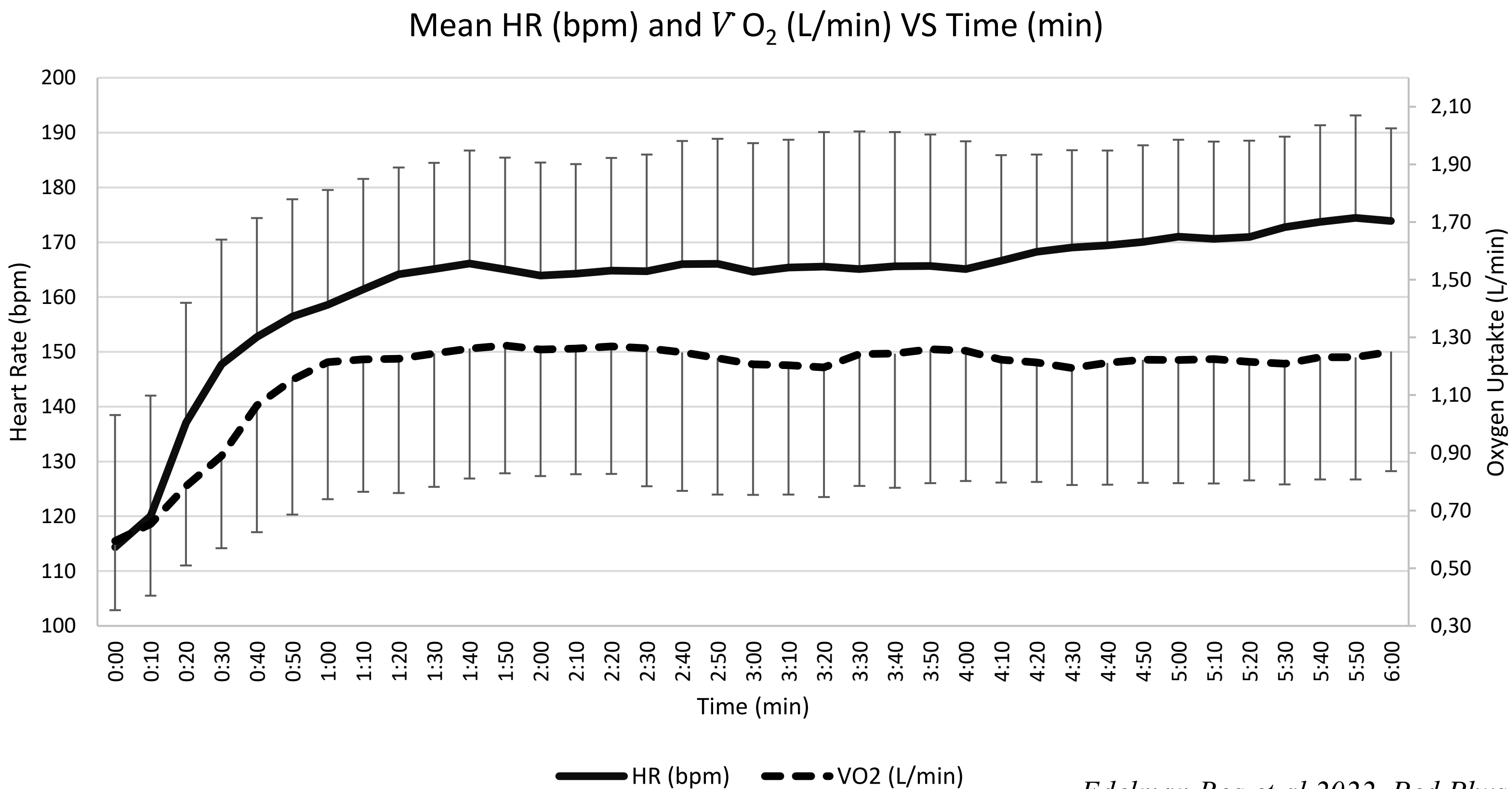


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Figure 1. Average heart rate (—) and oxygen uptake (L/min) (- -) with error bars (SD) of all participants during the 6-Minute RaceRunning Test.

Results

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Significant correlation between 6-MRT (distance) and VO_{2peak} (rho=0.75, 95% CI: 0.50 to 0.89).

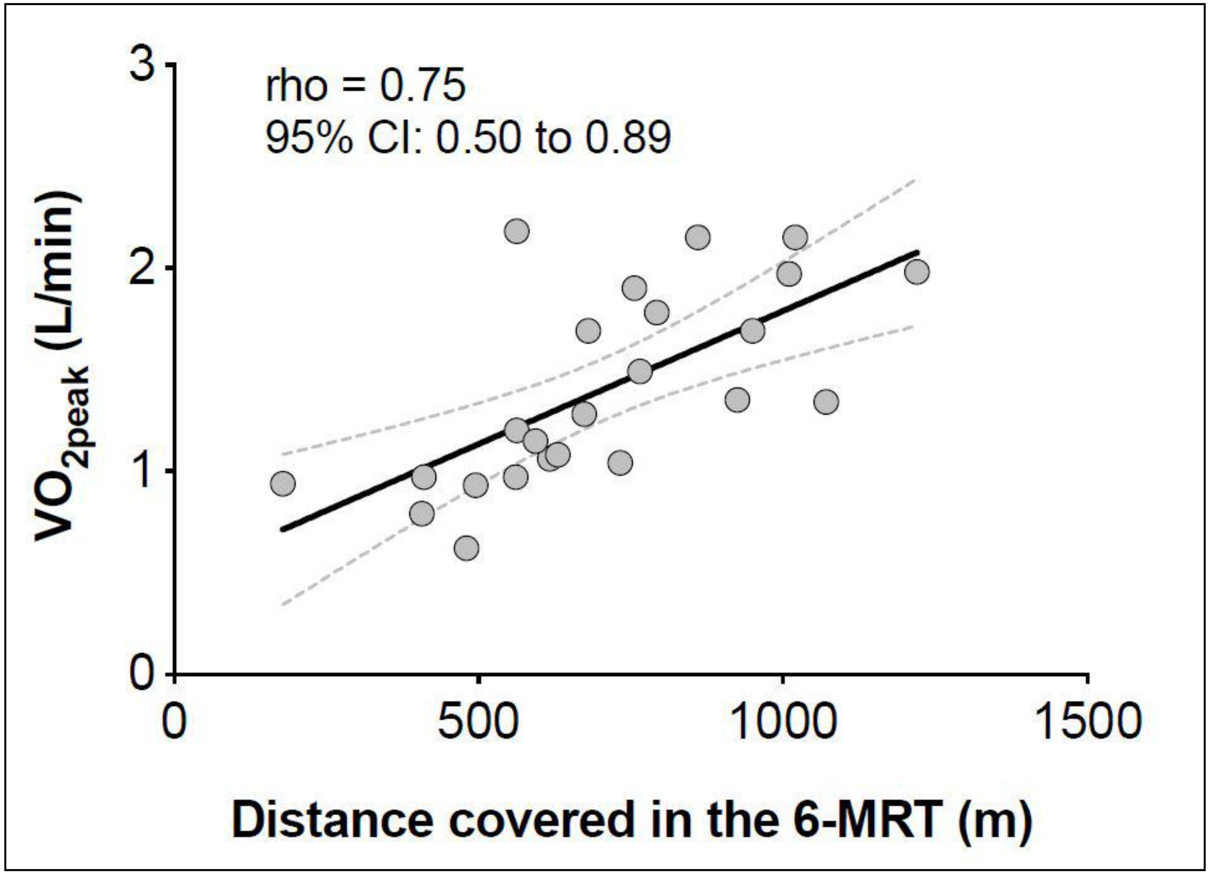

Figure 2. Scatterplot with $\dot{V}O_{2\ peak}$ (L/min) and distance covered in the 6-Minute RaceRunning Test (m). The dotted lines represent 95% confidence interval (95% CI: 0,50 to 0.89)

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Conclusions

- The response to 6-MRT indicates a (near) maximum effort for 75% (n=18) of the participants.
- The positive correlation between VO_{2peak} and distance on the 6-MRT suggests that the 6-MRT can serve as an estimation of oxygen consumption on an individual basis.

Ongoing work – VO_{2max} in CP

Material & Method

- Cross-sectional study
- VO2 max test
- Lactate threshold test

Population

- 14 (6 male) CP
- 30 (14 male) TD
- 13-40 years

- GMFCS II (1)
- GMFCS III (5)
- GMFCS IV (7)
- GMFCS V (1)

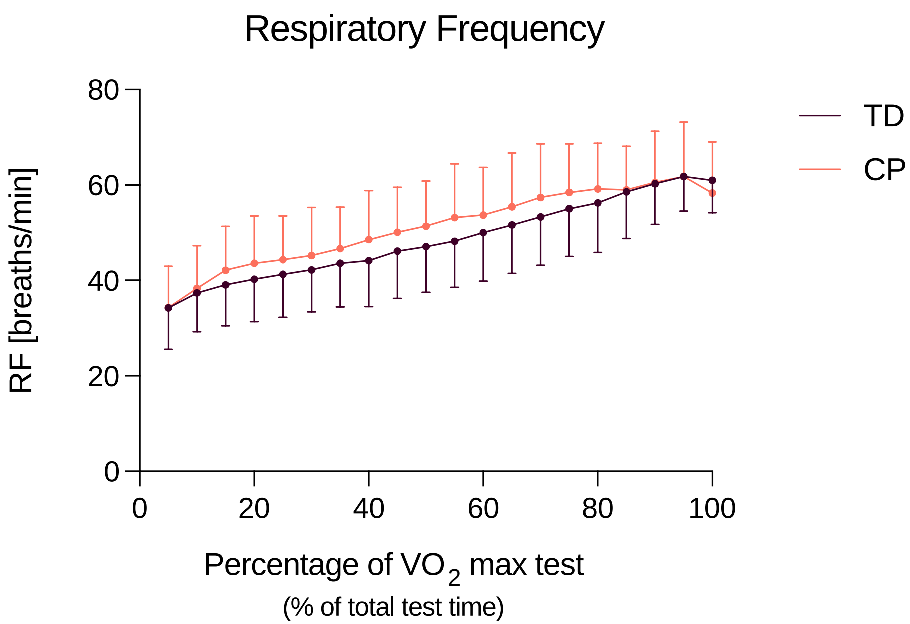
Experimental set up with a Frame Runner and a wide treadmill used for the lactate threshold test in individuals with CP

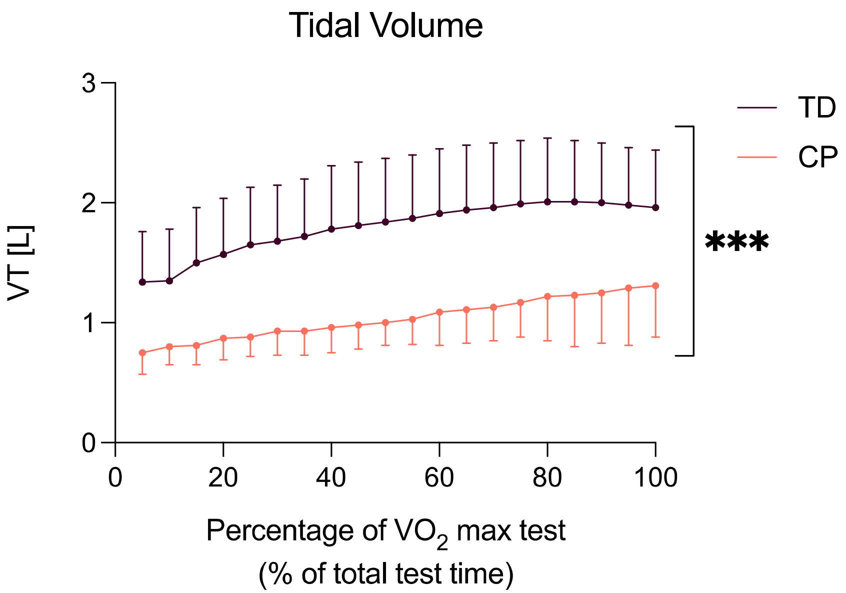
Example of an athlete performing Frame Running

Face mask used for gas exchange analysis

VO_2 maximal test

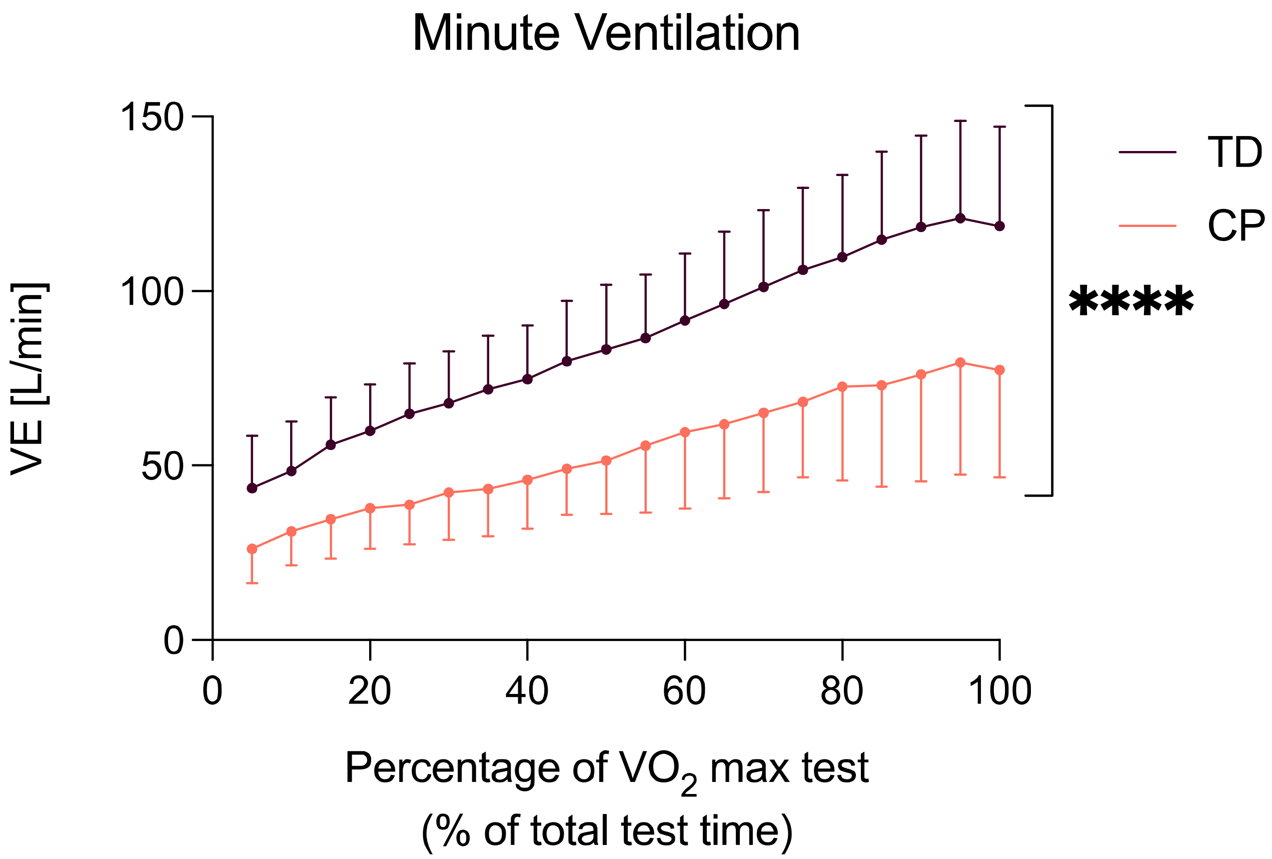
A maximal incremental exercise test





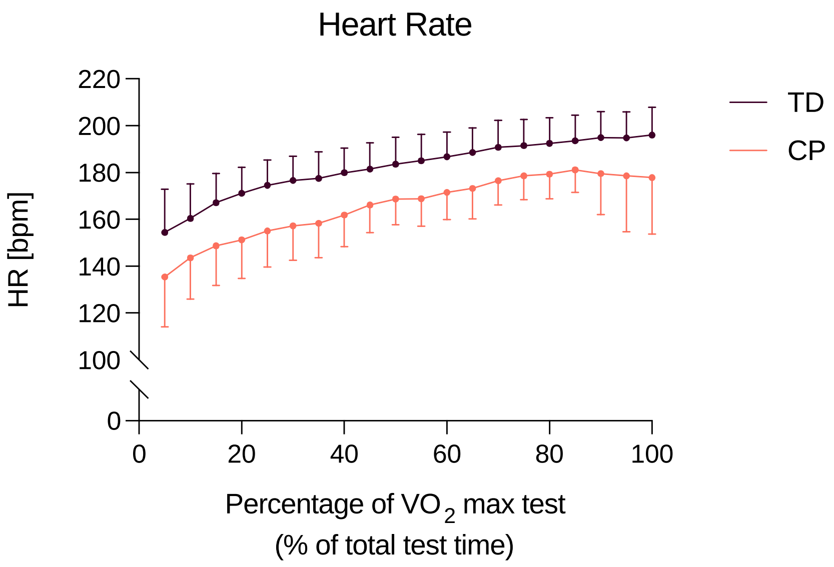
VO_2 maximal test

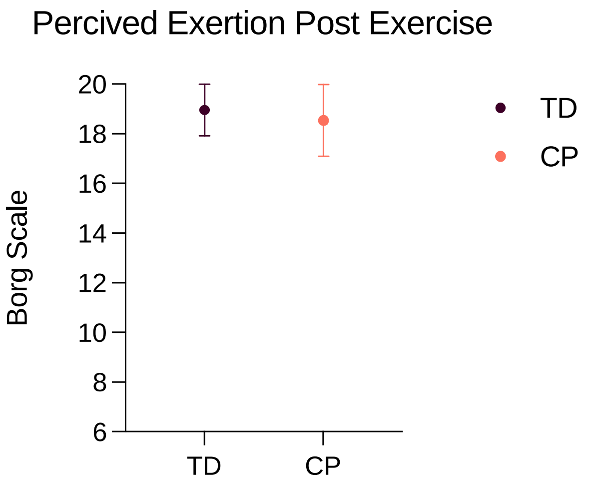
A maximal incremental exercise test



VO_2 maximal test

A maximal incremental exercise test

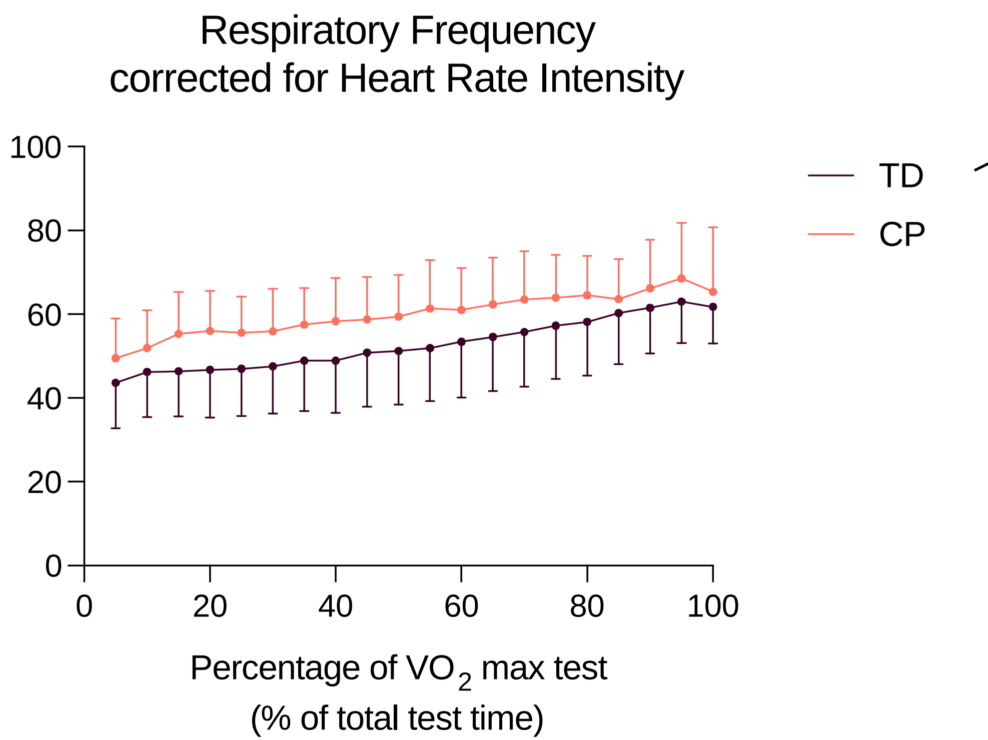




VO_2 maximal test

A maximal incremental exercise test

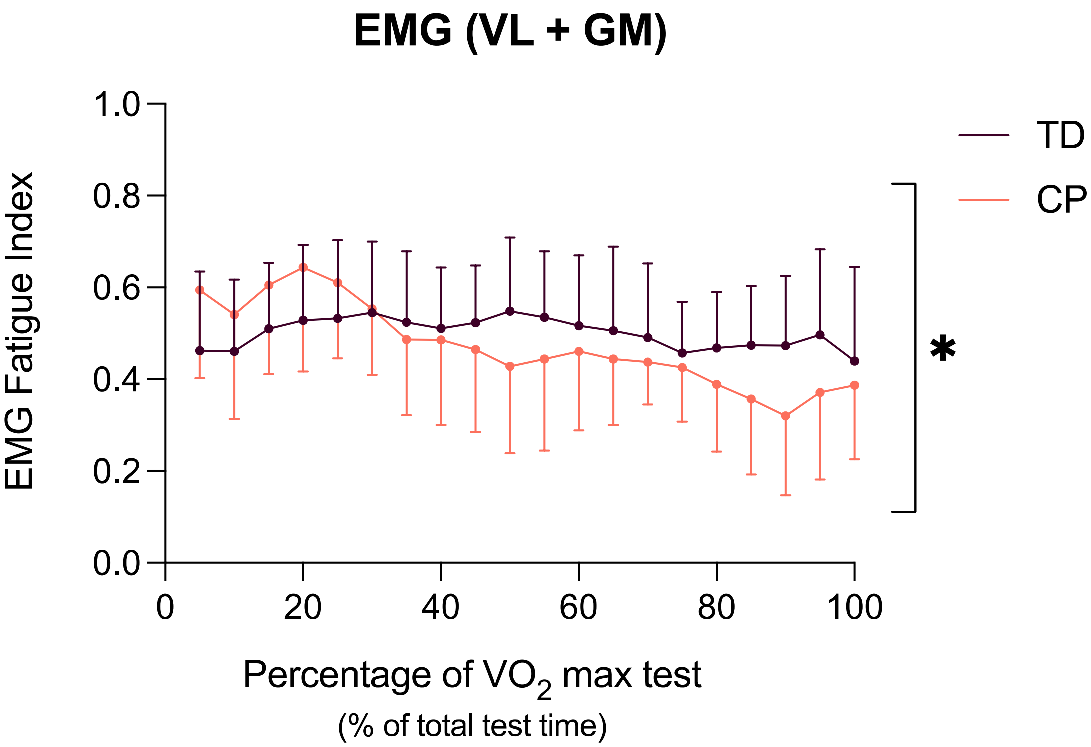
$$\frac{\text{HR}}{\text{Predicted HR max}}$$



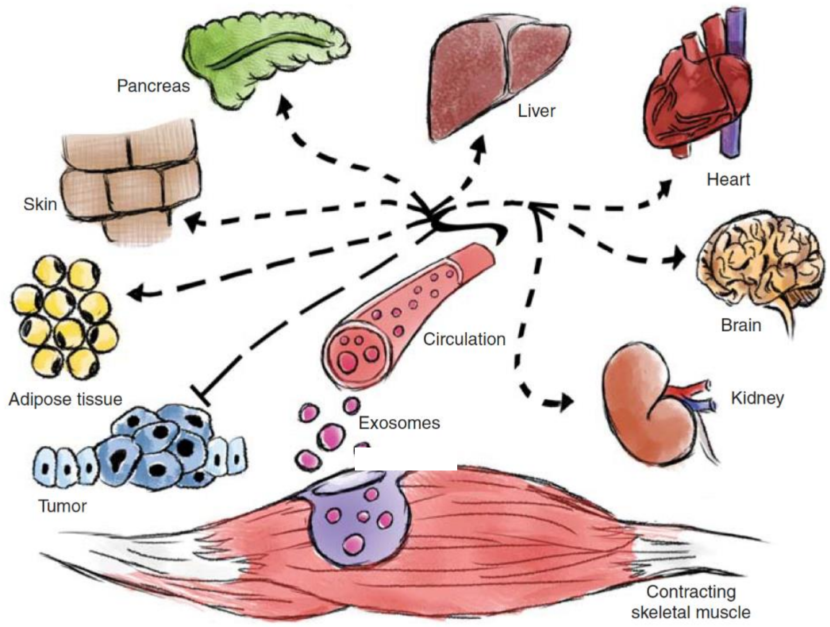
Respiratory frequency ”corrected” for heart rate intensity

VO_2 maximal test

Electromyography



Muscle as a secretory organ



Safdar & Tarnapolsky 2017. CSH Perspectives in Medicine

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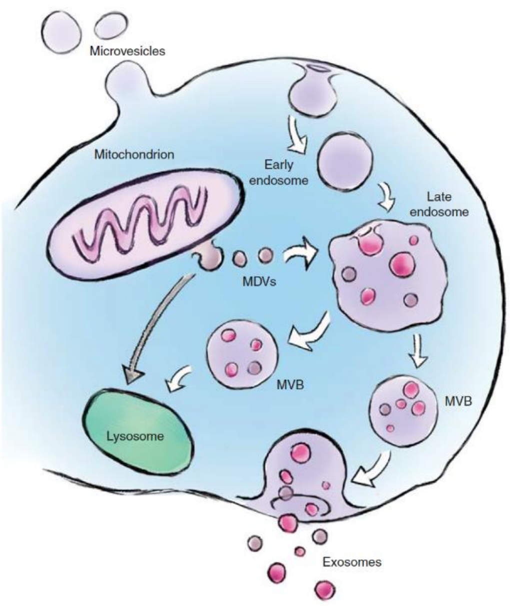
frontiers | Frontiers in Physiology

Extracellular vesicle characteristics and microRNA content in cerebral palsy and typically developed individuals at rest and in response to aerobic exercise

Ivan J. Vechetti[1], Jessica Norrbom[2], Björn Alkner[3], Emma Hjalmarsson[4], Alexandra Palmcrantz[4], Eva Pontén[4,5], Jessica Pingel[6], Ferdinand von Walden[4†] and Rodrigo Fernandez-Gonzalo[7,8*†]



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Acute endurance exercise

Group	Mean age	Weight (kg)	Height (cm)	BMI	Sex
TD PVC control	30±8	81.4±15.5	178±0.1	25.5±4.0	6 men/4 women
TD Exercise	28±7	78.7±17.0	176±0.1	25.2±4.7	6 men/4 women
CP Exercise	27±9	53.8±16.2	161±6.1	22.8±5.9	6 boys/4 girls

Lower concentration of extracellular vesicles in CP

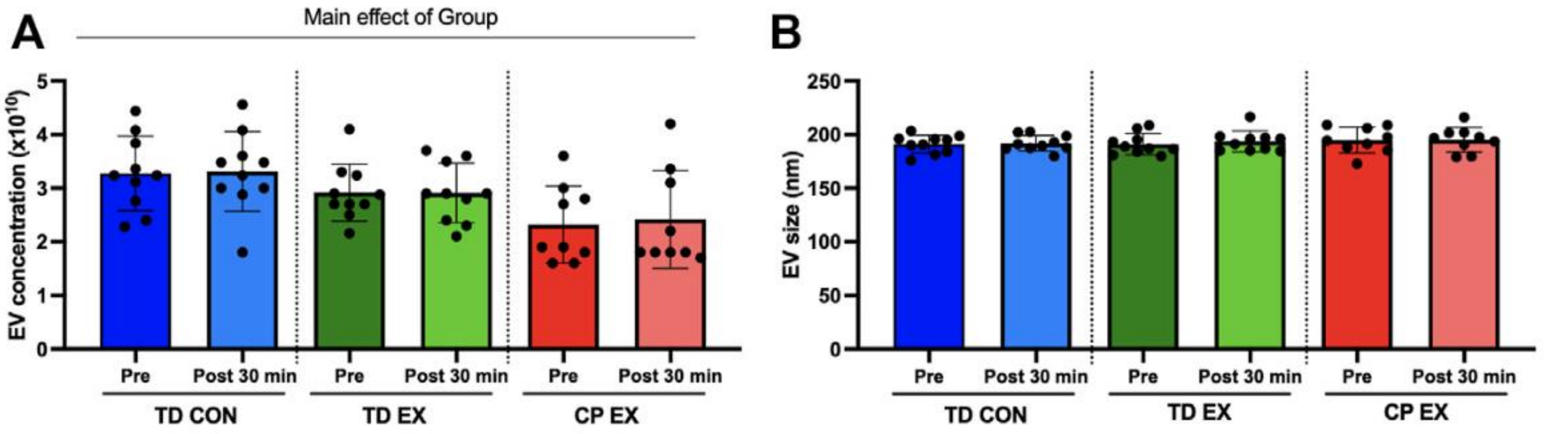
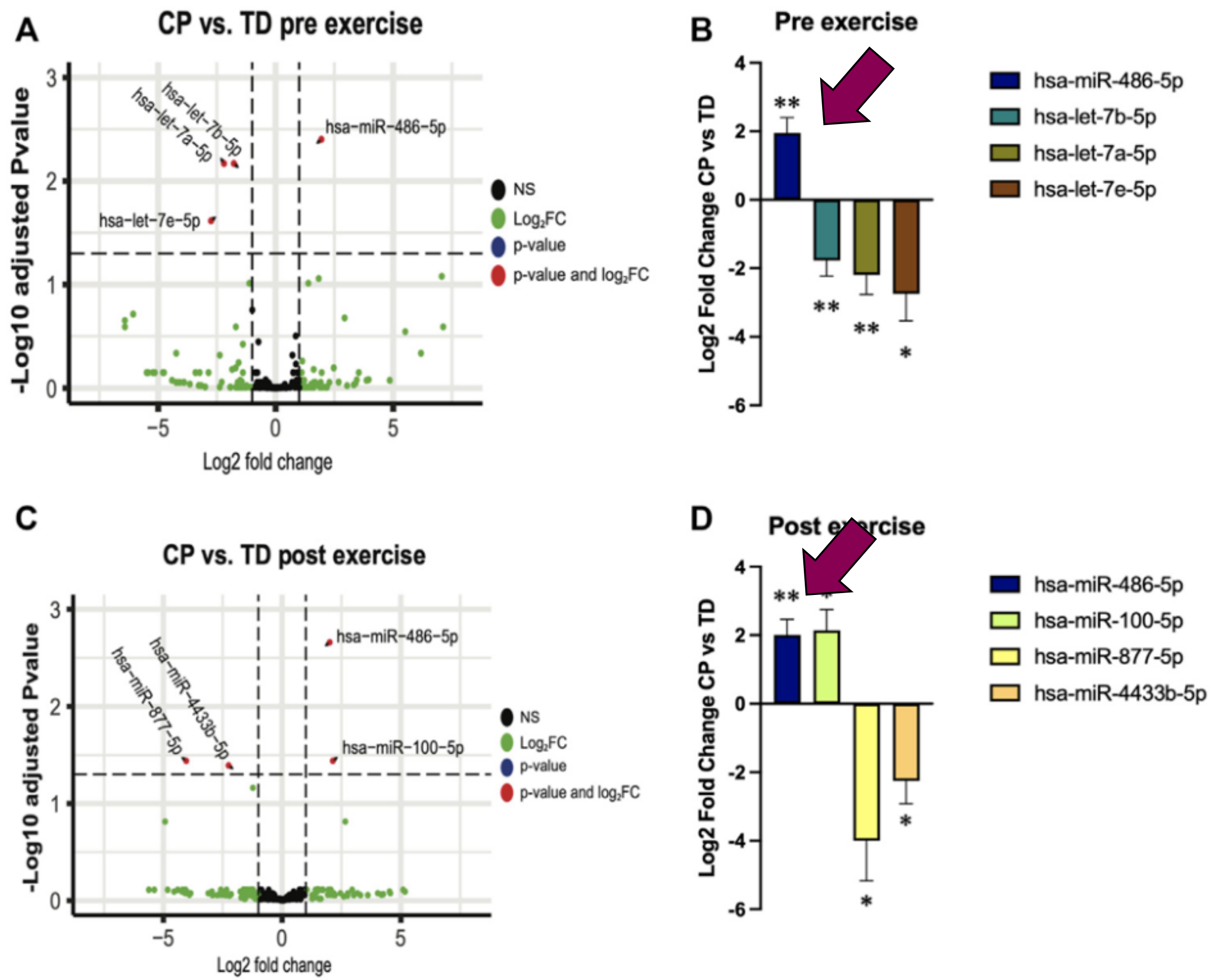
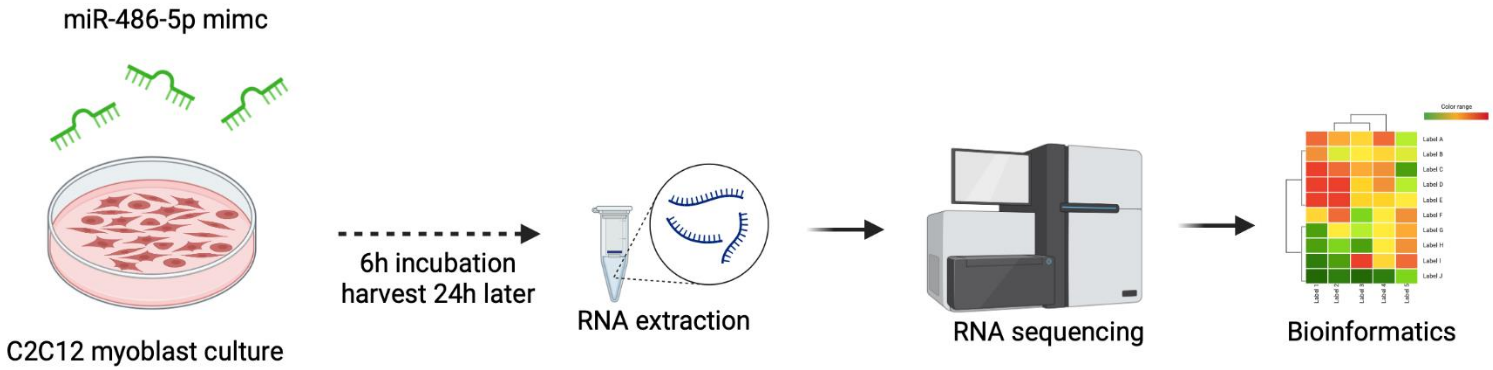


FIGURE 1
Extracellular vesicle (EV) characterization in typically developed (TD) and cerebral palsy (CP) individuals and its response to exercise. **(A)**; EV concentration (particles per mL of plasma) before (Pre) and after (Post) 30 min of aerobic exercise (EX) or control (CON). **(B)**; EV size before (Pre) and after (Post) 30 min of EX or CON condition.

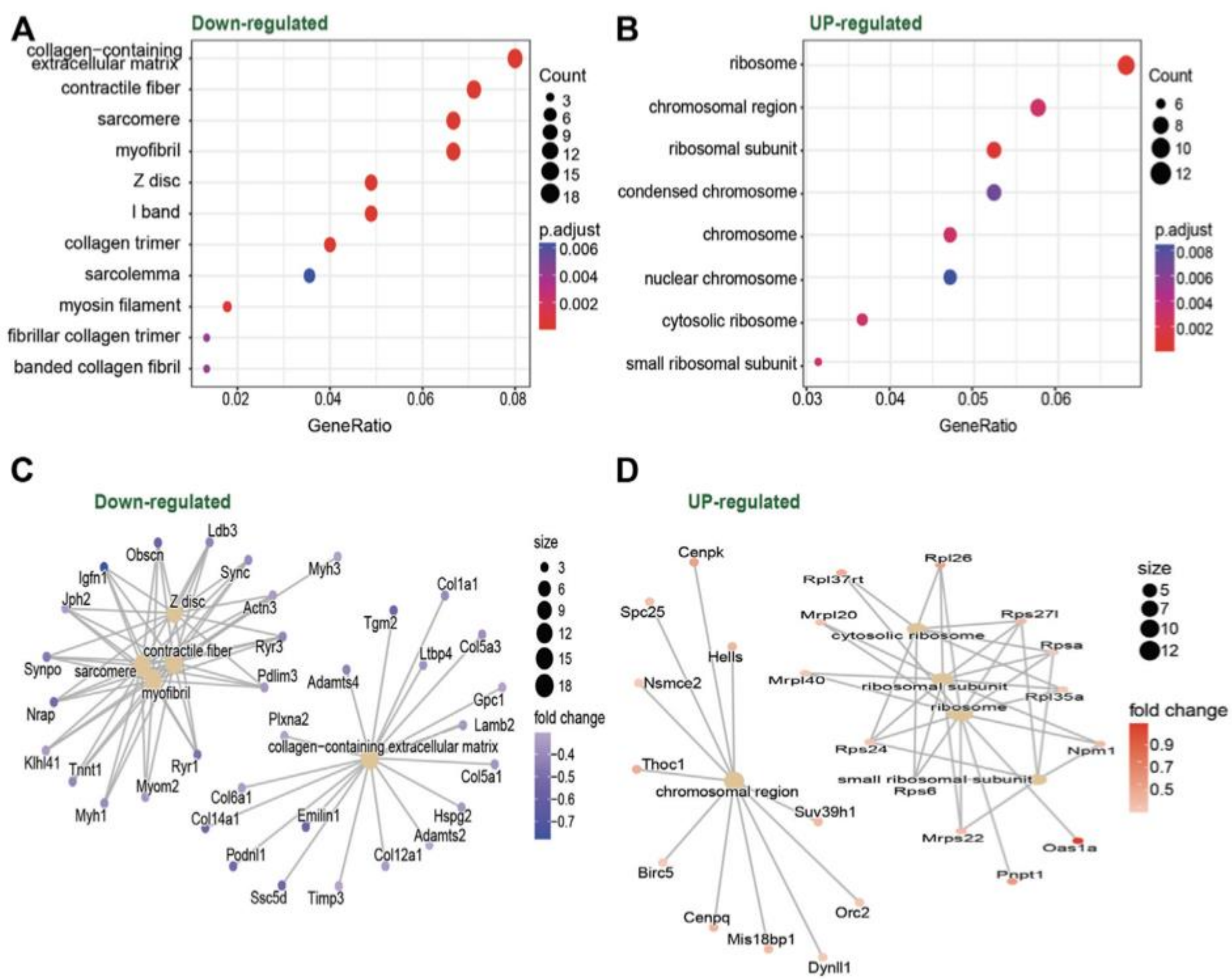
Extracellular vesicle miRNA levels in CP



In vitro experiments with synthetic miR486 on myogenic cells



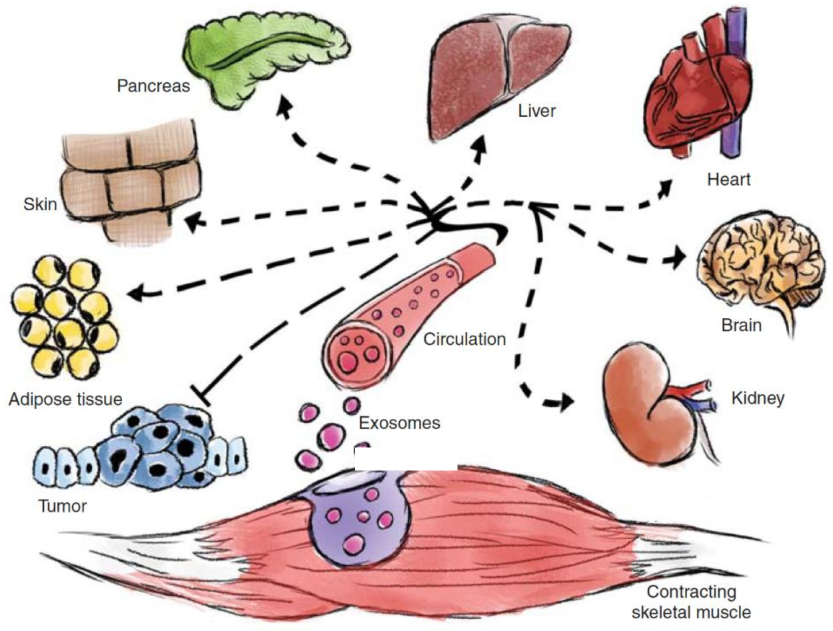
Influences ECM and growth pathways



Conclusions

- Plasma extracellular vesicle number is smaller in subjects with CP but size is the same.
- Extracellular vesicle miRNA content differs in subjects with CP.
- miR-486 is elevated in plasma Evs from indiviudals with CP.
- miR-486 influences ECM and growth related genes.

Muscle as a secretory organ



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Take home message

- Cerebral palsy is fairly common, 2/1000 kids.
- Skeletal muscle is macro/microscopically altered.
- Gene expression altered.
- Mitochondria fewer and less efficient?
- Physical fitness is low

- BUT trainable!
- Frame running is an efficient tool for moderate-high intensity exercise
- Ongoing research into aerobic capacity and metabolic function.

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Thank you!

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