

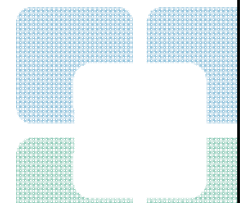
Aerobic Exercise and Nutrition as Tools in Stroke Recovery

Susan M. Linder, DPT, NCS



Disclosures

- I have no conflicts of interest to report related to this research
- I have received funding from the NIH and the American Heart Association/American Stroke Association



Course Objectives

At the end of the presentation, the participant will:

- Describe the potential mechanism underlying the recovery of motor function post-stroke via high intensity aerobic exercise
- Describe the methodology associated with applying aerobic exercise as an antecedent to motor task practice
- Discuss the motor and non-motor outcomes following aerobic exercise paradigms in individuals with chronic stroke
- Discuss the role of nutrition on stroke recovery

Historic Perspectives on Aerobic Exercise Training

Effects on cardiorespiratory fitness

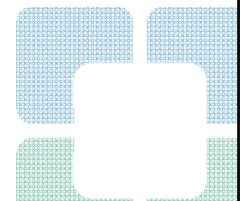
- Stroke: diminished peak aerobic capacity
- Moderate to vigorous intensity exercise has greater training effect than low intensity training



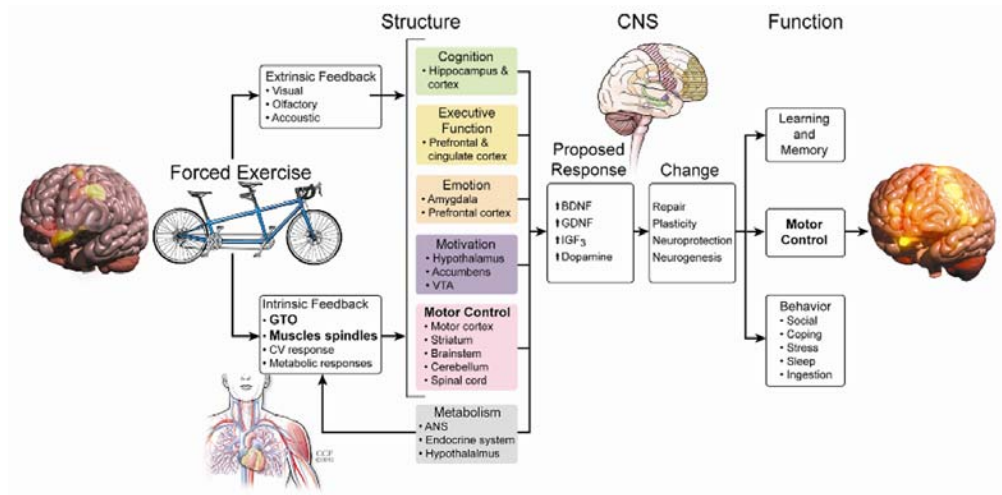
Taking A Serendipitous Finding from the Field into the Laboratory



Taking A Serendipitous Finding from the Field into the Laboratory



The Effects of Aerobic Exercise on Brain Function



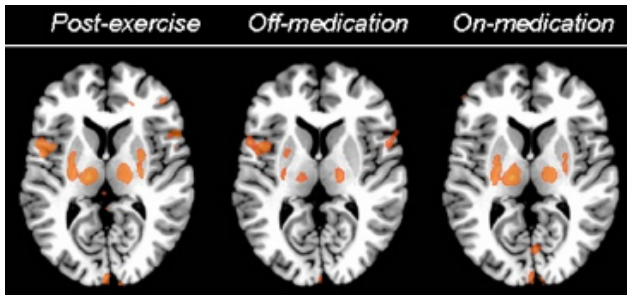
Alberts, 2011

What is Forced-Exercise in Humans?

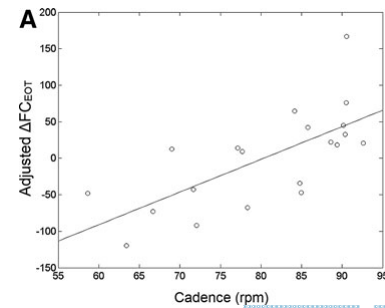
- Augmenting voluntary exercise effort
 - Exercise rate (cadence) increased by 30%
 - Consistent pedaling rate at high RPMs
- Designed to overcome barriers to intensive aerobic exercise training
- 60-80% target HR zone
- Participant is not passive



High Intensity Exercise Induces CNS Changes Measured with fMRI



FE and PD medication result in similar patterns of cortical and subcortical activation



Alberts 2011
Beall 2013
Alberts 2016

Can FE Enhance Recovery of Function after Stroke?

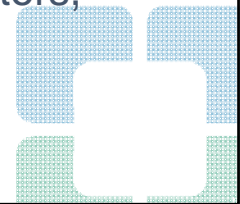
“I suppose it is tempting, if the only tool you have is a hammer, to treat everything as if it were a nail”

-Maslow, 1966



How Does Aerobic Exercise Relate to Stroke Recovery?

- Motor recovery post-stroke is largely reliant on motor learning-related neuroplasticity
 - BDNF, GDNF, IGF are mediators of neuroplasticity and motor learning post-stroke
 - Aerobic exercise has been shown to cause an endogenous upregulation of neurotrophic factors, including BDNF, GDNF, and IGF



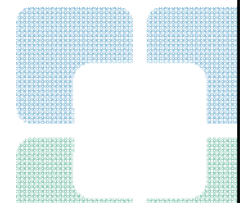
Forced Exercise Model Adapted to Stroke



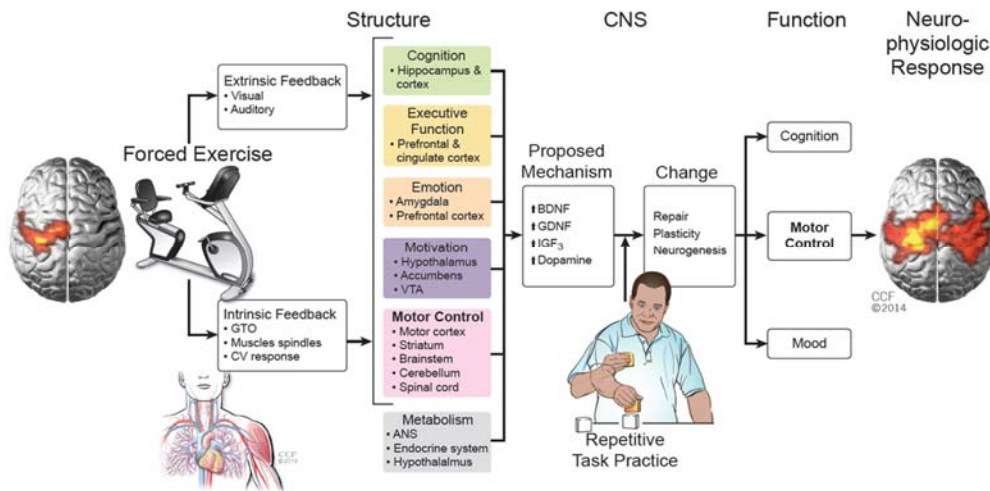
→ Prime the CNS →



→ Improved Rehabilitation Outcomes



Proposed Mechanism of Aerobic Exercise after Stroke



Investigating Two Time-Matched Modes of Aerobic Exercise Training

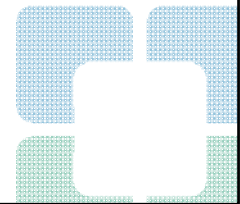
| | Forced Exercise | Voluntary Exercise |
|--|---------------------|--------------------|
| Exposure (sessions) | 24 | 24 |
| Duration (including 5-min warm up/cool down) | 45 min | 45 min |
| HR intensity | 60-80% HRR | 60-80% HRR |
| Rate (Cadence) | Self-selected + 30% | Self-selected |

Repetitive Task Practice (RTP)



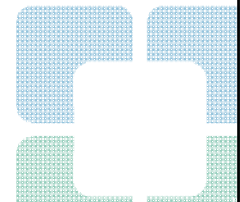
- Focus on maximizing reps
 - Selected 3-5 tasks/session
 - 75-100+ reps of each task
- Type of practice
 - ACTIVE
 - Incorporate ROM into functional activity
 - Blocked, target/goal-oriented, specificity of training
- Standing vs. Sitting
- Minimize rest time
- Grading of activities

 Cleveland Clinic



Study Aims

- To determine the effects of forced and voluntary exercise on motor function, non-motor function, and cardiovascular fitness in individuals with chronic stroke



Applying High Intensity Exercise to Individuals with Stroke

Hypothesis: Aerobic exercise will enhance motor recovery and non-motor function in individuals with stroke

Anticipated Outcome: Those in the FE group will have a greater recovery of motor and non-motor function than VE and RTP alone



↓
Prime the CNS for neuroplasticity



↓
Improved Rehabilitation Outcomes



Inclusion/Exclusion Criteria

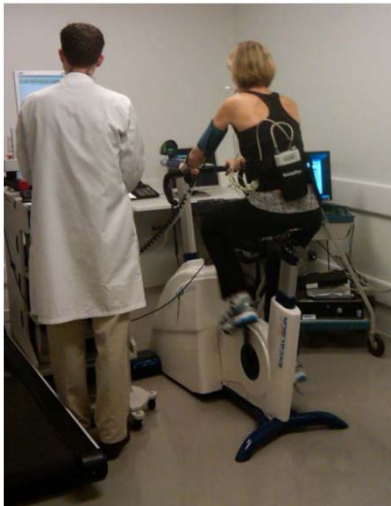
Inclusion

- 18-85 years old
- >6 months post ischemic stroke
- Approval from physician for stress test
- 19-55 on Fugl-Meyer upper extremity motor assessment
- Ability to follow 1-2 step commands

Exclusion

- Cardiac or pulmonary contraindication to exercise (cardiomyopathy, PE, A-fib, MI, etc.)
- Musculoskeletal contraindication to exercise
- Major psychiatric disorder
- Anti-spasticity injections (botox) within the past 3 mo
- Uncontrolled HTN

Cardiovascular Screening & Monitoring



Cardiopulmonary Exercise Test

- Target Heart Rate Established: 60-80% HRR

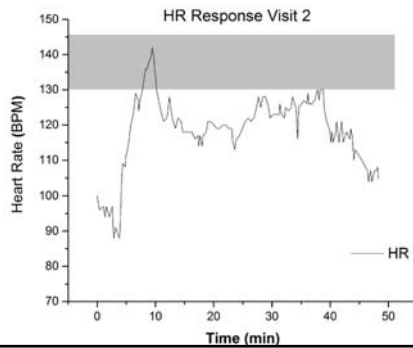
Monitoring During Exercise

- Continuous Heart Rate
- RPE
- Blood Pressure

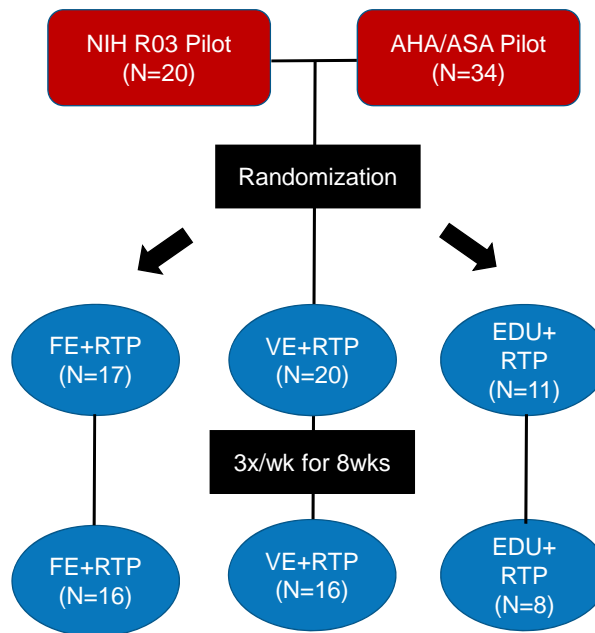
Cardiovascular Monitoring



- Continuous Heart Rate
- RPE
- Blood Pressure

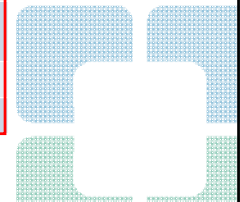


Study Overview: 2 Pilot RCT's

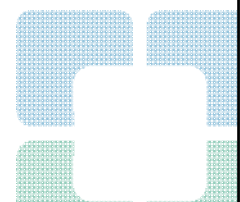


Baseline Demographics

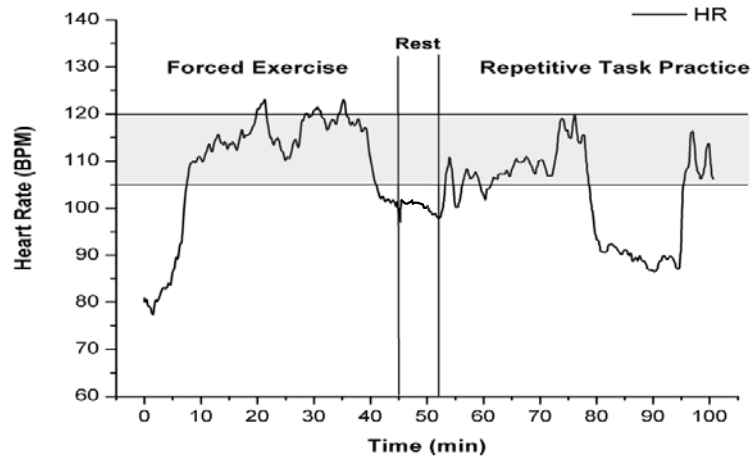
| Factor | FE + RTP (N=16) | VE + RTP (N=16) | RTP + Education (N=8) | p-value |
|--|--------------------|--------------------|-----------------------------|---------|
| Age | 51±12 | 60±14 | 58±12 | 0.14 |
| Female gender (versus male) | 12 (75%) | 10 (62%) | 7 (88%) | 0.43 |
| Race: | | | | 0.11 |
| African American | 8 (50%) | 3 (19%) | 4 (50%) | |
| Asian | 1 (6%) | 1 (6%) | 0 (0%) | |
| Other | 2 (12%) | 0 (0%) | 1 (12%) | |
| White | 5 (31%) | 12 (75%) | 3 (38%) | |
| Hispanic ethnicity | 1 (6%) | 0 (0%) | 1 (12%) | 0.67 |
| Dominant side affected (versus non-dominant) | 10 (62%) | 7 (44%) | 5 (62%) | 0.65 |
| Months since stroke | 12 [7,16] | 16 [11,32] | 17 [12,35] | 0.23 |
| Baseline Fugl Meyer score | 37±8 | 33±11 | 33±9 | 0.40 |



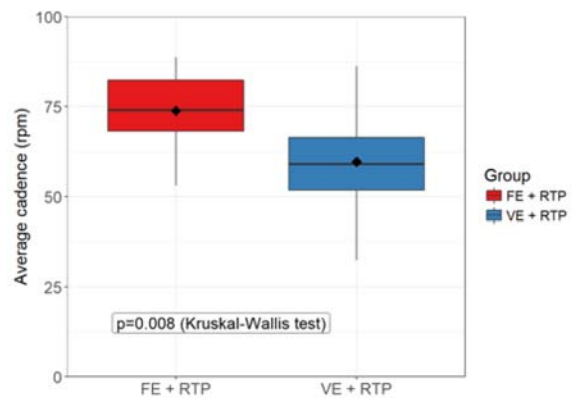
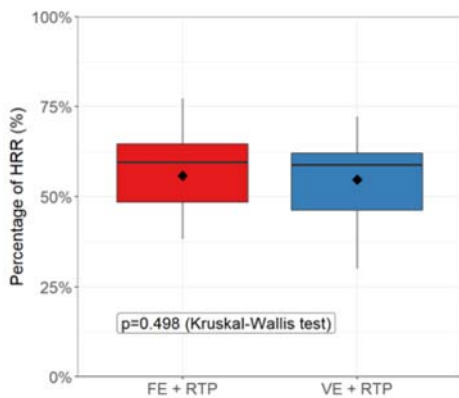
Training Variables



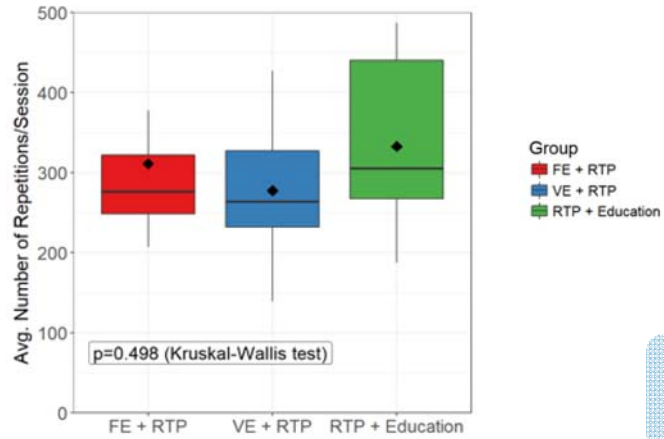
Representative Day of HR Data



Aerobic Exercise Training Variables

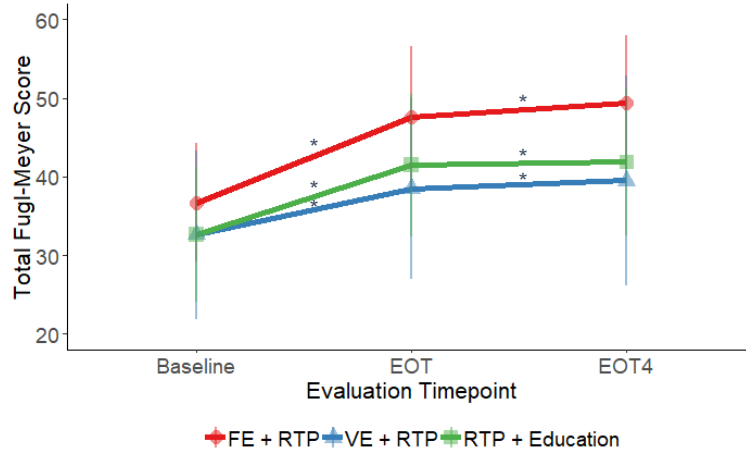


RTP Training Variables



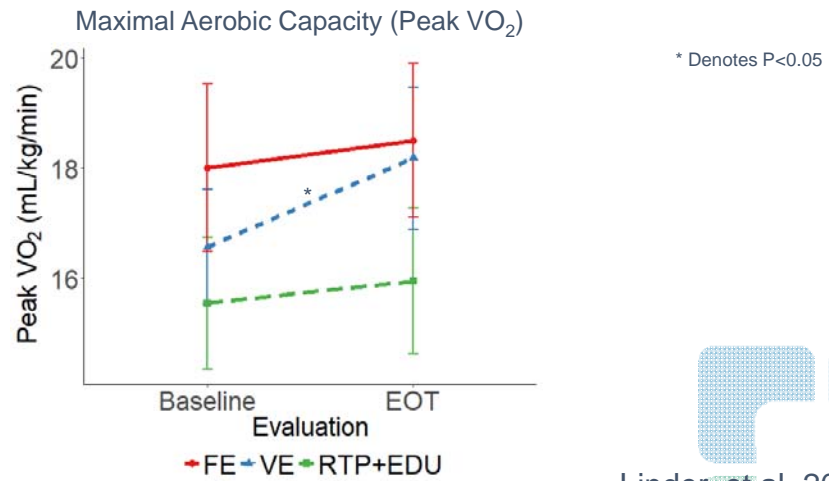
Motor Outcomes

Improved Motor Recovery: UE Fugl-Meyer Motor Score



Cardiovascular Outcomes

Improved Cardiovascular Function and Endurance

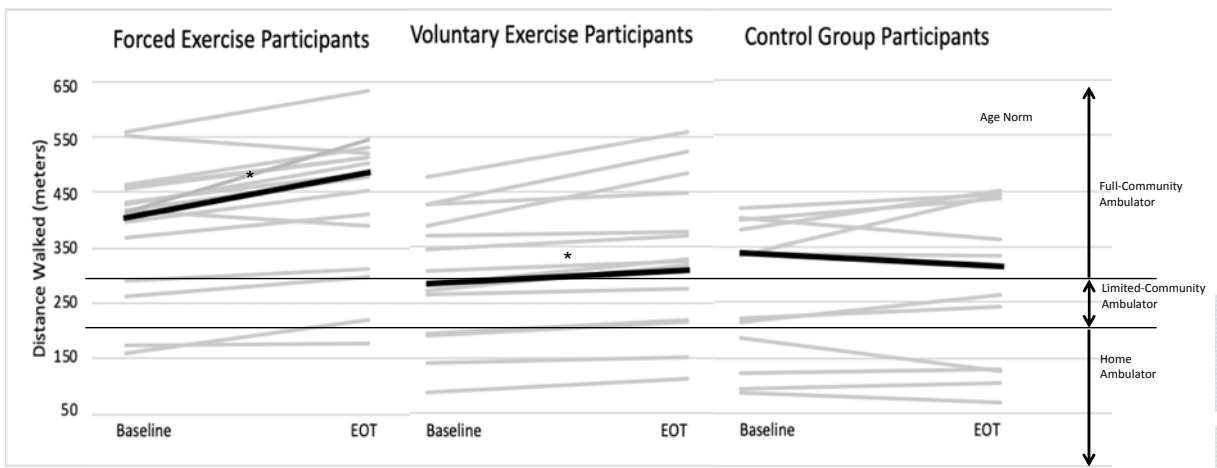


Linder, et al, 2020

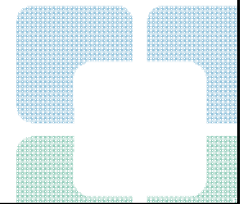
Improved Walking Capacity

Six-Minute Walk Test

* Denotes P<0.05

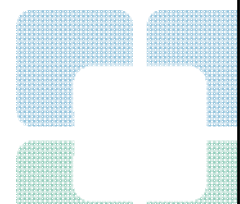


Quality of Life Outcomes

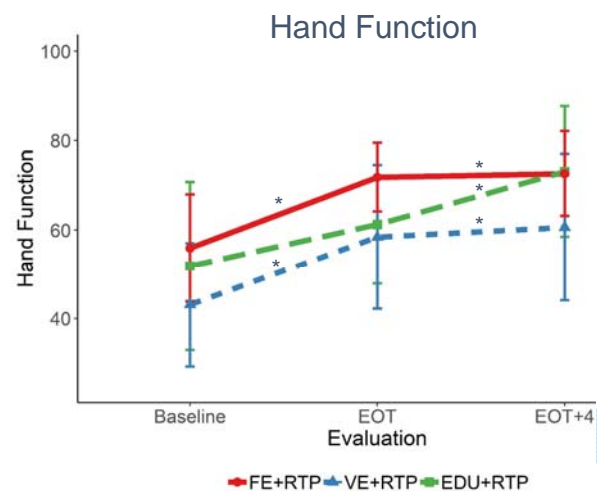
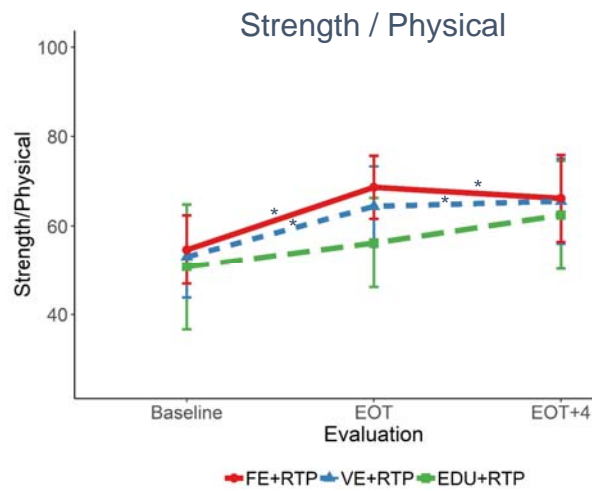


Stroke Impact Scale

- Physical / Strength
- Mobility
- Hand Function
- Activities of Daily Living
- Memory / Thinking
- Communication
- Mood / Emotions
- Meaningful Activities (Participation)
- Stroke Recovery (self-reported)



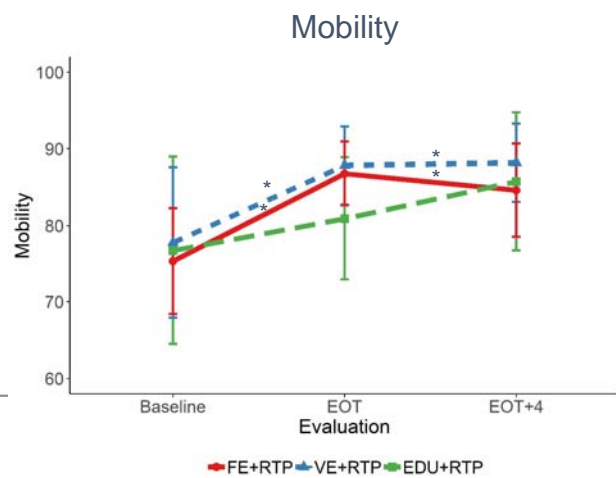
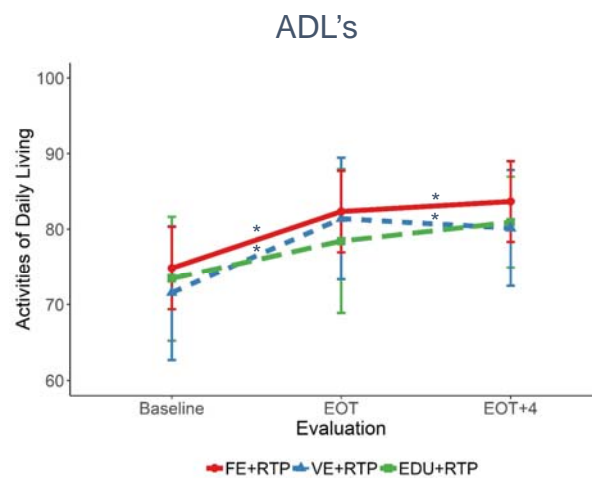
Aerobic Exercise Improved QOL



* Denotes P<0.05

Rosenfeldt, et al, 2019

Aerobic Exercise Improved QOL



* Denotes P<0.05

Conclusions

- Motor Function
 - All 3 groups improved significantly on the FMA
 - Improvements on the FMA by the FE+RTP group were greater than the other groups
- Cardiovascular Function
 - Significant improvements in cardiovascular fitness and walking capacity for exercisers

Conclusions

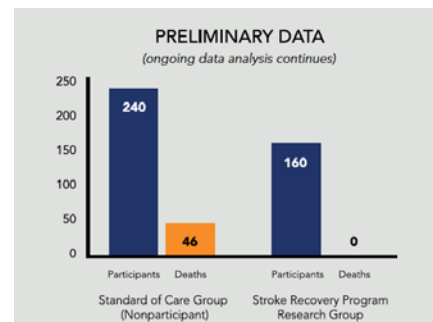
- Quality of Life
 - FE and VE groups improved in all motor domains
- Killing 4 birds with 1 stone? (Ploughman, 2016)
 - Reparative
 - Neuroplastic
 - Cardiorespiratory
 - Metabolic

Other Studies Corroborate Our Findings

- High intensity interval training (Boyne, 2019)
 - Improved recovery of gait
 - Higher levels of peripheral BDNF
 - Increased corticospinal excitability (TMS)
 - Intensity sufficient to accumulate blood lactate was important for eliciting BDNF response
- Single bout of high-intensity cycling (Mang, 2014)
 - Improved implicit motor learning

JFK Rehabilitation Institute

Stroke Recovery Program- Stroke HEART™ Trials



[Cuccurullo S](#), Fleming TK, Kostis WJ, Greiss C, Gizzi M, Eckert A, Ray AR, Scarpati R, Cosgrove N, Beavers T, Cabrera J, Sargsyan D, Kostis JB. *Impact of a Novel Stroke Recovery Program Integrating Cardiac Rehabilitation on All-cause Mortality, Cardiovascular Performance and Functional Performance.*

Clinical Translation

Aerobic exercise



Motor Task Practice



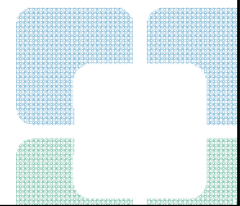
 Cleveland Clinic

StEP: Long-term Group Exercise Program



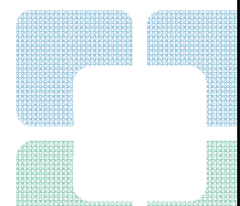
- Hospital-based group cycling class for stroke survivors
- Supervised by PT or PTA

Nutritional Considerations in Stroke Recovery



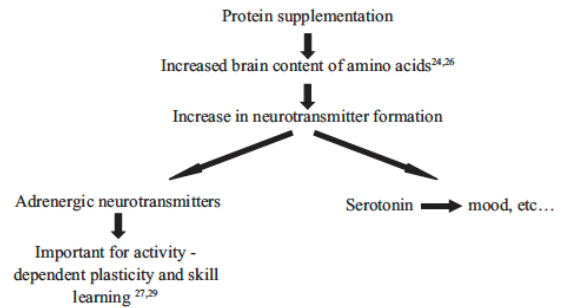
Nutrition for Brain Recovery – Acute Ischemic Stroke

- Acute ischemia induces profound alterations of brain protein synthesis and brain glucose metabolism
- Primarily due to alterations in cellular homeostasis



Nutrition for Brain Recovery – Acute Ischemic Stroke

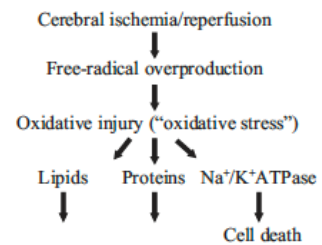
- Protein supplementation
 - Greater reductions in NIHSS scores at 21 days
- Excess carbohydrate intake
 - May increase lactate production leading to greater neuronal destruction



Aquilani R, et al. Nutrition for Brain Recovery After Ischemic Stroke: An Added Value to Rehabilitation. *Nutrition in Clinical Practice*. 2011;26(3):339-45.

Nutrition for Brain Recovery – Acute Ischemic Stroke

- Cellular damage in cerebral ischemia partly caused by oxidative damage due to free radical formation and lipid peroxidation
- Vitamins E & C – potent anti-oxidants
- B-group vitamins may also mitigate oxidative damage



- Damage to:
- plasma and mitochondrial membranes
 - enzymes
 - receptors
 - membrane transport systems

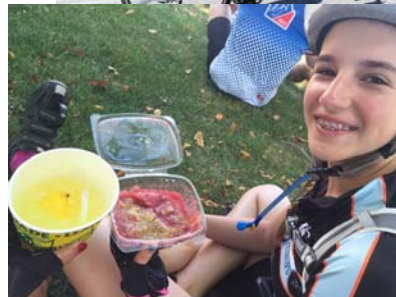
Aquilani R, et al. Nutrition for Brain Recovery After Ischemic Stroke: An Added Value to Rehabilitation. *Nutrition in Clinical Practice*. 2011;26(3):339-45.

Nutrition for Brain Recovery – Considerations for Chronic Stroke

- Most common factors associated with suboptimal nutritional status
 - Excess caloric intake
 - Reduced protein intake
 - Micronutrient deficiencies (B-vitamins, Vitamin D, Omega 3's)
- Mitigating the risk of recurrent stroke by addressing cardiovascular risk factors

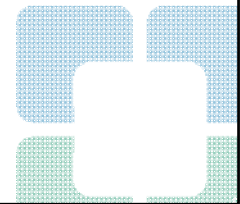
Serra M. The importance of assessing nutritional status to ensure optimal recovery during the chronic phase of stroke. *Stroke Research and Treatment*. 2018;1-8.

Pedaling for Parkinson's - Iowa



Acknowledgements

- Jay Alberts, PhD
- Anson Rosenfeldt, DPT, MBA
- Sara Davidson, PTA
- Cindy Clark, OT/R
- Amanda Penko, PhD
- Mandy Miller Koop, PhD
- Nicole Zimmerman, MS



Every life deserves world class care.

References

1. Miller EL, Murray L, Richards L, et al. Comprehensive overview of nursing and interdisciplinary rehabilitation care of the stroke patient: a scientific statement from the American Heart Association. *Stroke*. 2010;41(10):2402-2448.
2. Rosamond W, Flegal K, Furie K, et al. Heart disease and stroke statistics--2008 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2008;117(4):e25-146.
3. Dobkin BH, Dorsch A. New evidence for therapies in stroke rehabilitation. *Current atherosclerosis reports*. 2013;15(6):331.
4. Winstein CJ, Wolf SL, Dromerick AW, et al. Effect of a Task-Oriented Rehabilitation Program on Upper Extremity Recovery Following Motor Stroke: The ICARE Randomized Clinical Trial. *JAMA*. 2016;315(6):571-581.
5. Dobkin BH. Clinical practice. Rehabilitation after stroke. *N Engl J Med*. 2005;352(16):1677-1684.
6. Mang CS, Campbell KL, Ross CJ, et al. Promoting neuroplasticity for motor rehabilitation after stroke: considering the effects of aerobic exercise and genetic variation on brain-derived neurotrophic factor. *Phys Ther*. 2013;93(12):1707-1716.
7. MacKay-Lyons MJ, Makrides L. Cardiovascular stress during a contemporary stroke rehabilitation program: Is the intensity adequate to induce a training effect? *Archives of Physical Medicine and Rehabilitation*. 2002;83(10):1378-1383.
8. Singh AM, Neva JL, Staines WR. Aerobic exercise enhances neural correlates of motor skill learning. *Behavioural brain research*. 2016;301:19-26.
9. Singh AM, Duncan RE, Neva JL, et al. Aerobic exercise modulates intracortical inhibition and facilitation in a nonexercised upper limb muscle. *BMC Sports Sci Med Rehabil*. 2014;6:23.
10. Singh AM, Staines WR. The effects of acute aerobic exercise on the primary motor cortex. *J Mot Behav*. 2015;47(4):328-339.
11. Knaepen K, Goekint M, Heyman EM, et al. Neuroplasticity - Exercise-induced response of peripheral brain-derived neurotrophic factor. *Sports medicine*. 2010;40(9):765-801.
12. Ploughman M, Austin MW, Glynn L, et al. The effects of poststroke aerobic exercise on neuroplasticity: a systematic review of animal and clinical studies. *Transl Stroke Res*. 2015;6(1):13-28.
13. Mang CS, Brown KE, Neva JL, et al. Promoting Motor Cortical Plasticity with Acute Aerobic Exercise: A Role for Cerebellar Circuits. *Neural Plast*. 2016;2016:6797928.

References

14. Ploughman M, Windle V, MacLellan CL, et al. Brain-derived neurotrophic factor contributes to recovery of skilled reaching after focal ischemia in rats. *Stroke*. 2009;40(4):1490-1495.
15. Coelho FG, Gobbi S, Andreatto CA, et al. Physical exercise modulates peripheral levels of brain-derived neurotrophic factor (BDNF): a systematic review of experimental studies in the elderly. *Arch Gerontol Geriatr*. 2013;56(1):10-15.
16. Gatti R, De Palo EF, Antonelli G, et al. IGF-I/IGFBP system: metabolism outline and physical exercise. *J Endocrinol Invest*. 2012;35(7):699-707.
17. Statton MA, Encarnacion M, Celnik P, et al. A Single Bout of Moderate Aerobic Exercise Improves Motor Skill Acquisition. *PLoS one*. 2015;10(10):e0141393.
18. Mang CS, Snow NJ, Campbell KL, et al. A single bout of high-intensity aerobic exercise facilitates response to paired associative stimulation and promotes sequence-specific implicit motor learning. *Journal of applied physiology*. 2014;117(11):1325-1336.
19. Smith AE, Goldworthy MR, Garside T, et al. The influence of a single bout of aerobic exercise on short-interval intracortical excitability. *Exp Brain Res*. 2014;232(6):1875-1882.
20. Cotman CW, Berchtold NC, Christie LA. Exercise builds brain health: key roles of growth factor cascades and inflammation. *Trends in neurosciences*. 2007;30(9):464-472.
21. Erickson KI, Miller DL, Roecklein KA. The aging hippocampus: interactions between exercise, depression, and BDNF. *Neuroscientist*. 2012;18(1):82-97.
22. Rand D, Eng JJ, Liu-Ambrose T, et al. Feasibility of a 6-month exercise and recreation program to improve executive functioning and memory in individuals with chronic stroke. *Neurorehabil Neural Repair*. 2010;24(8):722-729.
23. Baker L FL, Foster-Schubert K, Green PS, Wilkinson CW, McTiernan A, Plymate SR, Fishel MA, Watson GS, Cholerton BA, Duncan GE, Mehta PD, Craft S. Effects of aerobic exercise on mild cognitive impairment. *Archives of neurology*. 2010;67(1):71-79.
24. Colcombe S, Kramer AF. Fitness effects on the cognitive function of older adults: a meta-analytic study. *Psychological science*. 2003;14(2):125-130.
25. Basso JC, Suzuki WA. The Effects of Acute Exercise on Mood, Cognition, Neurophysiology, and Neurochemical Pathways: A Review. *Brain Plast*. 2017;2(2):127-152.
26. Morgan JA, Singhal G, Corrigan F, et al. The effects of aerobic exercise on depression-like, anxiety-like, and cognition like behaviours over the healthy adult lifespan of C57BL/6 mice. *Behavioural brain research*. 2018;337:193-203.

References

27. Alberts JL, Linder SM, Penko AL, et al. It is not about the bike, it is about the pedaling: forced exercise and Parkinson's disease. *Exercise and sport sciences reviews*. 2011;39(4):177-186.
28. Alberts JL, Phillips M, Lowe MJ, et al. Cortical and motor responses to acute forced exercise in Parkinson's disease. *Parkinsonism & related disorders*. 2016;24:56-62.
29. Beall EB, Lowe MJ, Alberts JL, et al. The effect of forced-exercise therapy for Parkinson's disease on motor cortex functional connectivity. *Brain connectivity*. 2013;3(2):190-198.
30. Ridgel AL, Vitek JL, Alberts JL. Forced, not voluntary, exercise improves motor function in Parkinson's disease patients. *Neurorehabil Neural Repair*. 2009;23(6):600-608.
31. Alberts JL, Linder S, Penko AL, Lowe MJ, Phillips M. It is not about the bike, it is about the pedaling: forced exercise and Parkinson's disease. *Exercise Sports Science Reviews*. 2011;37(4):177-186.
32. Ridgel AL, Vitek J, Alberts JL. Forced, not voluntary, exercise improves motor function in Parkinson's disease patients. *Neurorehabil and neural rep*. 2009;23(6):600-608.
33. Linder SM, Rosenfeldt AB, Rasanow M, et al. Forced Aerobic Exercise Enhances Motor Recovery After Stroke: A Case Report. *The American journal of occupational therapy : official publication of the American Occupational Therapy Association*. 2015;69(4):6904210010p6904210011-6904210018.
34. Linder SM, Rosenfeldt AB, Dey T, et al. Forced Aerobic Exercise Preceding Task Practice Improves Motor Recovery Poststroke. *The American journal of occupational therapy : official publication of the American Occupational Therapy Association*. 2017;71(2):7102290020p7102290021-7102290029p7102290029.
35. Ryan AS, Dobrovolsky CL, Smith GV, et al. Hemiparetic muscle atrophy and increased intramuscular fat in stroke patients. *Arch Phys Med Rehabil*. 2002;83(12):1703-1707.
36. Riebe D, Franklin BA, Thompson PD, et al. Updating ACSM's recommendations for exercise preparticipation health screening. *Medicine Sci Sport Exer*. 2015;2473-2479. DOI: 10.1249/MSS.0000000000000664
37. Tajiri N, Yasuhara T, Shingo T, et al. Exercise exerts neuroprotective effects on Parkinson's disease model of rats. *Brain Res*. 2010;1310:200-207
38. Ploughman M, Windle V, MacLellan CL, White N Doré JJ, Corbett D. Brain-Derived Neurotrophic Factor Contributes to Recovery of Skilled Reaching After Focal Ischemia in Rats. *Stroke*. 2009;40:1490-1495.

