Accelerated Cure Project for MS

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Accelerating research towards a cure for multiple sclerosis

Physical fitness and Multiple Sclerosis: To exercise or not to exercise?

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Earlier this week I was moderating a group discussion among first year medical students on a hypothetical medical case where a physician prescribed his diabetic patient to lose fifty pounds and exercise regularly in order to manage their chronic condition. The students initially thought nothing of this statement, but as we revisited the *prescription*, they realized the prescription was non-specific without an actionable plan to encourage adherence and compliance of the diabetic patient to the *treatment*. The physician did not give any practical advice on nutrition, healthier food substitutes, best practices for weight loss, or where to begin with exercise – thus, the hypothetical patient would have been left uninformed and unfortunately be stuck with the same old habits. The students and I spoke about various approaches to improving the *prescription*, for example motivational interviewing by the physician as a means of identifying the patient's values and desires, and using that information to facilitate and encourage personal behavior change. I am the first to admit I have always been biased to the positive possibilities of exercise on physical and mental health, but for several years I saw exercise as a luxury, competing with the limited time I had to spend on *more* important things. Fortunately, I had an academic coach use

motivational interviewing to help me realize exercising was a cornerstone of my daily life, and by exercising, I was more productive and effective when I applied myself to other activities. This month there were several publications, not on motivational interviewing, but on physical activity – suggesting exercise improves various outcomes in MS.

The first publication, by Claflin *et al*, was a systematic review of 9 exercise studies published between 2001 and 2016[1], which included 260 persons with MS (PwMS). These studies were individually small, often exploratory (thus lacking replication), with varying study designs and health outcomes measured. However, when the 9 studies were reviewed collectively, they demonstrated exercise improved health outcomes for PwMS, particularly mobility and muscular strength.

The second article was a randomized controlled trial of 62 PwMS with substantial mobility disability (EDSS>4 [significant disability but able to walk without aid or rest for 500m] and <6 [requires a walking aid to walk 100m]), conducted by Sandroff *et al*[2]. PwMS were assigned to one of two 6-month programs: 1) multimodal exercise training (a combination of aerobic, resistance and balance exercises – this was the *intervention*), or 2) stretching-and-toning (the *placebo/control* activity). The two groups of PwMS did not differ at baseline, and multiple aspects of mobility, gait, physical fitness, and cognitive processing speed were measured. After 6 months, the participants in the multimodal exercise group significantly improve their walking speed (distance covered in 6 minutes), peak power (a measure of physical fitness), and scores on a cognitive processing speed test (3' Paced Auditory Serial Addition Test; PASAT), compared to the stretching-and-toning group. Overall, this study provide preliminary evidence suggesting multimodal exercise training might be a useful rehabilitative approach to improve various outcomes in PwMS who already have substantial disability, and adds support to Claflin's systematic review.

[1] https://www.ncbi.nlm.nih.gov/pubmed/28768821

[2] https://www.ncbi.nlm.nih.gov/pubmed/28732757

The last study that caught my attention was by Souza *et al*, and was not a study of humans, but of mice with experimental autoimmune encephalomyelitis (EAE), an animal model of MS[3]. The mice were randomly distributed to 4 groups: naïve, EAE, EAE plus strength training (ST), and EAE plus endurance training (ET). How does one strength train a mouse? Well the animals were first familiarized to climbing a ladder from bottom to top. Then a small load was secured to the base of each animal's tail, and the animals were then trained to climb the ladder for 30 minutes in a series of repetitions and breaks. The training last 5 days a week, for 4 weeks. The load was also increased over time. The mice in the ET group were habituated to a treadmill at 10m/min for 10min/day – the *running* program was increased in speed and duration to 13-17 m/mins for 5 days/week for 4 weeks also. The researchers evaluated many outcomes, and ST and ET had numerous positive outcomes. The most striking and relatable are the observations for the accrual of disability after initiation of EAE (**Figure 1**). Both the ST and ET groups had lower clinical scores (less severe disease), and the ET group had a delayed onset of symptoms (~day 15), compared to the EAE group that did not exercise. The study also demonstrated ST and ET reduced oxidative stress, the production of inflammatory cytokines, and permeability of the blood-brain-barrier – these results are fascinating.

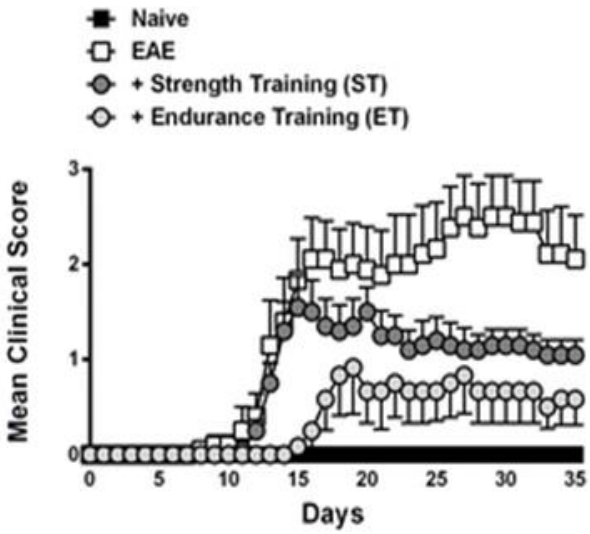

Figure 1: ST and ET inhibited the development of EAE. (Adapted from Souza, P.S., Gonçalves, E.D., Pedroso, G.S. et al. Mol Neurobiol (2017) 54: 4723)

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[3] https://www.ncbi.nlm.nih.gov/pubmed/27447807

Overall, these 3 publications continue to emphasize that exercise has a positive impact on various outcomes in PwMS. The U.S. Department of Health and Human Services recommends for adults of any age, that some physical activity is better than none – and health benefits can be gained from as little as 60 minutes of aerobic activity per week (there is no need to "feel the burn")[4]. PwMS should have honest conversations with their neurologists and primary care physicians about possible fitness programs and seek recommendations for a physical therapist. In the least, one can benefit from being informed, and should the opportunity arise to start exercising, I encourage one to first identify one's motives (Why exercise? How will my family and I benefit if I exercised?); then develop a plan that is simple and manageable with **actionable** goals (i.e. walking 5 more minutes a week); and lastly, try something new, such as aquatic Tai Chi with a friend.

[4] https://www.nhlbi.nih.gov/health/health-topics/topics/phys/recommend