

Exercise therapy as supplemental treatment in early multiple sclerosis: a randomised controlled trial



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1 Introduction

Early initiation of medical disease-modifying treatments is considered crucial in the *Time matters* notion in multiple sclerosis (MS). However, patients do still experience disease activity, neurodegeneration, and physical disabilities will progress. Consequently, supplemental treatment strategies are warranted.

Exercise therapy is a promising non-pharmacological approach with recent evidence indicating potential disease-modifying and neuroprotective properties, in addition to the well-known positive effects of exercise on physical function.

An overlooked "window of opportunity"

No previous study have investigated the effects of exercise therapy in the early stages of the disease course of MS.

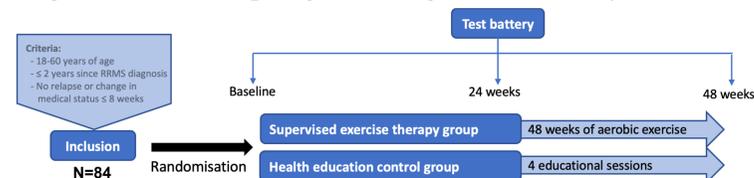
2 Objectives

To investigate the effect of an early exercise intervention on:

- ↳ Relapse rate
- ↳ MRI: global brain atrophy and microstructural integrity
- ↳ Physical function

3 Methods

National multicentre randomised controlled trial including patients diagnosed with relapsing remitting MS within 2 years.



Study groups included 48 weeks of:

- ↳ Supervised progressive aerobic exercise
- ↳ Control group with optional health education

Outcomes were obtained by:

- ↳ Extraction of relapses from medical records, annualised
- ↳ Structural and diffusion-kurtosis MRI imaging
- ↳ Maximal aerobic capacity test
- ↳ Timed 25-foot walk test (T25FWT), 6-minute walk test (6MWT) Six-spot step test (SSST), 9-hole peg test (9HPT)

4 Results

The current RCT sample had a mean disease duration of 10.6 (6.8) months, and a mean EDSS score of 1.63 (1.02) and was overall a good representation of the early Danish MS population.

In the 48-week intervention period, the mean (95 % CI) annualized relapse rate was 0.12 (0.00;0.24) and 0.23 (0.02;0.44) in the exercise group and control group, respectively. However, as indicated by the variation in the calculated incidence-rate-ratio it can not be concluded that exercise lowers the relapse rate in early MS (see Table 1).

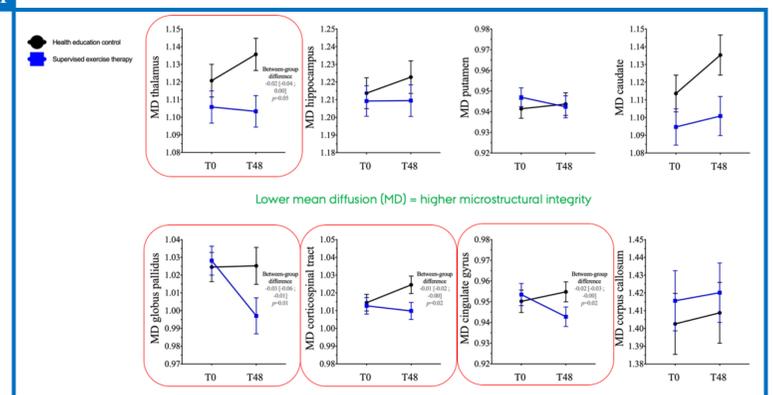
Table 1

	Supervised exercise therapy group	Health education control group
Incidence-rate-ratio	0.49 (0.15; 1.66), $p = 0.25$	Reference

The rate of annualized global brain atrophy, as per mean (sd) percental brain volume change was -0.34 (0.03) % and -0.30 (0.03) % in the exercise group and control group, respectively, with no between-group difference (-0.04 (-0.48; 0.40), $p = 0.87$).

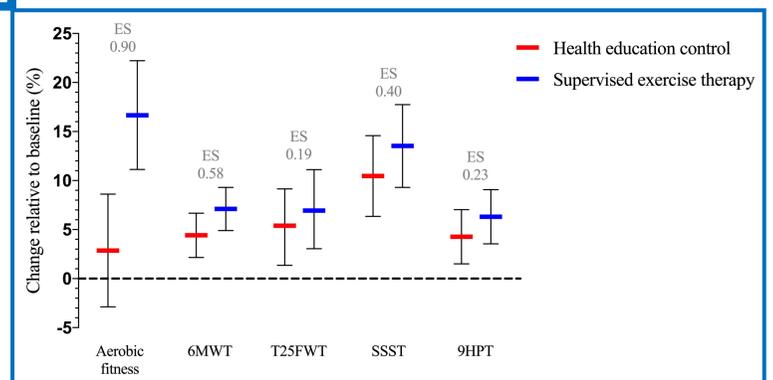
Diffusion-kurtosis imaging revealed a higher microstructural integrity in favor of the exercise group in four of eight a priori defined brain regions (see Figure 2).

Figure 1



Measures of physical function, including aerobic capacity, walking and upper limb function, revealed small-large mean effect sizes in favor of the exercise group.

Figure 2



5 Discussion

In a representative early sample of patients with MS (≤ 2 years since diagnosis) 48 weeks of supervised progressive aerobic exercise did not affect neither the relapse rate nor the global brain atrophy rate, when compared to a control group with optional health education. However, the microstructural integrity was higher in the exercise group in important a priori defined brain regions, including the central hubs of Thalamus and Corticospinal tract. This indeed do suggest a neuroprotective potential of early exercise in MS, possibly via beneficial exercise-induced effects on demyelinating/remyelinating processes. Moreover, early exercise initiation seem to positively affect the physical function of patients with MS.

Altogether these results suggest a microstructural neuroprotective potential of early exercise as well as building of physical functional reserve capacity, and this may over the long-term limit disability progression. Considering the low risk-profile of exercise, early exercise efforts are recommended alongside early medical disease-modifying treatment.

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