Exercise therapy as a supplemental treatment strategy early in the disease course of multiple sclerosis: a randomised controlled trial

Riemenschneider M. [1], Hvid L. G.[1], Ringgaard S. [2], Nygaard M. K. E. [3], Eskildsen S.F. [3], Gaemelke T. [1], Magyari M. [4], Jensen H. B. [5,6], Nielsen H. H. [7], Kant M. [8], Falah M. [9], Petersen T. [10], Stenager E. [6,8] and Dalgas U. [1]

[1] Exercise Biology, Department of Public Health, Aarhus University, Aarhus, Denmark
[2] The MR Research Centre, Aarhus University Hospital, Aarhus N, Denmark
[3] Center of Functionally Integrative Neuroscience, Department of Clinical Medicine, Aarhus University, Aarhus, Denmark
[4] The Danish Multiple Sclerosis Registry, Department of Neurology, University Hospital Rigshospitalet, Glostrup, Denmark.
[5] Brain and Nerve Diseases, Lillebaelt Hospital, Kolding, Denmark
[6] Department of Regional Health Research, University of Southern Denmark, Odense, Denmark
[7] Department of Neurology, Odense University Hospital, Odense, Denmark
[8] MS-Clinics of Southern Jutland (Sønderborg, Esbjerg), Department of Neurology, Sønderborg, Denmark
[9] MS-Clinic Hospital Unit of Western Denmark, Department of Neurology, Holstebro, Denmark
[10] The Multiple Sclerosis Clinic, Department of Neurology, Aarhus University Hospital, Aarhus, Denmark

Introduction: Time matters in persons with multiple sclerosis (MS), and supplemental disease-modifying and neuroprotective treatment strategies are warranted. Exercise is a promising non-pharmacological approach, but an uninvestigated "window of opportunity" exist early in the disease course.
Objectives: To investigate the effect of an early exercise intervention on relapse rate, MRI-outcomes of global brain atrophy and microstructural integrity, and physical function in patients with MS.
Methods: This national multicentre randomised controlled trial (RCT) (n=84, MS duration < 2 years) included 48 weeks of either aerobic exercise or a control condition with health education. In addition, a population-based control group based on data from the Danish MS registry was included (n=850, MS duration < 2 years). Relapse rates were obtained from medical records, and patients in the RCT underwent structural and diffusion-kurtosis MRI as well as a physical functional test battery.
Results: The annual relapse rates were 0.12 (0.00;0.24) and 0.23 (0.02;0.44) in the exercise group and the control group, respectively. No between-group differences were observed. The rate of global brain atrophy did neither differ between groups, as per percental brain volume change (-0.04 (-0.48;0.40), p=0.87). Diffusion kurtosis imaging revealed between-group differences in favour of the exercise group in four of eight a priori defined brain regions of interest in mean diffusivity, including thalamus, globus pallidus, corticospinal tract, and cingulate gyrus. Measures of aerobic capacity, walking and upper limb function showed small-to-large mean effect sizes in favor of the exercise group.
Conclusions: The present study do not support supplemental disease-modifying effects of exercise, when measured by relapse rate. Despite not showing a global neuroprotective effect, the supervised exercise intervention did lead to higher microstructural integrity in four of eight important brain regions, suggesting beneficial effects of exercise on demyelination/remyelination processes. Importantly, early exercise efforts also seem to build physical functional reserve.