Brain atrophy in multiple sclerosis could be ameliorated with aerobic exercise

L. Savsek[1,2], V. Strojnik[3], A. Ihan[4], Z. Spiclin[5], S. Sega Jazbec[2]

[1]Department of Neurology, General Hospital Celje, Celje, [2]Neurology Clinic, University Medical Centre Ljubljana, [3]Faculty of Sport, [4]Faculty of Medicine, [5]Faculty of Electrical Engineering, University of Ljubljana, Ljubljana, Slovenia

OBJECTIVE

- Although most disease modifying drugs exert high antiinflammatory effect on multiple sclerosis (MS), their neuroprotective effect is still rather unclear and is subject to many clinical studies. However, even less is known about additional neuroprotective and regenerative strategies in MS. Previous studies on elderly populations and Alzheimer's disease patients suggest a beneficial effect of exercise on neurodegeneration.
- The aim of present study is to test the effect of aerobic exercise as a strategy to ameliorate functional disability and brain atrophy progression on patients with MS.

SUBJECTS: 25 age- and sex-matched patients with MS, treated with fingolimod for ≥6 months, no relapses within 3 months prior to start of study and EDSS ≤ 6.5, were randomized into intervention group (IG; n=12) and control group (CG; n=13).

INTERVENTION: 12 weeks of supervised aerobic exercise twice a week (60 minutes´ duration).

IMAGING AND VOLUMETRIC ANALYSIS: Baseline 3T magnetic resonance imaging (MRI) was performed at start of study and follow-up at study end. Volumetric analysis of brain structures was performed on baseline MRI and corresponding regional atrophy changes were calculated between baseline and followup MRI scans using automated brain segmentation and deformation analysis techniques (MS Markers; ms.quantim.eu).

SECONDARY OUTCOMES:

- walking speed (10-Meter Walk Test),
- resting state brain-derived neurotrophic factor (BDNF),
- interleukin-6 (IL6) and interleukin-2 (IL2) serum levels.

Table 1: Baseline characteristics

	IG (n=12)	CG (n=13)	p value
Age (mean ± SD; years)	39.7 ± 6.7	42.3 ± 5.7	0.30
Sex (female/male)	9/3	11/2	0.54
Disease duration (mean ± SD; years)	8.4 ± 6.1	14.8 ± 4.5	<0.01
Median EDSS (range)	2.5 (1.0-6.5)	3.0 (1.0-6.0)	0.95
Median 10MWT (range; seconds)	5.9 (4.32-9.32)	5.8 (3.98-11.42)	0.85
BDNF (SD)	1818.9 ± 789.3	1770.5 ± 688.4	0.87
IL2 (SD)	346.4 ± 127.7	250.3 ± 93.4	0.02
IL6 (SD)	2.1 ± 0.3	2.2 ± 0.7	0.59
T2 lesion volume (mL)	10.9 ± 3.9	15.9 ± 10.3	0.12
Active T2 lesion volume (mL)	0.1 ± 0.1	0.1 ± 0.1	0.19
Normalized thalamus volume	15.5 ± 1.2	15.0 ± 1.6	0.42
Normalized hippocampus volume	12.8 ± 1.1	12.8 ± 1.0	0.97
Normalized parahippocampus volume	8.8 ± 0.7	8.8 ± 0.7	0.96
Normalized basal ganglia volume	90.9 ± 5.8	91.6 ± 5.4	0.77

IG = Intervention Group; CG = Control Group; SD= Standard Deviation; EDSS = Expanded Disability Status Scale; 10MWT = 10-Meter Walking Test; BDNF : brain-derived neurotrophic factor; IL2 = interleukin-2; IL6 = interleukin-6

Table 2: Rates of volumetric change after 12 weeks of RCT

	IG (n=12)	CG (n=13)	p value
Parahippocampal gyrus percent change	0.34 ± 0.38	0.01 ± 0.29	<0.01
Hippocampus percent change	-0.06 ± 0.43	-0.02 ± 0.60	0.59
Thalamus percent change	-0.06 ± 0.66	-0.48 ± 0.82	0.04
Precentral gyrus percent change	0.13 ± 0.29	-0.05 ± 0.32	0.05
Putamen percent change	-0.39 ± 0.28	0.24 ± 0.70	<0.01
Pallidum percent change	0.02 ± 0.86	-0.21 ± 0.98	0.71

RCT = randomized controlled trial; IG = Intervention Group; CG = Control Group

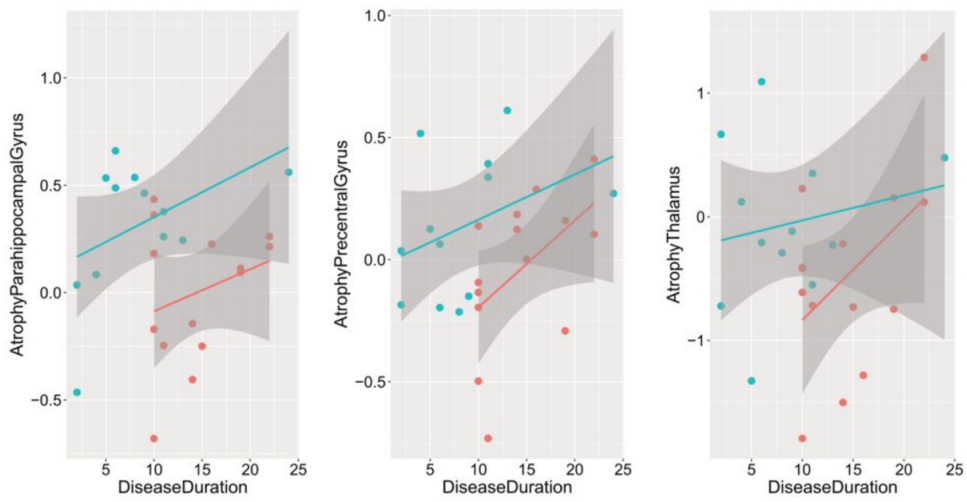

Figure 1: Regional atrophy changes in control (CG) and intervention (IG) patient groups shown with respect to disease duration as a covariate.

RESULTS

- Exercise improved EDSS score and walking speed in IG, while in CG a slight worsening of both measures was detected, but none of these changes were significant.
- Statistically significant regional increase in the volume of thalamus (p=0.039), parahippocampal (p=0.001) and precentral gyrus (p=0.048) was found in IG compared to CG (Table 2, Figure 1).
- After 12 weeks, resting state BDNF levels were significantly higher in the IG (p=0.004) compared to baseline, while in CG a mild, but not significant, increase was observed (p=0.8).
- Levels of IL6 and IL2 remained stable in both groups.

CONCLUSION

- Our study supports findings from previous studies that certain brain structures remain pliable throughout lifetime and can be modified through simple techniques, like aerobic exercise.
- Results suggest that regional brain atrophy, reflecting the neurodegenerative process, could be ameliorated by promoting aerobic exercise among patients with MS.

univerzitetni klinični center ljubljana
University Medical Centre Ljubljana

Splošna bolnišnica Celje
Predani življenju