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FACULTEIT GENEESKUNDE EN LEVENSWETENSCHAPPEN

master in de revalidatiewetenschappen en de kinesitherapie

Masterproef

The impact of a community-based aerobic running program on the cognitive capacity in persons with multiple sclerosis

Promotor :
Prof. dr. Peter FEYS

Copromotor :
Mevrouw Lousin MOUMDJIAN

Andrea Dufour

Scriptie ingediend tot het behalen van de graad van master in de revalidatiewetenschappen en de kinesitherapie

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Andrea Dufour

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A.D.

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1 Research Context

This thesis is situated within the domain of neurological rehabilitation. Patients with multiple sclerosis (MS) are often confronted with cognitive decline [1]. This decline has consequences on the activities of daily living and on the psychosocial functioning[2]. Therefore, it is important to include this in the rehabilitation program of the MS patient.

This thesis is situated in a research project, namely 'MS run project', from Dr. Inez Wens and Prof. Dr. Peter Feys. Paul Van Asch is the president of the non-profit organization Move To Sport, which is the sponsor of this research project. The title of the research project is 'The effect of rehabilitation therapy on cognitive and motor functioning and neuroplasticity in patients with Multiple Sclerosis'. This thesis focuses on the cognitive parameters of this research project. The first part of my thesis was a literature search about which parameters are the best outcome measures for dual-task rehabilitation. Because a further study concerning this subject was not possible I had to change of subject for the second part of my thesis. Because of change of subject I had no part in the development of the research design nor in the data acquisition of this study. I was responsible for the data processing of the neuropsychological tests. I have reviewed the literature and written the thesis and my promotor has reviewed it. I have assisted drs. Lousin Moumdjian in the administration of cognitive and dual-task tests in another study concerning the effects of an exercise study, led by Inez Wens and Bert Op 't Eijnde, on identical outcome measures of cognitive, motor and dual-task performance.

The impact of a community-based aerobic running program on the cognitive capacity in persons with multiple sclerosis

The effect of rehabilitation therapy on cognitive and motor functioning and neuroplasticity in patients with multiple sclerosis

2 Abstract

Background: Patients with Multiple Sclerosis often present cognitive dysfunction as the disease progresses. Previous research has shown that physical training programs have a tendency to improve cognitive performance.

Objectives: To investigate the effects of an aerobic exercise program on the cognitive performance in patients with MS.

Participants: 42 participants diagnosed with Multiple Sclerosis, able to walk 5km without rest or a walking aid and an EDSS score ranging from 0,5- 3 were included in this study.

Measurements: The primary outcome measure of the study is cognitive function and was measured through neuropsychological tests. The Paced Auditory Serial Addition Test, Brief Repeatable Battery of Neuropsychological tests, the Trail Making Test and STROOP test were used. These neuropsychological tests were carried out before and after the intervention, a 12-week aerobic running program.

Results: There was a significant group and time interaction effect on the Spatial Recall test, total score (p< 0,05) confirming previous studies in that there is a significant effect towards an improvement in cognitive performance. However, other tests were not impacted.

Conclusion: Findings indicate that an aerobic running program improves cognitive performance in patients at early stage of the disease and with mild cognitive impairment**.** More studies with longer interventions and participants with worse EDSS scores are needed to generalize the conclusion to persons with cognitive impairment or to patients with a mild form of MS.

3 Introduction

Multiple Sclerosis is a chronic non-traumatic disease of the nervous system in which the immune system produces antibodies that attack oligodendrocytes and thereby causes areas of demyelination. This occurs in the entire central nervous system. Signs and symptoms vary from muscle weakness and a decreased motor performance to cognitive impairment (CI). About 45-65% of patients with MS have cognitive impairment, which are seen in different domains. Cognitive processing speed (CPS), working memory, learning and memory, attention and executive control are primarily impaired in patients with MS [1-4]. Cognitive impairment has an impact on the activities of daily living (ADL), social functioning and is associated with depression and loss of independence [2]. There is no pharmacological treatment to alleviate cognitive decline [2, 3]. Therefore, it is important to investigate if there is a way to slow down or to reverse the deterioration in both the cognitive as in the motor performance. Recent studies have been focusing on the coupling of motor and cognitive performance, by evaluating walking when combined with a cognitive load. The Dual-Task Cost (DTC) is a parameter that gives a reflection about the deterioration in the walking performance when combined with a cognitive load [5-7]. Cognitive performance is evaluated with use of neuropsychological assessment [1-4]. Few studies have investigated the effects of cognitive training in persons with MS. These studies focused specifically on processing speed and working memory, which are the most effected cognitive deficits in persons with MS. Studies were included when participants followed a cognitive training program. Cognitive training was found to improve processing speed, attention and visual and verbal sustained memory. This suggests that cognitive training may influence neuroplasticity and induce cortical reorganization [8-10].

Little is known about the impact of aerobic exercise on the cognitive performance in persons with MS. There is growing scientific literature indicating that there is an improvement in several domains of cognition and a reduction or a delay in cognitive decline in older adults and patients with neurological disorders after physical exercise, but mostly interventions are relatively short or the duration of aerobic exercise was not long enough[1-4, 11, 12]. Sandroff et al. found that aerobic capacity is significantly associated with cognitive processing speed (p=0,036) [18]. Briken et al. found that exercise significantly improves verbal learning and delayed recall, measured by the Verbal Learning and Memory Test

(VLMT). Patients were randomized to four different modalities, namely an arm ergometry group, a rowing group, a bicycle ergometry group or to a non-exercise control group. All three exercise groups improved significantly compared to the waitlist control group [13]. Also Prakash et al. found that there is a correlation between moderate intensity aerobic exercise and gains in neural plasticity[14]. These findings suggest a correlation between aerobic exercise and an improvement of the cognitive function. The aim of present study is to examine if aerobic training is beneficial to improve cognitive performance. Specifically, our study investigates the effects of a gradual community-based running program of 5 kilometers, over a 12 week period on the cognitive status in persons in the early phase of MS. The cognitive status will be measured in several cognitive domains with use of 3 neuropsychological tests and 1 neuropsychological test battery which consists of 4 different neuropsychological tests.

4 Method

4.1 Participants

Patients were identified and recruited from the MS clinic of Melsbroek and Overpelt, through the website of the MS League, Move to Sport and through social media. Criteria for inclusion were EDSS-score ranging from 0,5- 3, being able to walk 5km without rest or walking aid. Reasons for exclusion were having a pacemaker, being able to run 5km or participating in another study concerning physical exercise training. After screening 42 patients met our inclusion criteria and were randomly assigned to the experimental group or the wait list control group. 21 patients were assigned to the wait list control group and 21 patients to the experimental group. All the participants completed a set of tests at the beginning of the study. These were administered at 2 locations. One part of the test administration took place at REVAL – Rehabilitation Research Center in Diepenbeek, Belgium. It consisted of a maximal exercise test and a series of cognitive tests to evaluate the physical condition and to measure the cognitive status at baseline. An MRI (Magnetic Resonance Imaging), fMRI (functional Magnetic Resonance Imaging) and a DTI (Diffusion Tensor Imaging) scan were carried out in a hospital in Antwerp to measure brain structure, diffusivity and connectivity.

4.2 Procedure

The study procedures were approved by the local medical ethical committee of the Virga Jesse Hospital, Hasselt, Belgium as well as the ethical committees of Hasselt university. The positive advice of the ethical committees is in accordance with the declaration of Helsinki, the Belgian Legislature and the Belgian Law of may 7th 2004. Patients were tested at two time points, at the beginning and at the end of the study. The patients completed a 12-week gradual running program and were instructed to train 3 times per week between these two time points. The running program is designed for MS-patients, it starts with alternately walking and running and evolves to running 5km. The initial exercise level was based on a maximal endurance test. At the end of each running program, there was a public running event in which all participants ran together, supervised by the therapists. 3 patients dropped out of the experimental group and 4 patients dropped out of the control group. Reasons for dropout were finding the combination with work to exhausting, moving to another country during pre- and post-test and encountered too much discomfort during the pre-test.

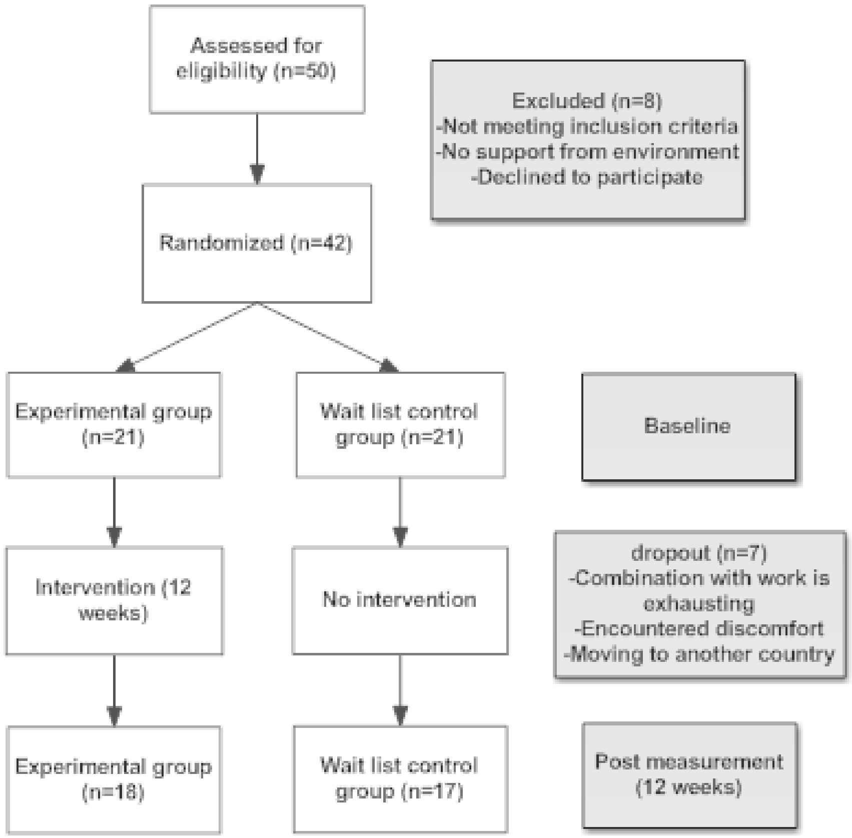


Fig. 1 Participant flow chart

4.2.1 Outcome measures

Seven neuropsychological tests were used for the assessment of the cognitive status and to measure cognitive decline.

- The Paced Auditory Serial Addition Test (PASAT) was used to measure attention, concentration, working memory, and speed of information processing [15]. Digits from 1-9 are read to the patient with a three second interval. The participant had to add this number to the one prior to it, this is repeated for 60 times. The PASAT raw score was used as a primary outcome measure.
- The Brief Repeatable Battery of Neuropsychological Tests consists the Digit Symbol Substitution Test (DSST), Word List Generation (WLG), Selective Reminding Test (SRT) and the Spatial Recall Test (SPART). The test battery provides a sensitive measure of cognitive decline [16, 17].
    - The DSST measures sustained attention and concentration. Participants are presented with a sheet of paper with 9 symbols paired with a number. Below the 9 symbols and numbers is a random sequence of numbers. The participants have 120seconds to write as many symbols possible to the corresponding number. The raw score of the DSST test is also a primary outcome measure.

- The WLG examines semantic verbal fluency, which is a spontaneous production of words [16]. It is a verbal test in which the examiner gives a letter to the participant and he/she has to give as many words as possible starting with that letter in 15s. Patients were tested with letter 'N', 'A' and 'K'. The total score, a sum of the amount of words that were found with the given letters with correction for education and gender, was included as one of the primary outcome measures.
- The SRT makes an assessment about the long-term aspects of memory [16]. In this test the Long-Term Storage (LTS) and Consistent Long Term Retrieval (CLTR) were evaluated. It is a verbal test in which the examiner presents the participant with 12 words. The participant is asked to recall as many as possible. Both scores were corrected for age and gender. The LTS and the CLTR were both included as a primary outcome measure.
- The SPART is a visuospatial learning and delayed recall test [16, 17]. The test makes an assessment about visual-spatial perception/ analysis, memory, reasoning, and/or processing speed[18]. The participant is presented with a checkerboard with 7 checkers in specified places for 10 seconds. After that the participant is requested to place seven checkers at the same place on a blank checkerboard. The participant is also asked to recall the same checkers after 30min. The total score is a sum of the correct checkers at each trial and was used as a primary outcome measure.

– The Trail Making Test (TMT) was developed to assess visual search and sequencing tasks which focusses on attention, resistance to distraction, concentration and cognitive flexibility [19]. In subtest A, the participant has to connect dots, which are numbered, in a sequential order on a sheet of paper. In subtest B, the patient had to connect the dots, also in a sequential order, but alternating between letters and numbers. The score of Trail Making Test part A minus the Trail Making Test part B is a primary outcome measure.

– The Stroop Test is a measure for processing speed, cognitive control, selective attention and resistance to distraction [20]. The participant is presented with a sheet of paper with written color names, which differ from the color ink there are printed with. The participants have to read out loud the written word. On a second trial, the participant must say the color it is printed with. The subtest C of the Stroop test is a primary outcome measure.

4.3 Data analysis

The statistical program JMP® Pro 12 of the SAS® Enterprise Miner™ as used for the statistical analysis. Normality of the data was evaluated through visual inspection of a residual quantile plot, also called the quantile-quantile plot. The quantiles were plotted against the quantiles of a standard normal distribution. The paired T-test was applied to compare data for the experimental group and the control group at baseline. The two groups were compared by means of a linear mixed model analysis which is useful for longitudinal studies and accounts for fixed and random effects. This means that these models adjust for confounding variables and accounts for dropout bias. The magnitude of group differences between the experimental group and the control group was expressed with delta.

5 Results

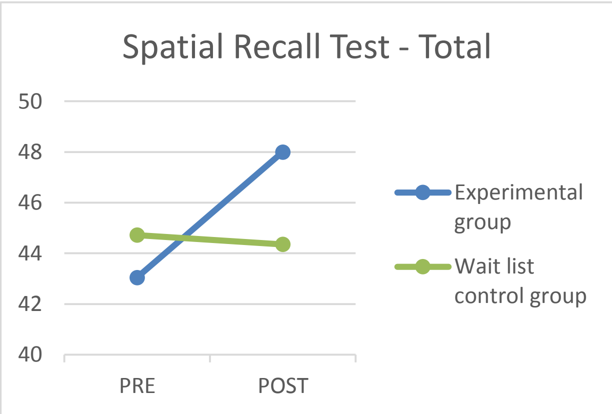
5.1 Baseline characteristics

There were no significant differences in demographic factors between the experimental group and the wait list control group as shown in table 1. An unpaired t-test was conducted to compare the baseline characteristics between both groups. The descriptive statistics of the cognitive measures are presented in table 2. There were significant differences between groups for the Stroop A performance ($p < 0.0018$) with a higher score for the experimental group, the Stroop B performance ($p < 0.0372$) with a higher score for the experimental group, the DSST performance ($p < 0.0102$) with a higher score for the experimental group and the Trail Making Test A- Trail Making Test B performance ($p < 0.0171$) where the score was better in the wait list control group.

5.2 Effects of aerobic exercise on cognitive performance

Table 3 presents a summary of the results for experimental and wait list control group. All main group and time effects as well as group x time interaction effects were evaluated. The DSST evaluates sustained attention and concentration, results show a tendency to a significant group and time effect ($p < 0.0904$ and $p < 0.0698$ respectively). Both the experimental and control group improved their time for the DSST. The experimental group improved more compared with the control group. There was no group x time interaction effect ($p < 0.5670$) for the DSST.

The group effect was found not to be significant ($p < 0.5459$). The time effect showed a tendency to significance ($p < 0.0851$) and the group x time interaction effect showed a significant result ($p < 0.0457$). The wait list control group showed a small decrease after the intervention.



The WLG examines the semantic verbal fluency, effects found not to be significant for the group effect, time effect or the group x time interaction effect ($p < 0.8701$; $p < 0.3747$; $p < 0.3468$ respectively).

The Long-Term Storage of the SRT failed to show significant results for any of the effects (group effect $p < 0.6011$; time effect $p < 0.6591$ and group x time interaction effect $p < 0.1987$).

Also the Consistent Long-Term Retrieval of the SRT did not show significant results (group effect $p < 0.1188$; time effect $p < 0.9798$ and group x time interaction effect $p < 0.2974$).

Attention, concentration, working memory and speed of information processing are assessed through the PASAT performance. There was no significant effect for the group effect, time effect or the group x time interaction effect ($p < 0.8142$; $p < 0.1790$; $p < 0.5191$ respectively).

Visual Search and sequencing tasks was measured by means of the TMT. The TMT, subtest A minus B shows a significant group and time effect ($p < 0.0294$ and $p<0.0147$ respectively). This was not the case for the group x time interaction effect, which was not significant ($p < 0.1638$).

The Stroop test, subtest C did not show any significant results for the group effect, time effect or the group x time interaction effect ($p < 0.2118$; $p < 0.5600$; $p < 0.5075$ respectively).

Table 1. Patient characteristics at baseline

Variable	**EXP**	**WLC**	**P-Value**
Age (yrs)	36.64 ± 8.53 (19.5-51.3)	44.35 ± 8.54 (29.2-62.4)	n.s.
Height (m)	1.68 ± 0.06 (1.57-1.79)	1.69 ± 0.07 (1.55-1.80)	n.s.
Weight (kg)	67.20 ± 15.22 (50.7-105.0)	76.13 ± 9.55 (58.0-92.0)	n.s.
Sex (M/F)	1/20	3/18	n.s.

EXP: experimental group; WLC: Wait list control group

Table 2. Baseline comparison of cognitive function between the experimental group and the wait list control group.			
Variable	**Experimental group**	**Wait list Control group**	**P-value**
TMT_A-TMT_B	-16.27 ± 12.67 (-20.44- -12.11)	-23.82 ± 14.25 (-28.51- -19.14)	<0.0171
Stroop_corrected_A	44.76 ± 9.23 (41.73- 47.79)	38.11 ± 8.5 (35.27- 40.94)	<0.0018
Stroop_corrected_B	50.32 ± 13.24 (45.96- 54.67)	44.92 ± 8.18 (42.192-47.646)	<0.0372
Stroop_Corrected_C	54.16 ± 13.62 (49.68- 58.63)	50.05 ± 9.40 (46.92- 53.19)	ns
DSST	93.08 ± 15.18 (88.16- 97.997)	84.46 ± 12.90 (80.03- 88.89)	<0.0102
PASAT_rawscore	49.14 ± 8.01 (46.46- 51.80)	48.30 ± 9.19 (45.05- 51.56)	ns
Bushke_LTS	48.92 ± 8.58 (46.1- 51.74)	50 ± 7.20 (47.53- 52.47)	ns
Bushke_CLTR	57.38 ± 8.57 (54.52- 60.24)	60.63 ± 8.57 (57.43- 63.83)	ns
SPART_Tot	45.33 ±6.75 (43.15- 47.52)	44.54 ± 5.63781 (43.15-47.52)	ns
WLG_Tot	31.5 ± 7.97 (28.88- 34.12)	31.14 ± 8.71 (28.15- 34.14)	ns
TMT_A- TMT-B: Trail Making Test A- Trail Making Test B; DSST: Digit Symbol Substitution Test; PASAT: Paced Auditory Serial Addition Test; LTS: Long Term Storage; CLTR: Consistent Long Term Retrieval; SPART: Spatial Recall Test; WLG: Word List Generation; Tot: Total; ns: not significant.			

Table 3. Changes of cognitive outcome measures after a three months intervention or waiting period							
Neuropsychological test	**Group**	**Pre-measurement**	**Post-measurement**	**Delta**	**p-value group effect**	**p-Value time effect**	**p-value interaction effect**
DSST	*EXP*	92 ± 14.89 (85.22 - 98.78)	94.33 ± 15.85 (86.45-102.21)	-2.33 ± 4.95 (-12.38 - 7.71)	ns	ns	ns
	WLC	83.5 ± 13.82 (76.62-90.37)	85.47 ± 12.18 (79.21-91.73)	-1.97 ± 4.4 (-10.91-6.98)			
TMT_A-TMT_B	*EXP*	-21.4 ± 9.59 (-25.88- -16.91)	-10.583 ± 13.46 (-17.28 - -3.89)	-10.81 ± 3.83 (-18.63 - -2.99)	0.03	0.02	ns
	WLC	-25.03 ± 16.12 (-32.37- -17.70)	-22.324 ± 11.8484 (-28.42- -16.23)	-2.71 ± 4.54 (-11.92-6.50)			
Stroop_Corrected_A	*EXP*	43.2 ± 7.92 (39.49-46.90)	46.5 ± 10.44 (41.30-51.69)	-3.3 ± 3.03 (-9.48- 2.88)	0.03	ns	ns

	WLC	38.80 ± 7.95 (35.19-42.43)	37.2 ± 9.36 (32.2-42.17)	1.62 ± 2.91 (-4.33 - 7.58)			
Stroop_Corrected_B	*EXP*	48.95 ± 12.49 (43.10 - 54.79)	51.83 ± 14.22 (44.75-58.91)	-2.88 ±4.37 (-11.75-5.99)	ns	ns	0.05
	WLC	45.76 ± 7.53 (42.34-49.19)	43.81 ± 9.09 (38.97-48.65)	1.95 ± 2.81 (-3.79- 7.69)			
Stroop_Corrected_C	*EXP*	52.8 ± 13.57 (46.45-59.15)	55.67 ± 13.9 (48.75-62.58)	-2.87 ± 4.47 (-11.93-6.19)	ns	ns	ns
	WLC	49.91 ± 10.51 (45.12-54.69)	50.25 ± 8.06 (45.95-54.55)	-0.34 ± 3.05 (-6.54-5.85)			
DSST	*EXP*	92 ± 14.89 (85.22-98.78)	94.33 ± 15.85 (86.45-102.21)	-2.33 ± 4.95 (-12.38-7.71)	0.09	0.07	ns
	WLC	83.5 ± 13.82 (76.63-90.37)	85.47 ± 12.18 (79.21-91.73)	-1.97 ± 4.39 (-10.92 - 6.98)			
PASAT_rawscore	*EXP*	47.8 ± 7.7 (44.2-51.40)	50.71 ± 8.33 (46.42-54.99)	-2.91 ± 2.65 (-8.30-2.49)	ns	ns	ns

	WLC	48 ± 10.95 (42.37-53.63)	48.63 ± 7.2 (44.79-52.46)	-0.61 ± 3.20 (-7.20-5.96)			
Buschke_LTS	*EXP*	50.45 ± 6.18 (47.56-53.34)	47.22 ± 10.57 (41.96-52.48)	3.23 ± 2.85 (-2.62- 9.08)	ns	ns	ns
	WLC	49.22 ± 6.74 545.86-52.58)	50.82 ± 7.78 (46.82-54.82)	-1.60 ± 2.47 (-6.63-3.43)			
Buschke_CLTR	*EXP*	58.35 ± 7.23 (54.97 -61.73)	56.24 ± 10.04 (51.08-61.39)	2.11 ± 2.92 (-3.86-8.09)	ns	ns	ns
	WLC	59.72 ± 8.18 (55.64-63.79)	62 ± 9.31 (56.08- 67.92)	-2.28 ± 3.31 (-9.15-4.59)			
SRT_Tot	*EXP*	43.05 ± 6.8 (39.95-46.14)	48 ± 5.78 (45.13-50.87)	-4.95 ± 2.01 (-9.03- -0.87)	ns	ns	0.0457
	WLC	44.72 ± 4.96 (42.26-47.19)	44.35 ± 6.43 (41.05-47.66)	0.37 ± 1.95 (-3.61- 4.36)			
	EXP	30.6 ± 8.52 (26.61-34.59)	32.5 ± 7.41 (28.81-36.19)	-1.9 ± 2.59 (-7.14- 3.34)	ns	ns	ns

WLG_Tot	*WLC*	30.89 ± 9.73 (26.05-35.72)	31.41 ± 7.78 (27.41-35.41)	-0.52 ± 2.97 (-6.57-5.53)			

TMT_A- TMT-B: Trail Making Test A- Trail Making Test B; DSST: Digit Symbol Substitution Test; PASAT: Paced Auditory Serial Addition Test; LTS: Long Term Storage; CLTR: Consistent Long Term Retrieval; SPART: Spatial Recall Test; WLG: Word List Generation; Tot: Total; EXP: experimental group; WLC: control group; ns: not significant.

6 Discussion

The aim was to investigate if an aerobic running program has a positive effect on the cognitive performance in persons with mild levels of disability. Previous research was promising to find an effect in different cognitive domains. We expected to find results that would confirm these conclusions. Few studies have tested the effect of aerobic exercise on the cognitive performance in MS, results are very promising but only very few were significant.

The findings of this study are consistent with the previous studies in that there is a beneficial effect of aerobic exercise and an improvement in cognitive performance. Briken et al. found a significant improvement for the Verbal Learning and Memory Test (VLMT), VLMT delayed recall, the Test Battery of Attention (TAP) subtest "tonic alertness", and the TAP subtest "shift of attention". These test are a reflection for declarative memory and learning abilities (VLMT) and tonic and phasic alertness (TAP) [13]. Although we found a significant effect for the total score of the SPART, this was not the case for the delayed recall were p=0.302. The PASAT, DSST and STROOP C are tests which also test attention, we did not find these to be significant after the intervention. These tests did not only test attention, a more specific test about attention could give us a better reflection about the changes in attention.

Baseline comparison showed a significant difference between the experimental group and the wait list control group for the STROOP A, STROOP B, DSST and the TMT_A minus TMT_B performance. The experimental group scored higher for the STROOP A, STROOP B and the DSST at baseline. The wait list control group scored better for the TMT_A minus TMT_B performance. These results could explain why the changes in these cognitive parameters were not significant after the intervention.

The results of this study indicate that there is a clear tendency to improve the cognitive performance, the Spatial Recall Test showed a significant group x interaction effect. Both groups improved after the intervention, but the experimental group improved significantly more compared to the wait list control group.

When a score falls below the 10th percentile of the total cognitive assessment score on age- and educational adjusted norms, this was evaluated as cognitive impaired for that domain. For the Spatial recall test, we found that the mean number of persons with cognitive impairment from all the subtests was less after the intervention for the experimental group whilst this number of persons with cognitive impairment increased in the wait list control group. Mean number of cognitive impairment decreased from 7,75 to 4 for the experimental group and increased from 5,5 to 6 for the wait list control group. For the LTS subtest of the selective reminding test we found that the number of persons with cognitive impairment decreased from 3 to 1 in the control group and increased from 1 to 4 in the experimental group. For the STROOP C test the number of persons with cognitive impairment increased from 2 to 3 for the experimental group and decreased from 2 to 1 person in the wait list control group. The amount of persons of with cognitive impairment decreased from 15 to 11 in the experimental group, for the wait list control group there were 13 persons with cognitive impairment and remained 13 after the intervention. There were not a lot of persons with cognitive decline, this could give us an explanation why there were only few significant effects after the intervention

Few weaknesses were found and taken into account with the interpretation of the results. Lack of significant data could be due to the fact that the sample size was relatively small in comparison with other studies. Also, this study was a remotely supervised study during the intervention. A more controlled evaluation during and at the end of the study could be beneficial. It is possible that a longer intervention program is needed to have a significant and permanent effect on the neuroplasticity in the brain and thereafter on the cognitive performance.

Despite a few weaknesses this study contains several strengths which make it valuable. Firstly, therapists were instructed by a neuropsychologist to administer and evaluate the neuropsychological test. The intervention program consisted of progressive increases in the running duration which makes the program suitable for persons with a lower physical fitness. This is an important factor to account for in the MS population. Several neuropsychological tests were used so not only one cognitive domain was evaluated in this study. A wait list control group was used so data was compared with reliable baseline data. A mixed model analysis was used, it provides a framework for analyses with subject dropouts or missing data.

More research is needed to explore the effects of an aerobic training program on the cognitive performance and cognitive decline in MS. It is important to take into account that all the participants were at the beginning stage of the disease. All the participants had an EDSS score of 3 or less. Because of the confined group, it is questionable whether these results would also be found in MS patients with worse EDSS scores. This study has focused on the chronic effects of exercise training. It could be beneficial to administer the tests immediately after exercise so that there is a distinction between the acute and chronic effects of aerobic exercise on the cognitive performance. Also, future studies should use a longer training program with a follow-up after the end of the training program.

7 Conclusion

Results from a community-based aerobic running program points towards a promising approach for the cognitive performance, more specific cognitive processing speed, in patients with MS as was shown by the significant interaction effect of the spatial recall test. Cognitive impairment might be managed through adaptations in the rehabilitation program. Future research should compare more outcome measures from different running programs to see which parameters are most effective.

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