Comparison of the influence of different rehabilitation programmes on clinical, spirometric and spiroergometric parameters in patients with multiple sclerosis

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Purpose The aim of this study was to compare the effect of four different programmes on spiroergometric, spirometric and clinical parameters in multiple sclerosis (MS) patients.
Methods One hundred and twelve MS patients were divided into four groups. The first group underwent neurophysiologically based physiotherapy, the second aerobic training, the third combined therapy (neurophysiologically based physiotherapy and aerobic training) and the fourth did not change any habits. Seventeen patients did not finish the study. Patients were examined on impairment (Expanded Disability Status Scale), disability (Barthel Index), handicap (Environment Status Scale), quality of life (Multiple Sclerosis Quality of Life), fatigue (Modified Fatigue Impact Scale), depression (Beck Depression Inventory Score), respiratory function (spirometric parameters on spirometry) and physical fitness (spiroergometric parameters on a bicycle ergometer).
Results The patients who participated in one of our training programmes showed a significant improvement of the examined parameters in comparison to those who did not change their present habits. Each of the four training programmes had a different impact on the parameters, which means that each of them had a different effect. The neurophysiologically based physiotherapy had the greatest impact on impairment, and the aerobic training on spirometric and spiroergometric parameters. All methods (the neurophysiologically based physiotherapy, the aerobic training and the combined programme) had an impact on fatigue. *Multiple Sclerosis* 2006; **12**: 227–234. www.multiplesclerosisjournal.com

Key words: aerobic training; fatigue; multiple sclerosis; neurorehabilitation; spirometric and spiroergometric parameters

Introduction

Nowadays, the approach to physical activities recommended to multiple sclerosis (MS) patients within rehabilitation as well as within the activities of daily living has changed. Until recently, patients were recommended to rest and fatigue was considered the limit of load [1,2]. It was assumed that physical activities raise body temperature, which results in slow conduction through a demyelinated

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nerve and consequently to the aggravation of the disease symptoms, mainly of fatigue. Nevertheless, inactivity has a great negative impact on the health condition of patients and leads to the development of several complications [1–3]. That was why scientists started becoming interested in these problems. At first Schapiro *et al*. who proved that physical activity of the aerobic character has no negative impact on examined parameters [4]. Then Petajan *et al*. proved its positive impact on many parameters, including even fatigue [5].

Fatigue in MS patients represents a great problem that has to be dealt with. That is why we decided to monitor the influence of physical activities on fatigue in MS patients in this study. We have chosen three different programmes (neurophysiologically based physiotherapy, aerobic training, and combined programme consisting of aerobic training and neurophysiologically based physiotherapy) and these were compared to the group of patients who did not change their habits. The mechanisms influencing fatigue differ in the individual therapeutic techniques. Neurophysiologically based physiotherapy influences the symptoms associated with fatigue, spasticity, pain, balance disorders, tremor, muscle weakness and the influence on psyche [6–10]. Aerobic training is based on the improvement of cardiorespiratory fitness and muscle performance [4,5,11].

Further, we evaluated the impact of these physical activities on the symptoms (depression, decondition and cardiorespiratory dysfunction) that can contribute to the aggravation of fatigue and we compared their impact on impairment, disability, handicap and quality of life. Spiroergometric and spirometric parameters normally reflect changes in clinical status, mainly cardiorespiratory dysfunctions and decondition [12]. That is why we decided to detect clinically significant change based on spiroergometric and spirometric parameters.

First, we assumed a great difference in the change between the examined parameters in the patients who took part in any of the programmes and those who did not change their present habits. Second, we assumed that the changes would differ in the individual approaches and that the patients who took part in one of the treatments would differ at the beginning and at the end of the therapy in terms of the improvement; while the patients who did not change their present habits would not differ.

Method

Choice and characteristics of the patients

One hundred and twelve patients participated in this study from January 2002 to April 2004 in the MS Centre at the Department of Neurology, 1st Medical Faculty, Charles University and General Hospital in Prague. The patients were chosen from all consecutive outpatients with MS who attended the centre those days and who showed no progression in the last three months, no attack of MS in the last 28 days and no acute manifestation of other disease or injury, who were able to move independently and walk at least 20 m with the help of crutches (Expanded Disability Status Scale (EDSS) 0–6.5) and who were indicated and able to undergo the programme (eg, agreement to participate in the study, motivation to co-operate actively, ability to attend the centre regularly). The patients were allocated to groups on the basis of next one, next group, if space, so the patients were not randomized and the groups were not matched.

The patients were examined at the beginning and at the end of the experiment by an independent examiner who did not know which patients belonged to which group.

Examination

In the groups of rehabilitated and nonrehabilitated patients an independent therapist examined the measures of impairment, disability, handicap and quality of life. Impairment was examined by means of the EDSS [13]. Other scales were used to evaluate fatigue (Modified Fatigue Impact Scale, MFIS [14]), depression (Beck Depression Inventory Score, BDIS [15]), disability (Wade and Collin's version of Barthel index scored from 0 to 100, BI [16]), handicap (Environment Status Scale, ESS [16]) and quality of life (Multiple Sclerosis Quality of Life-54, MSQOL [16]).

Spirometric parameters were obtained by flow/volume method; specialized SW application on the automatic analyser of respiratory gases Oxycon Delta (Jaeger, Germany) [17]. The examination of the static and dynamic spirometric values was performed under standard conditions at rest [18]. Basic spirometric parameters, forced vital capacity (FVC), forced expiratory volume in one second (FEV 1) and peak expiratory flow (PEF) were chosen to be monitored in the study. The absolute values of spirometric parameters of each patient were compared to average value of healthy age- and sex-matched untrained population.

Spiroergometric parameters were obtained by spiroergometry on a bicycle ergometer. The examination was executed under standard conditions [18] and it was carried out by means of the method called 'anaerobic threshold' [19]: continuously increased load on the bicycle ergometer EL 800, Ergoline/FRG, at intervals of one minute till the subjective maximum of a patient, with the evaluation of changes in respiratory gases and the calculation of spiroergometric parameters on the automatic analyser of respiratory gases Oxycon Delta (Jaeger, Hochberg bei Würtzburg, Germany). ECG was continuously monitored and blood pressure was monitored during the spiroergometry (see more details in [20]). At the end of testing, the patients evaluated the rate of perceived exertion (RPE) according to the Borg Scale [21]. Basic spiroergometric parameters, peak muscle performance (watt/kg), peak heart rate (HR/min), peak pulmonary ventilation (VE/kg), peak oxygen uptake (VO_2/kg), peak oxygen pulse (VO_2/HR per kg), were measured. The absolute values of spiroergometric parameters of each patient were compared to average value of healthy age- and sex-matched untrained population of the same age and gender.

Therapy

Group 1

Twice a week during the two-month period, patients were given neurophysiologically based physiotherapy operating on the well known principles of sensory-motor learning and adaptation, lasting approximately one hour. Individual facilitation techniques were combined to achieve the most ideal function. We employed various elements of several treatment methods in an eclectic way (reflexive locomotion, neurodevelopmental concept, sensory-motor stimulation, proprioceptive neuromuscular facilitation, Brüger concept and yoga) [22,23].

Group 2

Twice a week during the two-month period, the patients of Group 2 underwent training on a bicycle ergometer. The intensity and length of load was set individually on the basis of a spiroergometric examination on a bicycle ergometer and of a neurological finding. Derived training load corresponded approximately to 60% of individual maximal oxygen uptake. The length of load was based on our experience in the pilot project [24]. Patients with EDSS ≤ 3 (lower level of impairment) were able to start training for a period of 5–10 minutes and gradually, according to the reaction to load, they extended the training time up to 20–30 minutes. Patients with EDSS >3 and ≤ 6.5 (higher level of impairment) were able to start training for a period of 2 minutes, and gradually, according to their abilities and reaction, they extended the time of training up to 10–15 minutes. The recommended speed of training was approximately 60-wheel speed per minute. During the load we monitored heart rate using Sporttester (Polar, Kempele, Finland). Before and after aerobic training patients rode on a bicycle for 3 minutes without load. The training was interrupted in the case of an increase of muscle weakness, tremor, spasticity, pain, etc.

Group 3

Twice a week during the two-month period, the patients of Group 3 underwent a mixed programme, which consisted of aerobic load and physiotherapy. In this mixed programme we used the same physiotherapeutic methods as in Group 1 and the same exercise paradigm as in Group 2. The length of physiotherapy decreased with the extension of the aerobic training. The aerobic training preceded physiotherapy. The whole mixed programme lasted one hour.

Group 4

The patients of Group 4 did not change the their present habits during the two-month period.

Statistical evaluation

For testing the hypotheses, we chose the nonparametric tests. The comparison of the patients who went through any of the physiotherapeutic programmes and the patients who did not change their habits was carried out by means of a two-sample Wilcoxon test (see Table 1). The comparison of the four therapeutic groups at the beginning of the experiment and also the differences after the experiment was carried out by means of a Kruskal–Wallis ANOVA (see Table 2). The comparison of the parameters of each group at the beginning and at the end of the experiment was carried out by a paired Wilcoxon test (see Table 3). Data of patients who dropped out were not used at all. All the differences were considered statistically significant if the significance level of the test was lower than or equal to 0.05. As the number of performed comparisons in one batch is relatively large ($k = 31$, even though only 16 of them are mentioned in this article), the Bonferroni correction should be applied: each difference should be considered statistically significant only if the level of the test significance is lower or equal to 0.05/31, which means lower or equal to 0.0016. Using this approach, the overall significance level of the whole batch of tests is lower than or equal to 0.05. Nevertheless, since the Bonferroni correction is very strict for our data, we mention all the differences significant at the 5% level of significance for

Table 1 The comparison of the untreated (Group 4) and treated (Groups 1–3) patients before the experiment and the difference after the experiment

	Before the experiment		Difference after the experiment	
	Untreated	Treated	Untreated	Treated
watt/kg %	58.69	53.91	0.35	4.89*
HR/min %	85.36	82.53	−4.38	0.04
VE/kg %	89.53	74.31*	−4.67	9.90*
VO_2/kg %	90.14	82.20	−4.47	2.68*
VO_2/HR %	106.37	97.97	−5.56	4.72*
RPE	14.62	14.13	0.20	0.45
FVC %	102.36	101.62	−1.81	2.26
FEV 1 %	108.28	104.19	−5.29	−1.00*
PEF%	93.78	84.79	−5.92	1.41*
MFIS	27.00	39.62*	3.86	−5.24
BDIS	4.14	7.14	0.29	−1.95*
EDSS	2.31	3.08	0.00	−0.17*
BI	99.44	96.84	0.63	1.06
ESS	0.86	4.27	0.29	−0.62
MSQOL phys.	58.04	55.22	1.45	6.50
MSQOL mental	67.04	63.62	−0.50	6.84

*$P < 0.05$.

single comparison, keeping in mind that such results should be validated by further research.

Results

Basic characteristics

The study comprised 112 patients. Seventeen patients did not finish the study (8 because of MS relapse, 5 because of other illness, 4 because of motivation loss). They were representative of the rest of the group. There is no intention to treat analysis.

Ninety-five patients finished the study: 24 patients (25.26%) underwent the neurophysiologically based physiotherapy, 36 patients (37.89%) underwent the aerobic training, 19 patients (20.00%) underwent the complex programme, which consisted of aerobic load and neurophysiologically based physiotherapy, and 16 patients (16.84%) did not change their habits. The four groups differed in some parameters before the experiment (Tables 1 and 2, first column).

Table 2 The comparison of the four groups before the experiment and the difference after the experiment

	Before the experiment				Difference after the experiment			
	Group 1 Physiotherapy	Group 2 Aerobic t.	Group 3 Mixed p.	Group 4 Without p.	Group 1 Physiotherapy	Group 2 Aerobic t.	Group 3 Mixed p.	Group 4 Without p.
watt/kg %	40.68	61.50	53.46	58.69*	2.00	7.39	3.33	0.35*
HR/min %	76.19	84.37	85.74	85.36*	−0.56	3.38	−5.46	−4.38*
VE/kg %	59.87	83.33	72.43	89.53**	7.32	11.52	9.64	−4.67*
VO_2/kg %	69.75	88.59	83.21	90.14*	4.97	1.37	2.68	−4.47*
VO_2/HR %	86.71	107.42	91.58	106.37*	5.61	0.28	12.37	−5.56*
RPE	13.57	14.18	14.53	14.62	0.50	0.83	−0.30	0.20
FVC %	95.83	104.77	103.05	102.36	1.61	2.61	2.46	−1.81
FEV 1 %	100.04	106.56	104.97	108.28	−1.57	0.47	−3.22	−5.29
PEF %	81.64	86.96	84.66	93.78	1.81	3.24	−2.94	−5.92
MFIS	42.48	36.19	42.32	27.00	−8.27	−3.97	−3.68	3.86*
BDIS	8.63	7.60	4.68	4.14*	−2.95	−1.69	−1.26	0.29*
EDSS	4.10	2.21	3.42	2.31*	−0.30	−0.01	−0.32	0.00**
BI	93.75	99.19	96.18	99.44*	1.25	0.17	2.35	0.63
ESS	6.68	1.97	5.65	0.86*	−0.78	−0.28	−1.03	0.29
MSQOL phys.	49.88	59.87	53.07	58.04	4.91	5.29	10.51	1.45
MSQOL mental	61.78	65.07	63.15	67.04	6.38	5.79	9.20	−0.50

*$P < 0.05$; **$P < 0.0016$, thus $P_{overall} < 0.05$.

Table 3 Impact of the four treatments on the examined parameters

	Neurophysiologically based physiotherapy		Aerobic training		Mixed programme		Without programme	
	Before	After	Before	After	Before	After	Before	After
watt/kg %	40.68	42.68	61.50	68.72**	53.46	56.79	58.69	59.04
HR/min %	76.19	75.62	84.37	87.36	85.74	80.27*	85.36	80.98*
VE/kg %	59.87	67.19*	83.33	94.04**	72.43	82.07*	89.53	84.86
VO_2/kg %	69.75	74.73	88.59	89.39	83.21	85.89	90.14	85.67*
VO_2/HR %	86.71	92.32	107.42	106.76	91.58	103.31*	106.37	100.80*
RPE	13.57	14.06	14.18	15.16*	14.53	14.38	14.62	14.64
FVC %	95.83	97.44	104.77	107.38*	103.05	102.84	102.36	97.57
FEV 1 %	100.04	98.47	106.56	106.91	104.97	99.77	108.28	94.72
PEF %	81.64	83.45	86.96	92.26	84.66	81.09	93.78	86.89
MFIS	42.48	34.25**	36.19	32.17*	42.32	38.65*	27.00	30.86
BDIS	8.63	5.65**	7.60	5.76**	4.68	3.41*	4.14	4.43
EDSS	4.10	3.80**	2.21	2.19	3.42	3.11**	2.31	2.27
BI	93.75	95.00	99.19	99.31	96.18	98.53	99.44	100.00
ESS	6.68	5.90*	1.97	1.79	5.65	4.62	0.86	1.14
MSQOL phys.	49.88	54.79*	59.87	65.97*	53.07	63.58*	58.04	59.12
MSQOL mental	61.78	68.16*	65.07	71.83*	63.15	72.35*	67.04	67.08

*$P<0.05$, **$P<0.0016$, thus $P_{overall}<0.05$.

The diversification of the difference at the beginning and at the end of the experiment between the treated and the untreated

The members of the treated group (any of the three types of treatment) significantly differ in the amount of change after the experiment in comparison with the non-treated ones (Table 1, second column).

The diversification of the difference at the beginning and at the end of the experiment between the four groups

The four programmes differ in the amount of change in some parameters after the experiment. Groups 1 and 3 (patients who underwent neurophysiologically based physiotherapy) significantly improved in neurological impairment, while Groups 2 and 4 did not show any changes. Groups 1, 2 and 3 improved in several spirometric and spiroergometric parameters, in fatigue and depression (Table 2, second column).

Comparison of the individual groups at the beginning and at the end of the experiment (Table 3)

Group 1: neurophysiologically based physiotherapy

Patients of Group 1 significantly improved in pulmonary ventilation, fatigue, depression, neurological impairment (EDSS evaluates eight subsystems, patients in this study improved mainly in the pyramidal, cerebellar and mental systems, in spasticity, and bowel and bladder problems) and quality of life (physical as well as psychical).

Group 2: aerobic training

In Group 2 we observed a significant improvement in muscle performance, pulmonary ventilation, perception of effort, FVC, fatigue, depression and quality of life (physical as well psychical).

We found a better reaction to aerobic load in patients with a lower degree of neurological impairment (EDSS ≤ 3), who significantly improved in muscle performance, pulmonary ventilation, and perception of effort, fatigue and depression. Nevertheless, the patients with a higher degree of neurological impairment (EDSS >3 and ≤ 6.5) also tolerated the aerobic training without greater problems and showed a tendency towards improvement in the mentioned parameters.

Group 3: complex physiotherapeutic programme consisting of aerobic load and a neurophysiologically based physiotherapy

The patients who underwent the complex physiotherapeutic programme showed a significant decrease in heart rate at a higher load, while they showed increased pulmonary ventilation and oxygen pulse. We also observed a significant decrease of the level of neurological impairment, fatigue and depression, and an improvement in the quality of life (physical as well as psychical), in these patients.

Group 4: no therapeutic programme

Patients with no therapeutic programme also showed significant changes in some parameters, mainly in terms of worsening. We observed decrease heart rate, oxygen consumption and oxygen pulse.

Discussion

At the beginning of the study, the number of patients in the groups was similar. We consider the difference in impairment to be the most important. Patients in Groups 1 and 3 were more impaired than patients in Groups 3 and 4 – this could have an impact on the accomplishment of participation in the study (more demanding to attend the programme due to more health complications). We explain the lower number of patients in Group 4 by the fact that patients were not motivated to come to output examination and we could not use their data.

The patients were divided into four groups according to the available places in the groups; nevertheless there were significant differences in the input parameters in the four groups. We do not know any reasons for these differences, mainly for the difference in impairment (EDSS), because the patients were not divided according to their impairment. As the patients in the groups differed in some parameters, we have to discuss the impact of ceiling and floor effect on the outcome measures. It is mainly the BI that is criticized for its definite ceiling effect (changes in higher levels of functioning are not detected or measured by it [16]).

Even though before the experiment the four groups differed in some parameters, it had no impact on the evaluation of changes after the experiment. We evaluated the amount of change after the experiment rather than the absolute value of the examined parameters after the experiment.

The patients who participated in any of our training programmes showed a significant improvement of the examined parameters in comparison to those who did not change their habits. Consequently, we conclude that it is very important for MS patients to have the possibility to undergo a rehabilitation programme (in our case aerobic training or neurophysiologically based physiotherapy). We assume that after longer or more intensive training the difference after finishing the programme would be even more significant.

On the basis of the results obtained by the comparison of the four groups at the beginning and at the end of the experiment and also on the basis of the detailed description of the impact of the individual programmes on the examined parameters, we conclude that the choice of a therapeutic programme plays a key role because each of the proposed programmes had an impact on different parameters. For example, the neurophysiologically based physiotherapy influenced mainly the degree of neurological impairment; while aerobic training influenced decondition. Therefore, it follows that the treatment of MS patients should be targeted (according to the type and disease process as well as according to individual symptoms of the disease).

We presupposed a positive impact of the neurophysiologically based physiotherapy from the literature, which describes an impact on MS symptoms [25–27] and on fatigue [6–10]. The decrease of depression was assumed on the basis of the relationship between fatigue and depression [10], on the basis of applied physiologic mechanisms leading to system harmonization [22], and therefore also on regular contact with therapist and regular work on health improvement. The improvement of impairment, fatigue and depression relates to the improvement of disability, handicap and quality of life. Neurophysiologically based physiotherapy was not primarily aimed at the improvement of spiroergometric parameters, so an impact on cardiorespiratory fitness was surprising for us. On the contrary, muscle performance improved only slightly, even though the function of lower extremities improved. This confirms that better functioning relates more to muscle co-ordination than muscle strength. The neurophysiologically based physiotherapy was not aimed at the training of certain respiratory function [28–31] but at the co-ordination of respiratory muscles, postural system function, the activation of the deep spinal cord stabilizing system and the activation of diaphragm postural function. That led to the improvement of spirometric parameters, similarly to the study of Olgiati and Di Prampero [32].

In this study aerobic training caused an improvement of several peak spiroergometric parameters, even though it was of lower volume and intensity in comparison to other studies in MS [4,5,11,33] or healthy populations [34,35]. Even though aerobic training is not primarily aimed at strengthening, it causes the improvement of muscle power.[4,5,11,35,36] and muscle performance in this study. In comparison with Mostert's study [11], spirometric parameters were not influenced in our study. This study confirmed the results of Schapiro *et al*. and Petajan *et al.* that aerobic training has no impact on impairment and disability [4,5]. Similarly to Petajan *et al.* and Mostert and Kesselring, we confirmed a positive impact on fatigue, depression, handicap and quality of life [5,11]. In this study, similarly to Schapiro *et al*. and Ponichtera-Mulcare, patients with a lower degree of neurological impairment (EDSS <3) responded better to aerobic training [4,36]. However, patients with a higher degree of neurological impairment (EDSS > 3) tolerated aerobic training without problems.

The combined programme had a similar impact on fatigue, depression and neurological impairment as well as the ability to perform activities of daily living, socioeconomic situation and quality of life compared to the impact of neurophysiologically based physiotherapy that was used independently. On the contrary, it did not have such a great impact on spiroergometric parameters in comparison to the group that underwent aerobic training only. This could have been caused by the difference between the groups (volume and intensity of aerobic training were influenced by neurological impairment).

Conclusion

The neurophysiologically based physiotherapy, the aerobic training as well as the combined programme have a positive impact on fatigue. Therefore a subjective symptom of fatigue should not be considered as a limit of load (within rehabilitation as well as within the activities of daily living); on the contrary, it should be the principal point of therapeutic interest.

Moreover, the neurophysiologically based physiotherapy has a great impact on the regulation of depression, impairment, disability, handicap and quality of life, as it causes changes of spiroergometric and spirometric parameters. Aerobic training influences, above all, spiroergometric and spirometric parameters and depression and therefore it consequently improves quality of life (also in patients with a higher motor deficit).

We conclude that it is very important for MS patients to have the possibility to undergo a physiotherapeutic programme. We think that this programme should be specific to each patient's symptoms and disease progression, it should be applied already in the early stages of disease and in the long term, and it should be a part of complex MS rehabilitation programme.

Nevertheless, the results of this study should be verified in further research.

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