Multiple Sclerosis relapses are not associated with exercise

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Keywords:
Multiple sclerosis, physical activity, exercise, disease activity, immunotherapy, relapses.

Running title:
Exercise and MS relapses

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Summary. Since Multiple Sclerosis often affects physically active young individuals, it is important to know if exercise can result in an increased disease activity. Therefore we used a self-report questionnaire to examine the relation of different levels of sports activity and relapses in 632 MS patients. In order to analyze if subjective recall might have biased the results, we performed, in a subgroup of our sample, an objective assessment of clinical data and physical fitness parameters.

We could not find any association between sports activity and clinical relapses in any of the two analyses. The highest active group even shows the lowermost mean values, standard deviations and range concerning the number of relapses.

In order to finally approve that even high levels of physical activity have no detrimental influence on disease activity, results from our cross-sectional study should be confirmed in a large prospective epidemiological study.

Introduction. Multiple sclerosis (MS) is the most common autoimmune inflammatory disease in young adults and is characterized by recurrent neurological deficits. Although many studies have shown a positive effect of physical activity and exercise on muscle strength and aerobic capacity in MS patients [1,2], there is still an uncertainty about the relation between exercise and clinical relapses among patients and physicians, which often results in a “prophylactic” reduction of activities. In order to clarify if high levels of sports activity are associated with an increased inflammatory disease activity, we examined the relation between the level of sports activity and MS relapses in a german MS population.

Material and Methods. The study was approved by the local ethics committee. After written informed consent we collected questionnaires from 632 MS patients. Data included demographics, disease course, self-reported relapses within the last two years, immunomodulatory treatment and Expanded Disability Status Scale (EDSS). Physical activity was evaluated using the german version [3] of the Baecke questionnaire [4], which quantifies structured exercise (sport index), physical activity acquired in leisure time (leisure time index) and at work (occupational index). Each index adopts values from 1 to 5, with 5 indicating the highest possible physical activity. We stratified the patients into four groups according to their individual sport index value and compared the groups concerning relapse rate (Analysis of variance) and presence or absence of immunotherapy (Pearson´s Chi Square Test). We then performed a bivariate correlation analysis (Spearman´s rho) to quantify the strength of a possible relationship between number of relapses and sport index.

Since subjective recall might have biased the results concerning both relapse rate and physical activity, we invited the least (n=21) and the most (n = 21) physically active patients, according to the Baecke sport score, to our study center. All of these

patients were treated with interferon beta 1b according to the manufacturers instruction. Neurologic examination including clinical validation of relapses was performed by a neurologist (M.M., A.W.) who was not aware of the sport score. Spiroergometry on a bycicle ergometer was conducted to assess aerobic capacity. In the subgroup analysis, we performed a t-test and computed effect sizes (Cohen´s d) for group differences. Statistical analyses were performed with SPSS Statistics 17.0.

Results. From the 632 MS patients (460 female, 172 male) complete datasets were available from 546 Patients. Mean age was 43.3 ± 10.4 years, mean EDSS was 3.0 ± 1.8 and mean disease duration was 10.3 ± 7.8 years. While 357 (65%) patients were currently obtaining an immunomodulatory treatment, 189 (35%) patients were without a specific MS treatment. The mean relapse rate within the last two years for the entire group of patients was 1.4 ± 1.6 relapses. The mean sport index was 2.68 ± 0.95 for male and 2.62 ± 0.79 for female patients. We did not find significant overall differences between the four groups concerning the number of relapses within the last two years (p=.279). It is notable that the highest active group showed the lowermost mean and standard deviation as well as the lowest range of all groups (Table 1). The distribution of patients within the groups with respect to immunotherapy did not differ significantly between groups (p=.740). The bivariate correlation analysis indicated a significant (p=.015) but very small and negative correlation (Spearman´s rho = -.104) between the sport index and the number of reported relapses.

Table 2 shows significant and meaningful differences with large effect sizes between the subgroup of active and inactive patients concerning physical performance variables. The groups did not differ significantly concerning relapse rates.

Discussion. Several studies have highlighted the positive influence of physical activity and exercise on quality of life [5], muscle force and aerobic capacity in patients with MS [1, 2]. However MS patients show an even more distinct physical inactivity than the normal population [6].

Consistently, we found reduced sports activity in our MS sample compared to a healthy german sample (sport index 2,76 for female and 3,05 for male healthy participants [3]).

The inactivity of MS patients might be due to the former belief that physical activity and/or exercise and the associated elevation of body core temperature may be harmful for MS patients and result in clinical relapses. This unproven concept still leads to the recommendation of avoiding physical activity and exercise – or at least to stay away from the individual performance limit.

Therefore, we found it important to examine whether levels of habitual sports activity are associated with higher disease activity in a large german MS cohort. Patients in the highest sport index category did not differ significantly from the less active groups concerning the number of relapses within the last two years. The highest active group even showed the lowermost mean values, standard deviations and range concerning the number of relapses. The correlation between the sport index and self-reported relapses was significant and negative, but too small to be meaningful.. In order to find out if subjective recall of both relapses and physical activity might have biased our results, we performed a subgroup analysis of the most active and inactive patients according to the Baecke sport score. Relapses were clinically validated and aerobic capacity was determined via spiroergometry. The distribution of relapses among among the groups reproduced the results of our epidemiologic study quite well.

In our substudy, we assessed aerobic capacity as a measure of physical fitness, which has shown associations to physical activity but might as well be an

independent construct [7]. It has been used, though, as a measure for physical activity in epidemiological studies [8] and can be assessed objectively in a clinical setting.

The assessment of physical activity via questionnaire is not without pitfalls but considered appropriate in MS patients [9]. The psychometric properties of the Baecke-Questionnaire have been confirmed for the original version [10] and the german version [11] for non-diseased populations. There are no validation studies with MS patients for either version, which might be a drawback to the study. The fact that there is, to our knowledge, no german physical activity questionnaire which is validated in MS patients and the fact that the original version of the Baecke Questionnaire has shown sensitivity to change in exercise interventions with MS patients [12] seem to justify the choice of the questionnaire.

Consistently, the physical performance variables in our subgroup analysis differed significantly between groups, indicating a valid separation of active and inactive patients with the Baecke Sport Score. Moreover, when comparing the scores from the Baecke-Questionnaire with a triaxial accelerometer (Actibelt, Trium, Germany) and aerobic capacity yielded from performance diagnostics on a bycicle ergometer in 45 MS patients, the Baecke sport index showed significant correlations with accelerometer counts (r=.492, p=.001) and VO2peak (r=.487, p=.001) (Tallner, unpublished data). These results further reinforce the choice of the Baecke Questionnaire.

In order to relate the self-reported frequency of relapses to sports activity, the recall period of both variables should be comparable. Since relapses are rare, a two-year recall period seems adequate. The Baecke-Questionnaire measures habitual physical activity without a delineated recall period, which is not consistent with the two-year period but is long-term and appears to be acceptable.

We believe that the results of our retrospective analysis with high numbers of patients – being reinforced by a subgroup analysis using clinical and objective measurements – suggest that high levels of physical activity are not harmful to MS patients. We did not find statistical evidence that subjective recall might have compromised the validity of our data. In fact, our study is in line with a Cochrane review [2] that did not report any deleterious effects of exercise on the course of the disease. Seven of the studies included in this review reported a total of 12 relapses which were not, according to the relevant authors, related to the intervention. Due to the small number of relapses and small sample sizes, this assumption cannot be statistically verified. In this regard, our study gives first and statistically sound evidence that the number of relapses is not related to sports activities. Hence, our study might as well be a justification for further studies to explore high-intensity or high-volume exercise and the corresponding training effects on physical function and disease activity in MS patients prospectively.We acknowledge, though, the cross-sectional character of our data and underline that our results should be confirmed in a large prospective epidemiological study.

Acknowledgement: This study was supported by Bayer Vital GmbH, Germany.

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Table 1: Number of relapses within the last two years among the 4 patient groups discriminated according to the sport index.

	Groups according to sport index value				All groups
	1,0 - 1,99	2,0 - 2,99	3,0 - 3,99	4,0 - 4,99	
Patients per group	95	230	172	49	546
with immunotherapy	59 (62%)	150 (65%)	113 (66%)	35 (71%)	357 (65%)
Mean number of relapses (last 2 years)	1,51	1,44	1,42	,98	1,40
standard deviation	1,940	1,553	1,654	1,010	1,622
range	0-10	0-8	0-10	0-4	0-10

Table 2: Group differences concerning relapse rate among inactive and active patients

		Sport index	Relapses in 2 years	Max. heartrate	VO2peak	Max power (watts)	Watt/kg
Active (n=21)	mean value	**3.60**	**0.95**	**171**	**34.69**	**204**	**2.94**
	STD	.57	0.97	14	8.36	59	0.65
Inactive (n=21)	mean value	**2.33**	**1.6**	**170**	**27.31**	**150**	**2.24**
	STD	.49	1.64	18	6.09	42	0.47
Group differences	significance	.000	.137	.842	.002	.002	.000
	Effect size (Cohen´s d)	2,34	-.48	.06	.99	1.03	1.21