PACE

Effect of Physical ACtivity in Fingolimod Treated patiEnts (PACE) With Relapsing-remitting Multiple Sclerosis

Background

Multiple Sclerosis (MS) is a chronic, demyelinating, immune-mediated disease of the central nervous system affecting about 2.3 times as many women as men. It frequently occurs in young adults. Progress, severity and the individual symptoms like muscle weakness, depression, cognitive impairment and fatigue cannot be predicted. Especially fatigue is one of the most common and disabling symptoms of multiple sclerosis and it is reported by up to 80 % of all persons with MS (pwMS). Up to 40% of pwMS report fatigue as the most disabling problem, severely affecting daily activities and thus reducing quality of life. Fatigue may be directly related to primary disease mechanisms (inflammation, demyelinisation, axonal damage) or to secondary, non-disease-specific factors such as physical inactivity.

Since fatigue can be caused by physical inactivity, it seems intuitive that physical activity and exercise may ameliorate fatigue in terms of onset, severity and duration. Indeed, numerous studies have given evidence not only for positive effects of exercise on muscle force and aerobic capacity, but also for positive effects on walking ability and fatigue. Positive effects of exercise on fatigue are not consistently shown across all studies, though. Explanations are heterogeneous study samples that often included non-fatigued patients. In addition, only few studies defined fatigue as primary study goal and results seem to depend upon the fatigue measures that were used.

To carefully dissect the effect of exercise on fatigue outcomes in RRMS patients, disease modifying therapy has to be restricted to the least confounding factor. In the present study, only patients were included who received stable and efficient immunomodulatory treatment with Fingolimod.

Goal

The primary goal of this study is to evaluate the effect of a structured physical training program vs. no training on the primary outcome fatigue. Secondary outcomes are dynamic strength of the lower extremities (knee flexion/tension), isometric strength of the trunk muscles (trunk flexion/extension), health-related quality of life (HAQUAMS), depression (BID-II), aerobic capacity (treadmill spiroergometry) and physical activity levels (accelerometry, Baecke questionnaire). Exploratory objectives are the evaluation of the effect of physical training on the course of the disease and to explore physical activity relevant social-cognitive variables in this population.

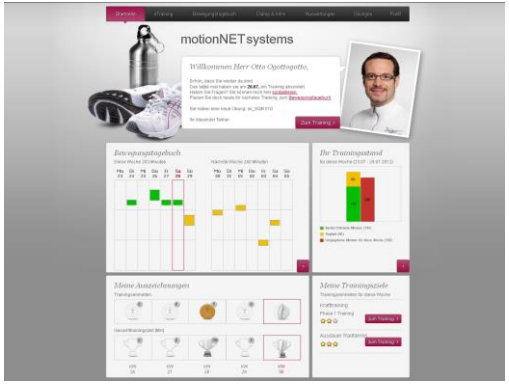
Methods

Prospective 6-month, multicenter, randomized, controlled parallel group study. Inclusion Criteria: Subjects with relapsing remitting MS defined by 2010 revised McDonald criteria, pwMS with Expanded Disability Status Scale (EDSS) score of 0-3.5 (including), immunomodulatory treatment with prescribed fingolimod for at least one month prior to baseline, fatigue score assessed by mFIS of equal or greater than 14 at screening, neurologically stable with no evidence of relapse within 30 days prior to inclusion date.

Participants are randomly assigned to a 6-month intervention of e-training or waiting group. Allocation of participant to one of the two arms was performed after the central training center had established the level of physical fitness.

The e-training intervention employs a web-based application to administer an adaptive and individualized exercise protocol with the emphasis on endurance and strength training but also containing additional balance and core stability exercises. All exercises can be easily performed at home without the need of further devices. The intervention phase could be extended by an additional 6-month intervention period. The waiting group started the exercise program after the first 6 month.

The primary outcome fatigue is assessed with the Modified Fatigue Impact Scale. It is defined as change (decrease) in mFIS immediately after 6 month of training compared to baseline.



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