EFFECT OF TREADMILL TRAINING ON FATIGUE IN MULTIPLE SCLEROSIS: A PILOT STUDY

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CONFLICT OF INTEREST

None declared

ABSTRACT

Purpose: People with multiple sclerosis (MS) tend to be less physically active than the general population. Limited physical activity increases fatigue possibly affecting other functions such as balance. Treadmill training is a promising method to ameliorate these sympthoms. The aim of the study was to assess the effect of treadmill training on fatigue and balance.

Method: Thirty subjects with MS were recruited; the mean age and (standard deviation) was 47.6 (9.2). The Median EDSS score was 5.5 (3-6.5). Subjects were randomized into a control group receiving 12 sessions of conventional therapy and an experimental group receiving conventional therapy including 15' of treadmill training. Rate of Perceived Exertion (RPE), Heart Rate (HR), Fatigue Severity Scale (FSS) and Berg Balance Scale were assessed before and after rehabilitation.

Results: In spite of a low HR (107 Beats/min) the RPE score was high (15,8) at baseline assessment. In the experimental group RPE significantly decreased to 12.8 (p= 0.04) after training. Treadmill training had also a positive effect on HR but no changes in FSS and balance were observed.

Conclusions: MS subjects showed a high level of exertion before treatment. Treadmill training was effective in reducing level of perceived fatigue with no impact on balance.

Keywords:

Training, fatigue, balance

INTRODUCTION

Multiple sclerosis (MS) is the most common progressive neurological disease in young adults. Because of the variable distribution of demyelisation throughout the central nervous system, people with MS (PwMS) may experience fatigue (Larocca NG, 2011), reduced aerobic endurance, coordination, strength, sensation and balance disorders leading to loss of functional capacity and physical inactivity (White LJ and Dressendorfer RH, 2004; Motl RW and Pilutti LA, 2012). In fact, people with MS tend to be less physically active than the general population, even when their MS has caused minimal disability. (White LJ and Dressendorfer RH, 2004) Limited physical activity and impairments lead to further decrease in activities and participation which again induce deconditioning and increase fatigue. This could affect other functions such as gait and balance. (Morrison EH et al., 2008)

Lapierre et al found that fatigue is the most disabling symptom in 28-40% of PwMS and also one of the most common: 78-90% of individuals experience fatigue and 40% of them reported to be fatigued every day across a 30-day period. (Lapierre Y and Hum S., 2007). Fatigue is a multidimensional construct comprising primary fatigue that is a result of the disease process, and secondary fatigue that is a result of disease-related manifestations. (Lapierre Y and Hum S, 2007) Several tools have been developed to assess multidimensional aspects of fatigue including physiological fatigue (Rampello A et al., 2007), perception of fatigue in activities of daily living (Krupp LB, 1989) and perception of fatigue during physical effort (Robertson RJ and Noble BJ, 1997), defined as physical and/or mental weariness resulting from exertion that leads to an inability to continue task at the same intensity without a resultant deterioration in performance. (Evans WJ and Lambert CP, 2007) The neurophysiological bases of perceived exertion are poorly understood and can be due to the complex integration of different inputs to the central nervous system (CNS). (Marcora SM et al, 2009) With respect to a psychobiological model of exercise performance, mental fatigue may limit exercise tolerance without any alteration of the cardiorespiratory and muscoloenergetic systems. (Marcora SM et al, 2009) The assessment of exertion is important because it can have a role in curtailment of activities of daily living and in social activities, as some days PwMS may experience an overwhelming sense of fatigue that cannot be alleviated with rest. Rate of Perceived Exertion (RPE) is a scale originally developed for healthy subjects that has also been used also with PwMS to assess exertion during efforts. It is frequently used both to assess and to set exercise intensity. (Robertson RJ and Noble BJ, 1997)

According to the task oriented approach, treatment for the reduction of fatigue should be incorporated into task related activities of daily living. Treadmill training is an example of a "task oriented" approach to treatment that is commonly used as an intervention for neurological conditions because it is a highly repetitive form of gait training.(Newman MA et al., 2007) Moreover, it promotes both specific practice and use of systems concerned with walking while providing an aerobic training stimulus. (Newman MA et al., 2007)

The effects of treadmill and aerobic training have been addressed and it has been found to be beneficial for healthy people and people with stroke, improving aerobic capacity and general fitness with concomitant changes in neuroactivation. (Luft AR et al.2005; Kramer AF et al. 2006)

Nowadays, it is recognized that exercise is safe and PwMS are encouraged to train to achieve aerobic cardiovascular benefits and improve their skills in tasks execution (Brown TR and Kraft GH, 2005) although there is some ambiguity as to its efficacy (Motl RW and Pilutti LA, 2012). Mostert and Kesselring (Mostert S and Kesselring J, 2002) found that a short training program can improve some aspects of aerobic fitness, fatigue, level of physical activity and improve perception of health status, without a change in maximal aerobic capacity; while Petajan et al (Petajan JH et al, 1996) found an increase (10%) in maximal aerobic capacity in an aerobic training group. Rampello et al. comparing aerobic training and traditional neurological treatment showed that aerobic training is more effective than neurological training in improving maximum exercise tolerance in terms of VO_2 while they found no differences between groups on the fatigue level as assessed by a self-administered questionnaire. (Rampello A et al., 2007) The impact of fatigue after physical exercise on balance has not been experimentally tested although it has been suggested that a rehabilitation programme can foster clinically relevant change in fatigue and balance. (Hebert JR et al., 2011) Given the importance of balance in activities of daily living and in fall risk the relationship between these two domains is an important aspect that needs exploring.

The aims of the present study were to provide further evidence in PwMS of the:

1. Effect of a single treadmill session on fatigue.
2. Effect of treadmill training:
   a. on perceived exertion, fatigue during activities of daily living and physiological adaptations.
   b. on balance.

MATERIAL AND METHODS

A convenient inpatient sample of 30 subjects (18 male), willing to participate in the study, was recruited; the inclusion criteria were: ability to stand independently in the upright position for 30 s, ability to walk for 6 meters even with assistive device, no history of cardiovascular, pulmonary and metabolic or other medical conditions. Following initial assessment, subjects were randomly assigned to two subgroups.

Table 1 About here

All subjects signed an informed consent to the protocol which was approved by the local Ethics Committee and conformed to the standards for human experiments set by the Declaration of Helsinki.

The following scales were collected. The first three scales measured three different aspects of fatigue while the other scales measure mood and balance.

The Borg Scale also called Rate of Perceived Exertion (RPE) was used to monitor exertion during the exercise testing. (Robertson RJ and Noble BJ, 1997) Perceived exertion is defined as subjective effort intensity and fatigue during physical exercise.
RPE ranges from 6 to 20 where 6 means “no exertion at all” and 20 means “maximal exertion”. A Rate of 11-14 represents “moderate intensity”. This scale is validated for healthy subjects and used also for PwMS. (Morrison EH et al., 2008)

Heart Rate (HR) was used to assess the physiological aspects and adaptations related to the effort. It was monitored by Technogym Polar Electro OY™ and reported as beat/minute; HR was assessed at rest with the subject seated on a chair (HR rest) and at the end of treadmill exercise (HR treadmill).

The Fatigue Severity Scale (FSS) is a tool designed to assess the impact of fatigue on daily function. (Krupp LB, 1989; Bergamaschi R et al., 1997) It was designed for MS patients and patients with chronic fatigue syndrome. It consists of 9 items: 3 items are related to physical exercise; 3 items to the psychosocial environment; the other 3 items are generic. The items are related to fatigue that the subjects rate according to their level of agreement measured on seven-point scale from 1, indicating “strongly disagree”, to 7 , indicating “strongly agree”. Maximum score is 7 that means high level of fatigue.

Fatigue can be associated with mood disorder (Dobkin BH, 2008) so we used Positive And Negative Affect Schedule (PANAS) to measure two dimensions of mood to exclude this confounding factor. PANAS is a self-administered scale comprising 20 items with a 10 positive and 10 negative descriptors ranging from 10 to 50, where higher scores indicate higher affect.

Reponses were scored on a 5-point likert scale ranging from 1 “very slightly or not at all” to 5 “very much or extremely”. The positive dimension refers to a state of emotional well-being, while the negative dimension refers to a state of emotional distress.(Watson D et al, 1988)

Berg Balance Scale (BBS) was used to assess static balance. This scale rates balance skills from 0 (cannot perform) to 4 (normal performance) on 14 items with a maximum total score of 56. The items explore the ability to sit, stand, lean, turn and maintain the upright position on one leg. (Cattaneo D and Jonsdottir J, 2009)

Dynamic Gait Index (DGI). This scale measures gait function and dynamic balance. The eight tasks of this scale include walking, walking with head turns, pivoting, walking over objects, walking around objects and going up stairs. Maximum score is 24 indicating good dynamic balance. (Cattaneo D et al., 2007)

Assessment procedures

After the informed consent was signed, the following assessments were carried out (see Figure 1).

Baseline 1 (T1): In this first evaluation baseline measurements were collected and subjects were familiarized with the treadmill.

The familiarization on the treadmill was carried out to make the patient confident with the task and to set velocity at which the patient felt max exertion. The subjects wore their usual shoes and walked with hand support. While on the treadmill, subjects were exposed to increased gait speeds. According to Dettmers the velocity was increased until the perceived level of exertion was 16-17 at RPE. (Dettmers C et al, 2009)

Outcome measures: BBS, DGI, FSS, PANAS.

Baseline 2 (T2): in this second baseline evaluation session, done the day after Baseline 1, the impact of a single treadmill session on fatigue, RPE and HR was assessed.

Subjects performed a test on the treadmill at a preset velocity (as determined in T1) with their usual shoes and with two hands supported.

Outcome measures: HR rest, RPE and HR after treadmill.

Post rehabilitation 1 (T3): the effect of 15 treadmill sessions on Balance, Mood and Fatigue during ADL, and physiological adaptations after rehabilitation was assessed.

Outcome measures: BBS, DGI, PANAS, FSS.

Post rehabilitation 2 (T4): This evaluation session was carried out the day after T3 with the same conditions in terms of velocity and duration used in the first treadmill session (T2) to assess the impact on perceived fatigue and HR.

Outcome measures: HR rest, RPE and HR after treadmill .

Figure 1. About Here

Treatment

The Experimental group (EXP) received 30’ of ‘conventional therapy’ such as the control group, as well as, 15 minutes of treadmill training. According to recommendations in the literature (Morrison EH et al., 2008),**Errore. Il segnalibro non è definito.** subjects were encouraged to walk at an intensity of 11 and 12 points of RPE. To promote gait adaptation slope and speed of treadmill were changed within sessions. No feedback were provided to improve walking skills and symmetry.

The Control group (CTRL) received 45 minutes of ‘conventional therapy’ aimed to increase joint range of motion, muscle strength, balance, gait or upper limb function according to treatment plan. In this way the experimental and control group received equal time in therapy.

Each subject, irrespective of group assignment, underwent 12 treatment sessions over a two weeks period.

Statistical analysis:

Mann-Whitney (U) test was used to assess statistically significant differences of the change scores between groups for FSS, DGI, BBS and PANAS: differences between T1 and T3, that is before and after the last treadmill session (Figure 1) were compared the effect of the rehabilitation protocol.

U test was also used to check statistically significance differences in HR and RPE between T2 and T4. An effective treatment would reduce the increment of RPE and HR at the end of this phase with respect to the beginning of the study.

The level of statistical significance test was set at $p < 0.05$.

RESULTS

The mean age and standard deviation (SD) of the sample was 47.6 (9.2) years. The average onset of the pathology was 15.0 (9.8) years before the start of the study the median EDSS score (min-max) was 5.25 (3-6.5). The percentage of subjects with relapsing remitting, primary and secondary progressive type of MS were respectively: 47.6% (n= 14), 19.0% (n=6), 33.3% (n=10).

No statistically significant differences were found in demographic characteristics or in baseline measures between treated and control group (Table 1).

1. Effect of a single treadmill session

Subjects walked on the treadmill at an average speed of (Mean and (SD)) 2.5 (0.9) Km/h for 4.05 (2.05) minutes before they had to stop walking because they had reached maximum exertion.

After this treadmill session the whole group of subjects showed high levels of exertion that were not correlated with HR: they reported 16 (1.8) points at RPE scale with a mean HR of only 107.6 (15.1) beat/minute corresponding to 62.5% of maximum heart rate.

2. Effect of treadmill training (RPE, HR, FSS, balance and gait)

Figure 2 depicts RPE scores for experimental and control group following treadmill. No differences were noted between groups pre intervention, all reported around 16 points on the RPE scale confirming that both groups were similarly fatigued at the end of the first treadmill session (T2).

After 12 treatment sessions (T4) the fatigue level in the experimental group decreased three points moving from “Hard exercise” (16 points) to “Somewhat hard” (13 points) using the same workload as in T2 while the fatigue level in the control group decreased around one point. The difference in between groups were statistically significant (p=0.04).

Figure 2. About Here

Table 2 shows HR at rest, after the first treadmill session (T2), and after the last intervention session (T4). The control group showed higher levels of HR at rest and HR after treadmill with respect to the experimental group; however these differences were not statistically significant. No statistically significant difference was observed between groups in change scores (before treadmill to after) after the first treadmill session (T2) indicating that the increment of heart rate was similar in both groups. From before the treadmill (T2) to after the 12 treadmill sessions

(T4) the change in HR were 21.00 (9.77) beat/min for the experimental group and 33.43 (16.69) beat/min for the control group; the difference in change scores between groups was statistically significant (p=0.02) indicating that the increment of heart rate after the treadmill session was lower for the experimental group with respect to the control group.

Table 2. About Here

FSS and PANAS scores are reported in Table 3. No statistically significant changes pre-post rehabilitation (T3-T1) were observed for fatigue during ADL and positive and negative affect (mood) as monitored with PANAS following rehabilitation.

Table 3. About Here

Table 4 shows data on static and dynamic balance pre and post treatment. No statistical differences were found between groups.

Table 4: About here.

DISCUSSION

The aims of the present study were to investigate the effect of a single treadmill session and the effect of an aerobic treadmill training on fatigue and balance in PwMS.

1. Effect of a single treadmill session on fatigue.

The first finding of the present study is that MS subjects have a high level of exertion as demonstrated by a score of RPE of 16 points at RPE with a relatively low HR of 107 beat/min. This rate of exertion can be considered abnormal since normative data on healthy subjects indicate that exercising at 107 beat/min corresponds to a score of 11 points at RPE. (Robertson RJ and Noble BJ, 1997)

The observed high level of RPE with a low HR after treadmill is in contrast with findings of Morrison and Mc Cullagh on PwMS (Morrison EH et al., 2008; McCullagh R et al., 2008) where it was reported that a HR of about 150 beat/min was found for a RPE score of 17 during a graded maximal test on a cycle ergometer (McCullagh R et al., 2008). These differences between our results and those obtained by Morrison and Mc Cullagh may be due to clinical differences since our sample had a higher level of disability (higher EDSS score) and a longer onset of the pathology. It is indeed possible that in our sample the higher level of disability and the high perceived rate of exertion prevented subjects from walking longer and faster reaching higher HR. Further, it is possible that compared to cycling walking on the treadmill requires a higher level of cognitive effort to control gait pattern and balance and it is known that cognitive effort is correlated with perceived exertion (Marcora S, 2009; Marcora S, 2009; Marcora SM and Staiano W, 2010) Compared to the study of Morrison and Mc Cullagh where cycling was applied the use of a more demanding walking task may have caused an increased perceived effort during the walking session thus increasing the level of perceived exertion.

2. Effect of treadmill training on three dimensions of fatigue and balance

Treadmill training was effective in reducing perceived exertion. These results are in agreement with those of Morrison and Mc Cullagh (McCullagh R et al,2008) who found a 3 points reduction in RPE after aerobic training comprising 5 minutes of warm up and cool down and 40 minutes of exercise. Treadmill training may have had an effect on RPE because it is a fatiguing task stressing cognitive and physiological factors. With respect to cognitive factors Marcora et al**Errore. Il segnalibro non è definito.** have suggested that cognitive resources may play an important role in perceived exertion.(Marcora S, 2009) Indeed, some experimental evidence come from a study on elderly subjects that found that walking on treadmill is a cognitively demanding task requiring attention and the use of frontal area associated with executive functions. (Luft AR, 2005) It is thus possible that treadmill training increased the availability of cognitive resources, and improved walking skills reducing the impact of the task on such cognitive factors. This may have reduced the rate of perceived exertion.

With respect to physiological factors a small improvement in physical conditioning (HR) was observed in the experimental group indicating cardiovascular adaptations. This is in agreement with studies involving healthy subjects indicating that endurance exercise training results in adaptations of the cardiorespiratory and neuromuscular systems with a reduction of HR and oxygen consumption. (Jones AM and Carter H, 2007)

The effect of training on HR in MS are controversial. Rampello, Newman and Petajan found that aerobic training induced a significant change in maximum aerobic capacity (VO_2) and HR (Rampello A et al, 2007; Newman MA et al, 2007; Petajan JH, 1996) while Van der Berg (Van der Berg M, 2006) found no difference in HR after aerobic training. The small reduction of HR observed in our study may be due to the low amount of workload, 10-12 treatment sessions might not be enough to promote HR adaptations. Further, as suggested by Marcora et al (Marcora SM and Staiano W, 2010), it is possible that perceived exertion limited the exercise tolerance of our subjects preventing them from reaching 65-90 % of maximum HR that is considered the threshold beyond which cardiovascular adaptations starts. (American College of Sports Medicine, 1990)

Robertson and Noble reported that psychological factors could influence the intensity of exertional perception in clinical situations. (Robertson RJ and Noble BJ, 1997) To take into account these factors we measured mood before and after training but found that while RPE was reduced there were no changes in mood.

While we found a change of RPE after training there was no reduction in fatigue as measured by the Fatigue Severity Scale. Similar results were observed by Van der Berg, Petajan and Rampello who used scales similar to FSS and found no improvement in fatigue after rehabilitation. (Van der Berg M et al, 2006; Petajan JH et al, 1996; Rampello Aet al, 2007) This may be due a lack of effect of training or to low sensibility to change of the FSS. The fact that our sample consisted of inpatients that were recovered during the study may also have influenced the results since they had to imagine how tired they would feel during their ordinary daily activities.

Our data do not support the theory that the adjunction of an aerobic treadmill training improves gait and static balance in PwMS. To our knowledge there are no firm conclusions on the effects of aerobic training on balance although Benedetti et al showed an effect of this training on postural stability in three PwMS. (Benedetti MG et al., 2009) The lack of transfer of treadmill training to balance stresses the importance of a multivariated intervention specifically tailored to subject's functional disorders.

Since this was a pilot study there were limitations: firstly, the assessment was not carried out by a blind assessor. We tried to reduce this bias by choosing a self-administered test and using instrumental measures of cardiofrequency as primary outcome variable. Secondly, we did not collect follow up data since we recruited only inpatients that were treated within a 3-week period and then discharged to home.

In conclusion treadmill training was effective in reducing level of perceived exertion with a small impact on heart rate while there was no effect on fatigue during daily activities and balance. Further studies are needed to assess the impact of treadmill training on ADL and balance.

Table 1. Demographic and clinical characteristics of the MS sample in Experimental and Control group.

EXP: Experimental group; CTRL: Control group; EDSS: Expanded Disability Status Scale; RR: Relapsing Remitting; PP: Primary Progressive; SP: Secondary Progressive

Table 2. Mean and (SD) of heart rate for experimental and control group

EXP: Experimental group; CTRL: Control Group; T2: Assessment on treadmill before rehabilitation; T4: Assessment on treadmill after rehabilitation

Table 3. Median and (Range) of Fatigue Severity Scale (FSS) and Positive and Negative Affect Schedule (PANAS)

EXP: Experimental Group; CTRL: Control Group; T1: Clinical assessment before rehabilitation; T3: Clinical assessment after rehabilitation

Table 4. Mean and (SD) of Berg Balance Scale (BBS) and Dynamic Gait Index (DGI) at baseline and at last session

EXP: Experimental Group; CTRL: Control Group; T1: Clinical assessment before first treadmill session; T3: Clinical assessment after rehabilitation

Figure 1. Flow chart of the study.

Figure 2. Rate of Perceived Exertion (RPE) scores for experimental and control group pre and post rehabilitation.

Mean of RPE scores, vertical bars represent 95% confidence interval of means*;* EXP: Experimental Group; CTRL: Control Group. T2: assessment after first treadmill session; T4: assessment after last treadmill session.

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Table 1. Demographic and clinical characteristics of the MS sample in Experimental and Control group.

	Age mean (SD)	Onset mean (SD)	EDSS Median (Range)	RR%	PP%	SP%
EXP (N=15)	49.6 (9.4)	14.5 (9.7)	5.0 (3-6.5)	37.5	25.0	37.5
CTRL (N=15)	45.7 (8.9)	15.5 (10.3)	5.5 (3.5-6)	54.6	18.2	27.3

Table 2. Mean and (SD) of heart rate for experimental and control group

	HEART RATE (Beat/Min)					
	BEFORE REHABILITATION (T2)			**AFTER REHABILITATION (T4)**		
	At rest	After treadmill	Change score	At rest	After treadmill	Change score
EXP	74.79 (14.22)	102.92 (17.22)	28.13 (11.09)	76.42 (11.94)	97.42 (14.53)	21.00 (9.77)
CTRL	80.66 (10.80)	112.40 (11.81)	31.74 (13.77)	78.53 (11.00)	112.46 (18.71)	33.43 (16.69)

Table 3. Median and (Range) of Fatigue Severity Scale (FSS) and Positive and Negative Affect Schedule (PANAS)

	BEFORE REHABILITATION (T1)		**AFTER REHABILITATION (T3)**		**CHANGE SCORES (T3-T1)**		**P-LEVEL OF CHANGE SCORES**
	EXP	**CTRL**	**EXP**	**CTRL**	**EXP**	**CTRL**	
FSS	5.4 (1.8-7)	5.4 (2.3-6.6)	5.5 (2.4-7)	5.3 (1.6-7)	0.10	-0.10	0.38
PANAS pos	29.0 (21-43)	28.0 (23-47)	30.0 (21-44)	33.0 (17-49)	1.0	5.0	0.86
PANAS neg	26.0 (10-43)	23.0 (10-44)	21.0 (9-35)	21.0 (10-46)	-5.0	-2.0	0.48

Table 4. Mean and (SD) of Berg Balance Scale (BBS) and Dynamic Gait Index (DGI) at baseline and at

last session

	BEFORE REHABILITATION (T1)		AFTER REHABILITATION (T3)		CHANGE SCORES (T3-T1)		P-LEVEL OF CHANGE SCORES
	EXP	**CTRL**	**EXP**	**CTRL**	**EXP**	**CTRL**	
BBS	43.61 (9.35)	47.13 (5.02)	47.62 (8.46)	50.28 (4.06)	4.01	3.15	0.33
DGI	15.38 (4.48)	16.00 (5.07)	17.54 (3.95)	18.07 (5.15)	2.16	2.07	0.51

Figure 1. Flow chart of the study.

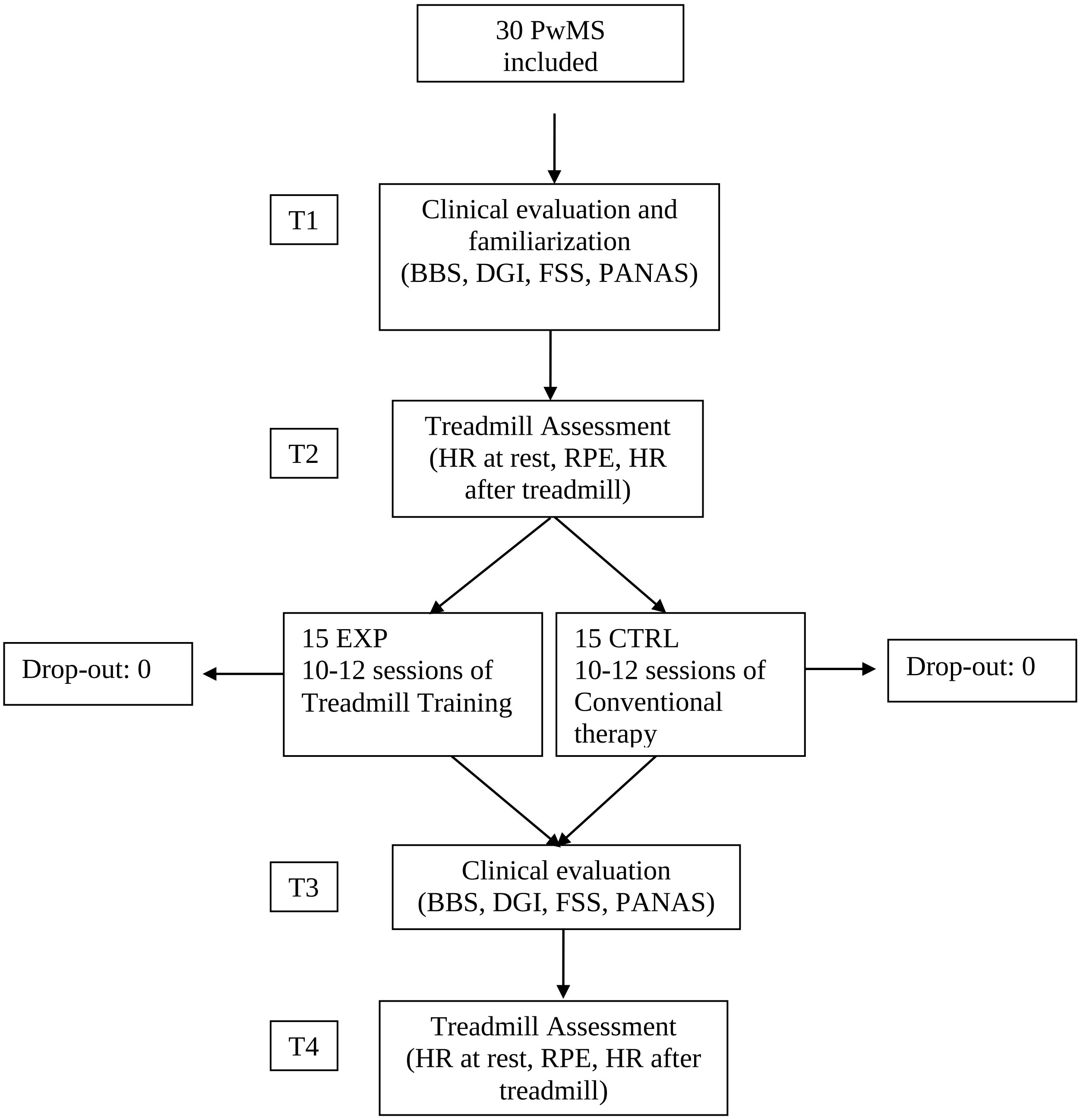

Figure 2. Rate of Perceived Exertion (RPE) scores for experimental and control group pre and post

rehabilitation.