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Effects of MOTOmed® movement therapy on the motor function and main symptoms of patients with Parkinson's disease: a systematic review

Efectos de la terapia de movimiento MOTOmed® sobre la función motora y los principales síntomas de pacientes con enfermedad de Parkinson: una revisión sistemática

Karina Pitombeira Pereira-Pedro, Iris Machado de Oliveira, José María Cancela Carral, Irimia Mollinedo Cardalda
University of Vigo (Spain)

Abstract. Introduction: Scientific findings show immediate improvements after forced assisted cycling at high pedaling speeds of up to 90 revolutions per minute in patients with Parkinson's Disease, thus this review aimed to estimate the efficacy of MOTOmed® movement therapy. to increase motor function and alleviate the main symptoms in these patients. Methods: Systematic review including randomized controlled trials examining MOTOmed® movement therapy interventions, alone or as an adjunct to rehabilitation, for patients with Parkinson's disease. The risk of bias assessment tool followed the recommendations of the Cochrane Handbook 5.1.0. All included studies reported the effects of mobility as primary outcomes. Standardized mean differences or mean differences with corresponding 95% confidence intervals (CI) were calculated. Results: In total, 7 trials with a total of 206 patients were included in the analysis. All studies were of moderate quality. MOTOmed® movement therapy resulted in statistically significant improvements in the MDS-UPDRS (Movement Disorder Society-Unified Parkinson Disease Rating Scale) Motor III score ($p<0.05$); Upper limb MDS-UPDRS score ($p<0.05$); Total MDS-UPDRS ($p<0.04$): Upper body function ($p<0.007$); bradykinesia ($p<0.044$); Cycling variables: higher cadence ($p<0.001$); Timed up and done ($p>0.05$); tremor score ($p<0.05$); Walking time ($p<0.05$); Gait steps ($p<0.05$); Pronation and supination ($p<0.05$); Parkinson's Disease Questionnaire -PQD8 (bandages and depressions $p<0.05$); Gait analysis: speed ($p<0.000$), stride length ($p<0.000$), monopedal posture ($p<0.000$), swing phase ($p<0.000$); Biodex® Balance System: Clinical Test of Sensory Integration of Balance-CTSIB1 ($p<0.007$). Conclusion: MOTOmed® movement therapy alone or combined with standard rehabilitation improves motor function and main symptoms in patients with Parkinson's disease.
Keywords: Parkinson´s disease, MOTOmed®, Physical Therapy, Physical Activity, Rehabilitation.

Resumen. Introducción: Los hallazgos científicos muestran mejoras inmediatas después de un ciclismo asistido y forzado en altas velocidades de pedaleo de hasta 90 revoluciones por minuto en pacientes con la Enfermedad de Parkinson, así esta revisión tuvo por objetivo estimar la eficacia de la terapia de movimiento MOTOmed® para aumentar la función motora y aliviar los principales síntomas en eso pacientes. Métodos: Revisión sistemática que incluyó ensayos controlados aleatorios que examinaron las intervenciones de terapia de movimiento MOTOmed®, exclusiva o como un extra a la rehabilitación, para pacientes con enfermedad de Parkinson. La herramienta de evaluación del riesgo de sesgo siguió las recomendaciones del manual Cochrane 5.1.0. Todos los estudios incluidos informaron los efectos de la movilidad como resultados primarios. Se calcularon las diferencias de medias estandarizadas o las diferencias de medias con los correspondientes intervalos de confianza (IC) del 95%. Resultados: En total, se incluyeron en el análisis 7 ensayos con un total de 206 pacientes. Todos los estudios fueron de calidad moderada. La terapia de movimiento MOTOmed® resultó en mejoras estadísticamente significativas en el puntaje del MDS-UPDRS (Movement Disorder Society-Unified Parkinson Disease Rating Scale), Motor III ($p<0.05$); Puntaje MDS- UPDRS de las extremidades superiores ($p<0,05$); MDS- UPDRS total ($p<0,04$): Función tren superior ($p<0,007$); bradicinesia ($p<0,044$); Variables de ciclismo: mayor cadencia ($p<0,001$); Temporizado arriba y listo ($p>0.05$); puntuación de temblor ($p<0,05$); Tiempo de caminata ($p<0,05$); Pasos de marcha ($p<0,05$); Pronación y supinación ($p<0,05$); Parkinson's Disease Questionnaire -PQD8 (vendajes y depresiones $p<0,05$); Análisis de la marcha: velocidad ($p<0,000$), longitud de zancada ($p<0,000$), postura monopedal ($p<0,000$), fase de balanceo ($p<0,000$); Sistema de Equilibrio Biodex®: Clinical Test of Sensory Integration of Balance-CTSIB1 ($p<0,007$).Conclusión: la terapia de movimiento MOTOmed® exclusiva o combinada con la rehabilitación estándar mejora la función motora y los principales síntomas en pacientes con enfermedad de Parkinson.
Palabras clave: Enfermedad de Parkinson, MOTOmed®, Fisioterapia, Actividad Física, Rehabilitación.

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Irimia Mollinedo Cardalda
irimia_mollinedo@hotmail.com

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease and the most common neurological disease of the basal ganglia (Cummings, 1999). It is projected that in the world's most populated nations, individuals diagnosed with PD will increase from between 4.1 and 4.6 million in 2005 to between 8.7 and 9.3 million in 2030 (Dorsey et al., 2005).

PD develops when dopaminergic neurons in the midbrain die and stop producing the neurotransmitter dopamine. This neurotransmitter is responsible for the ability of movement through the interaction of neurons in the basal ganglia and substantia nigra (Triarhou, 2013). This disease is defined as the presence of two out of four cardinal symptoms: akinesia (bradykinesia), tremor at rest, rigidity, and postural instability (Morris, Martin & Schenkman, 2010; Jankovic, 2008).

The degenerative nature of PD results in progressive deterioration of motor skills along with reduced sensory and cognitive function. The current treatment for PD is medication (levodopa, dopamine agonists) and surgical intervention (deep brain stimulation). These treatments only partially treat the symptoms and do not slow progression of the disease. Furthermore, they often have undesirable side effects, such as dyskinesia (Ahlskog & Muenter, 2001). These surgical and medical treatments are associat-

ed with excessive health care costs (Findley et al., 2003).

Physical activity can be seen as a complement to pharmaceutical treatment to manage the inherent decline associated with the disease. The notion of integrating physical activity in the therapeutic treatment of PD was introduced during the 1950's. Back then, physical activity had already been foreseen as a way of minimizing the limitations induced by the disease (Bilowit, 1956). Results of scientific examinations demonstrate that various movement therapies can lead to improvements in the symptomatology in Parkinson's patients (Farley & Koshland, 2005; Hackney & Earhat, 2009; Lee, Lee & Hwang, 2011).

Treatment options without a medical or surgical approach present an essential alternative in current PD treatment options. Exercise training has been shown to be a valid method to improve gait disturbances. Approaches such as body-weight supported exercises on a treadmill, lower leg strengthening and balance training have been shown to improve motor functions and gait disorders (Vitório et al., 2011). An exercise approach that is recently gaining popularity is forced exercise training, which can be conducted with either a passive assistive or an active assistive approach. The patients train on a movement exerciser and make movements like those made when cycling but at a higher cadence than they could normally manage. Both active and passive assistive forced exercise training have been shown to reduce Parkinsonian symptoms such as rigor, bradykinesia, and tremor (Laupheimer, Hartel, Schmidt & Bos, 2011).

New scientific findings show immediate improvements after assisted, forced cycling at high pedaling rates up to 90 revolutions per minute (Ridgel, Vitek & Alberts, 2009).

Movement therapy systems can help individuals to achieve and increase mobility and to improve endurance, thereby increasing independence in everyday life and improving quality of life (Diehl, Schule & Kaiser, 2008). The MOTOmed® system is an effective supplement to sports and movement therapy in medical facilities and at home; it can be used in passive or active assistance modes. Users execute movements like those performed when cycling. This system has been applied clinically in step-by-step therapy for patients with neurological diseases. MOTOmed® movement therapy provides patients with visual feedback during different periods of training; the flat exercise mode is a gentle, risk-free alternative to walking, jogging, or cycling, which can benefit patients with existing morbidity. The device enables safe training of the lower extremities, even in patients with very limited mobility and coordination, and it allows patients to train effectively and independently (Gao, Xu, Huang & Xiao, 2013).

The use of this type of therapy is recent and the studies do not use the same tools to evaluate the effectiveness of this therapy in patients with PD. Therefore, the aim of the study was an examination of the existing literature into the effects of an intervention with the movement therapy device MOTOmed® on fine motor skills, coordination, mobility, gait control and tremor as well as the mental state of the Parkinson's patients. We carried out a systematic review to examine the capacity of the MOTOmed® system to improve the main symptoms in patients with PD, analyzing studies found, with the intention of finding in the applications of the MOTOmed® cycling system in patients with PD, combined or not with conventional rehabilitation, influences the motor function and symptomatology of these patients.

Methods

Study Design

Systematic Review

Data Source and Search strategy

For this systematic review, the Embase (1974–), Web of Science (1900–), PubMed (1950–), OVID (1996–), Cochrane Central Register of Controlled Trials (1948–), Sportdiscus (1990–), Scielo (1990–), PEDRO (1990–), databases were searched to identify relevant articles published in English, Portuguese, and Spanish from the beginning of coverage through 10 May 2019. In addition, a manual retrospective search was conducted to identify articles published in Rehabilitation Medicine, Sports Science, Physical Therapy and Rehabilitation.

Study Selection

Two reviewers (KP and JC) examined the titles and abstracts of retrieved studies according to the following criteria. The findings were discussed regularly, and a third reviewer (IM) was consulted in cases of disagreement. The inclusion criteria were as follows: (1) randomized controlled trial; (2) medically confirmed Parkinson's diagnosis; (3) stage of disease 1 – 3 according to Hoehn & Yahr (1967); (4) inclusion of MOTOmed® movement therapy in the experimental protocol. The exclusion criteria were as follows: (1) the use of different cycling devices, rather than of MOTOmed® use with conventional therapy; (2) inability to extract data; and (3) duplicate data. In cases of duplicate reports, reviewers either extracted data from each report separately, then combined information from multiple data collection forms, or extracted data from all reports directly into a single data collection form, as appropriate.

Data extraction

Two independent reviewers (KP and JC) initially screened study titles and abstracts for eligibility, then screened and evaluated the full texts of all relevant articles. Disagreements were resolved through consultation with a third reviewer (IM). Then, pairs of review authors extracted data independently, with any disagreement resolved by consensus or consultation with a third reviewer (IM). The following information was extracted from selected studies: first author, date, and source of publica-

tion; sample size; patient age; average stage Hoehn & Yahr (1967); MOTOmed® intervention characteristics (frequency, duration, methodology); and outcome measures (motor function, PD symptoms, tremor and bradykinesia, physical tolerance, gait analyses and quality of life). Considering that the study focused on analyzing the influence of MOTOmed® cycling therapy on motor function and main symptoms in PD patients, the main results were considered those that are commonly analyzed in these patients, such as the Unified Parkinson's Disease Rating Scale (UPDRS), tremors, gait analysis, quality of life, balance and cycling performance data generated by the MOTOmed® system.

Risk of bias

We used the Cochrane (Higgins et al., 2011) tool to assess the risk of bias of selected studies in the following categories: random allocation, concealed allocation, blinding of participants and personnel, detection bias, attrition bias, reporting bias, and others. The risk of bias was recorded as high (3), low (2), or unclear (1). Reviewers (KP and JC) assessed all items independently, and disagreements were resolved by consensus in consultation with a third reviewer (IM).

Results

Description of the Included Studies

From the 23 studies identified in the systematic literature search, 2 duplicate records were removed. After the scanning of titles and abstracts, 11 publications remained eligible. Full-text examination led to the inclusion of 7 randomized controlled trials in this systematic review. (Figure 1) illustrates the selection process. Of the seven studies included for analysis, three performed cycling therapy with MOTOmed® exclusively with patients. Another three refer to the continuation of standard therapy, and only one study described the performance of a 30 minutes of resistance training, 20 minutes of flexibility training and 5 minutes neuromuscular activity, in which gait and balance were trained.

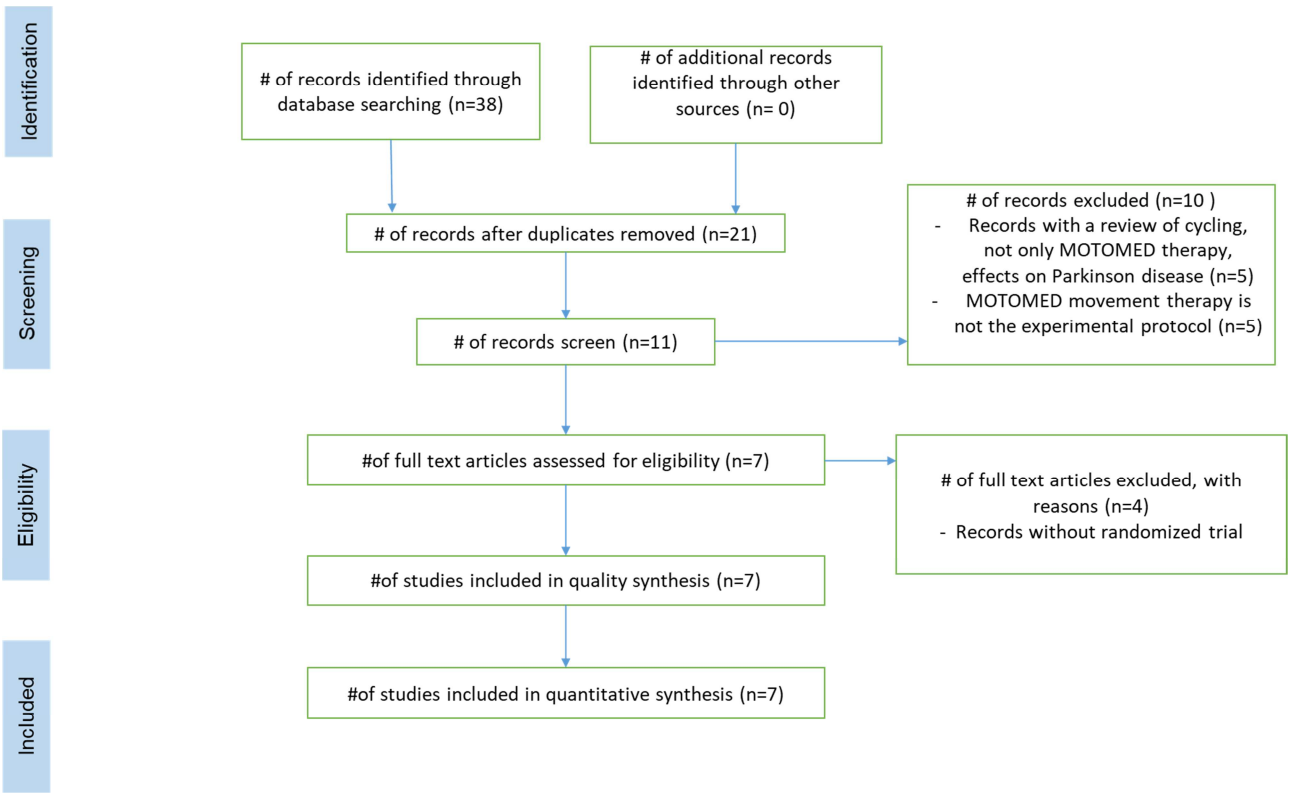

Figure 1. *Flow Chart*

Sample characteristics

Characteristics of and data from the selected trials are summarized in (Table 1). Six selected studies were performed in United States (Ridgel, Phillips, Walter, Discenzo & Loparo, 2015; Peacock, Sanders, Wilson, Fickes-Ryan, Corbett, Von-Carlowitz 6 Ridgel, 2014; Ridgel, Muller, Kim, Fickes & Mera, 2011; Laupheimer et al., 2011; Stuckenschneider, Helmich, Raabe-Oetker & Frobose, 2015; Wilson, 2013; Fickes, 2012) and one in Germany (Stuckenschneider et al., 2015), with a total of 206 participants. All studies were published in English. The participant sex was reported in five studies (Ridgel et al., 2015; Peacock et al., 2014; Ridgel et al., 2011; Laupheimer et al., 2011; Stuckenschneider et al., 2015) Mean (standard deviation) participant age ranged from 62.0 (7.3) to 71.5 (5.7) years. In all the included studies the patients had a medical diagnosis of Idiopathic Parkinson's disease.

Table 1.
Characteristics of randomized controlled trials

Study	n		Age Years	Hoehn & Yahr mean±sd (Interval)	Intervention Times/Week/Minutes	Intervention program		Outcomes
	Control	Experimental				control	Experimental	
Dynamic high-cadence cycling improves motor symptoms in Parkinson's disease. Ridgel, AL. et al., 2015	23 Static cycling	24 Dynamic cycling	EG: 67.2±1.6 CG: 67.3±0.9	EG: 2.1±0.2 CG: 1.8±0.1	4/1/40	MOTOMED® Static cycling without motor assist, speed not controlled. Preceded and concluded by a 5 min. passive cycling warm up/cool down at 40 to 50 rpm.	MOTOmed® Dynamic cycling 75-85 rpm. Preceded and concluded by a 5 min. passive cycling warm up/cool down at 40 to 50 rpm.	UPDRS Motor III score ($p<0.05$); UPDRS Upper extremity score ($p<0.05$); Cycling variables: higher cadence ($p<0.001$); Timed Up and Go ($p>0.05$).
Introducing a multifaceted exercise intervention particular to older adults diagnosed with Parkinson's disease: a preliminary study Peacock, CA. et al.,2014	9 Age-matched healthy	13	EG: 67.3±7.8 CG: 65.6±2.9	1 to 3	3/8/30	30 min. active-assisted cycling 70 to 75 rpm, 30 min. resistance training, 20 min. flexibility training, 5 min. neuromuscular (gait and balance).	MOTOmed® 30 min. active-assisted cycling 70 to 75 rpm, 30 min. resistance training, 20 min. flexibility training, 5 min. neuromuscular (gait and balance).	Cardiovascular performance: resting heart rate and exercised heart rate. Muscular endurance: curl-up test. Muscular strength: 1 RM bench press/leg press. Flexibility: sit and reach
Acute effects of passive Leg cycling on upper extremity tremor and bradykinesia in Parkinson's disease. Ridgel, AL. et al., 2011	12	20	EG: 62.8±8.5 CG: 64.6±5.8	CG: 1.6±0.5 EG: 2.0±0.8	1/4/40	Pre-enrollment activity level, off medication Motor function was assessed before and after watching a short instructional video about the MOTOmed® motorized cycle. Evaluation: 10 minutes before and after	Pre-enrollment activity level, off medication 12 hours. MOTOmed® 30 min. passive cycling - randomized 60, 70, 80 rpm. -preceded and concluded by a 5 min. passive cycling warm up/cool down at 40 to 50 rpm. Evaluation: 10 minutes before and after	Tremor Score ($p<0.05$). Kinesia® : Pronation-supination task, hand grasp task
Forced exercise - effects of MOTOmed® therapy on typical motor dysfunction in Parkinson's disease. Laupheimer, M. et al., 2011	23	21	EG: 67.5±7.8 CG: 71.3±4.0	EG: 2.7±0.7 CG: 2.7±0.6	5/10/40	Usual therapy	Usual therapy and a cycling program with a motor-assisted MOTOmed® Viva 2 Program. (5 min. passive cycling warm up/cool down and therapy with 90 rpm)	TMT Battery: walking time ($p<0,05$), walking steps ($p<0,05$), pronation and supination ($p<0,05$), Tremor spiral test PQD8 (dressing and depressions $p<0,05$).
Active assistive forced exercise provides long-term improvement to gait velocity and stride length in patients bilaterally affected by Parkinson's disease. Stuckenschneider, T. et al., 2015	12	10	CG: 71.4±4.9 EG: 71.0±4.6	CG: 3.0± 0.0 (3) EG: 3.0± 0.0 (2.5 a 4)	3/12/40	Standard course of therapy and medical treatment	Cycling on MOTOmed® active assisted forced exercise (5 min. passive cycling warm up/cool down). Standard course of therapy and medical treatment	Gait analyses: velocity ($p<0.000$), stride length ($p<0.000$), monopedal stance($p<0.000$), swing phase($p<0.000$). UPDRS. Kinesia® : Tremor test ($p<0,05$).
	10	12	CG: 71.0±4.6 EG: 71.5±5.7	CG: 3.0± 0.0 (2.5 a 4) EG: 3.0± 0.0 (3)	3/12/40	Follow up (EG 1º phase)	Cycling on MOTOmed® passive forced exercise (5 min. passive cycling warm up/cool down). Standard course of therapy and medical treatment	Gait analyses: velocity ($p<0,05$), stride length ($p<0.05$), monopedal stance($p<0.05$), swing phase($p<0.01$). UPDRS. Kinesia®: Tremor test
Interval active-assisted cycling intervention improves motor function in individuals with Parkinson's disease. Wilson, KA., 2013	4	3	CG: 62.0±7.3 EG: 69.7±5.0	CG: 2.2±1.3 EG: 2.3±0.6	3/4/40	Did not completed any exercise	Cycling on MOTOmed® : 5 min. passive cycling warm up/cool down (20-60 rpm) and 40 min. active assisted forced exercise (65-90 rpm).	UPDRS total ($p<0,04$): Upper body function ($p<0,007$); bradykinesia ($p<0,044$); Lower Body Function; Tremor; Posture; Gait; Rigidity. Kinesia®, Biodex® Balance System: CTSIB1 ($p<0,007$) CTSIB2; CTSIB3; CTSIB4. Postural Stability Fall risk test. Berg Balance scale PDQ39 3-minute step test.
Effects of interval active-assisted cycling on balance in individuals with Parkinson's disease. Fickes, E.J., 2012	10	10	CG: 65.3±8.6 EG: 70.9± 5.4	CG: 2.0±0.9 EG: 2.2±0.8	3/4/40	Only visited the lab for assessments	Cycling on MOTOmed® : 5 min. passive cycling warm up/cool down (45-70 rpm) and 40 min. active assisted forced exercise (65-90 rpm).	UPDRS Motor III ($p<0,04$): upper body motor function ($p<0.001$), lower body motor function ($p<0.001$), tremor ($p<0.001$), bradykinesia ($p<0.001$), posture ($p<0.001$) and gait. Kinesia® : resting tremor, posture tremor, kinetic tremor, overall tremor, average tremor. Balance: postural stability, CTSIB1, CTSIB2, CTSIB3, CTSIB4, Fall risk test. Berg Balance scale PDQ39: single index, mobility, activities of daily living, emotional wellbeing, stigma, social support, cognitive, communication, bodily discomfort. Hoffman Reflex.

EG: Experimental group; CG: Control group; rpm: rotations per minute; UPDRS: Unified Parkinson's Disease Rating Scale; RM: Repetition maximum; TMT Battery Timed Motor Battery Trail Making Test; PDQ8-39 Parkinson's Disease Questionnaire; CTSIB: Clinical test of sensory integration and balance.

The duration of MOTOmed® movement therapy sessions was 40 minutes in 6 studies (Ridgel et al., 2015; Ridgel et al., 2011; Laupheimer et al., 2011; Stuckenschneider et al., 2015; Wilson, 2012; Fickes, 2012), using a therapy with high speeds of revolutions per minute (60-90rpm), preceded and concluded by 5 minutes of cycling to warm up and cool down (30-50rpm). Four studies used the movement therapy active assisted cycling (Peacock et al., 2014; Laupheimer et al., 2011; Wilson, 2013; Fickes, 2012), one used the movement therapy passive cycling (Ridgel et al., 2011), and two studies used both types of training for different intervention groups (Ridgel et al., 2015; Stuckenschneider et al., 2015). Only one study used 30 minutes of active assisted cycling with the addition of 30 minutes of resistance training, 20 minutes of flexibility training and 5 minutes of neuromuscular training (Peacock et al., 2014).

The intervention period ranged from 1 to 12 weeks; in three studies the subjects underwent training for four weeks (Ridgel et al., 2011; Wilson, 2013; Fickes, 2012), in three other studies they performed longer courses, eight weeks (Peacock et al., 2014), ten weeks (Laupheimer et al., 2011) and twelve weeks (Stuckenschneider et al., 2015) and only in one study did the subjects undergo one week of exercises (Ridgel et al., 2015). In relation to frequency of training the variation was 1 to 5 times per week: four studies three times a week (Peacock et al., 2014; Stuckenschneider et al., 2015; Wilson, 2013; Fickes, 2012), one study five times a week (Laupheimer et al., 2011), one study four times a week (Ridgel et al., 2015) and one study once a week (Ridgel et al., 2011).

Description by Outcomes defined

The Unified Parkinson's Disease Rating Scale (UPDRS) was used in 4 studies (Ridgel et al., 2015; Stuckenschneider et al., 2015; Wilson, 2013; Laupheimer et al., 2011), for the assessment of both motor and non-motor symptoms of the disease. The tremors suffered by patients diagnosed with Parkinsons were evaluated by the following different tests: Tremor score, Tremor spiral test and Tremor test with Kinesia® were analyzed in 5 studies (Ridgel et al., 2011; Laupheimer et al., 2011; Stuckenschneider et al., 2015; Wilson, 2013; Fickes, 2012) and gait analyses were studied in 3 studies (Laupheimer et al., 2011; Stuckenschneider et al., 2015; Fickes, 2012). The patients´ quality of life was evaluated by the Parkinson's Disease Questionnaire (PQD8 and PQD39) in 3 studies (Laupheimer et al., 2011; Wilson, 2013; Fickes, 2012), the Clinical test of sensory integration and balance (CTSIB) in 2 studies (Wilson, 2013; Fickes, 2012), and the Berg balance scale in 2 studies (Wilson, 2013; Fickes, 2012). Other tests that were composed of only one study were: Cycling variables and Timed To Up and Go test (Ridgel et al., 2015); Cardiovascular performance, Muscular endurance, Muscular strength, and Flexibility (Peacock et al., 2014); Timed Motor Battery (Laupheimer et al., 2011); 3-minute step test (Wilson, 2013); and Hoffman Reflex (Fickes, 2012) (Table 1).

Table 2.
Cochrane methodological quality of included studies.

Study	Random sequence generation	Allocation concealment	Selective reporting	Other sources of bias	Blinding (participants and personnel)	Blinding (outcome assessment)	Incomplete outcome data	Total
Dynamic high-cadence cycling improves motor symptoms in Parkinson's disease. Ridgel, AL. et al., 2015	High (3)	Low (2)	Unclear (1)	Unclear (1)	High (3)	High (3)	Low (2)	15
Introducing a multifaceted exercise intervention particular to older adults diagnosed with Parkinson's disease: a preliminary study Peacock, CA. et al.,2014	Low (2)	Low (2)	Unclear (1)	Unclear (1)	Unclear (1)	Unclear (1)	Low (2)	10
Acute Effects of Passive Leg Cycling on Upper Extremity Tremor and Bradykinesia in Parkinson's Disease. Ridgel, AL. et al., 2011	Unclear (1)	Low (2)	High (3)	Unclear (1)	High (3)	Low (2)	Low (2)	14
Forced Exercise - effects of MOTOmed® therapy on typical motor dysfunction in Parkinson's disease. Laupheimer, M. et al., 2011	Low (2)	Low (2)	Unclear (1)	Unclear (1)	Unclear (1)	Unclear (1)	Low (2)	10
Active assistive forced exercise provides long-term improvement to gait velocity and stride length in patients bilaterally affected by Parkinson's disease. Stuckenschneider, T. et al., 2015	High (3)	Low (2)	Unclear (1)	Unclear (1)	Unclear (1)	Unclear (1)	Low (2)	11
Interval active-assisted cycling intervention improves motor function in individuals with Parkinson's disease. Wilson, KA., 2013	Low (2)	Low (2)	Unclear (1)	Unclear (1)	Unclear (1)	Unclear (1)	Low (2)	10
Effects of interval active-assisted cycling on balance in individuals with Parkinson's disease. Fickes, E.J., 2012	Low (2)	Low (2)	Unclear (1)	Unclear (1)	Unclear (1)	Unclear (1)	Low (2)	10

Risk of bias

The authors of four studies (Laupheimer et al., 2011; Peacock, 2014; Wilson, 2013; Fickes, 2012), reported the use of randomized sequence generation, whereas those of the other study (Ridgel et al., 2011) mentioned only randomization. Allocation concealment and reasons for dropout were described in all studies. With respect to Selective reporting, we must indicate that six studies (Ridgel et al., 2015; Peacock et al., 2014; Laupheimer et al., 2011; Stuckenschneider et al., 2015; Wilson, 2013; Fickes,

2012) do not present bias in the information, whereas in one study that information bias exists (Ridgel et al., 2011). No other study indicates the presence of other types of existing bias. Two studies (Ridgel et al., 2015; Ridgel et al., 2011) indicate that the participants and personnel are not blinds, while in the other studies this situation is not clarified (Peacock et al., 2014; Laupheimer et al., 2011; Stuckenschneider et al., 2015; Wilson, 2013; Fickes, 2012). The analysis of the Blinding of outcome assessment revealed that only one study (Ridgel et al., 2011) describes them adequately. The observation of outcome data in all studies revealed that these are presented in an adequate and detailed way in all of them. In view of the results obtained in (Table 2), we can indicate that there are four studies which present the lowest risk of bias and therefore the best methodological quality clarified (Peacock et al., 2014; Laupheimer et al., 2011; Wilson, 2013; Fickes, 2012), and that in one study the highest risk of bias occurs (Ridgel et al., 2015).

Discussion

The main finding of this systematic review is that MOTOmed® movement therapy effectively improves motor function and main symptoms in PD patients, since in all the studies analyzed in this review, significant improvements were found in some data analyzed with the intention of evaluating motor function and main symptoms in PD patients (Ridgel, Phillips, Walter, Discenzo & Loparo, 2015; Peacock, Sanders, Wilson, Fickes-Ryan, Corbett, Von-Carlowitz 6 Ridgel, 2014; Ridgel, Muller, Kim, Fickes & Mera, 2011; Laupheimer et al., 2011; Stuckenschneider, Helmich, Raabe-Oetker & Frobose, 2015; Wilson, 2013; Fickes, 2012; Stuckenschneider et al., 2015)

With the increased prevalence of age-related diseases such as PD, it is of the greatest importance to review and seek the standardization of the best model of exercises that are both tolerable and beneficial to the PD population. This examination focused on motor function and containment of the main symptoms, essential elements of rehabilitation for patients with PD.

The improvement in motor function and symptoms of PD patients due to therapy with the MOTOmed® system can be explained by the fact that during the cycling, proprioceptors measuring joint angles, muscle length and force, and cutaneous receptors on the bottom of the foot (Ericson, 1986) would be activated. Improvements in motor function and mobility after bouts of cycling in individuals with PD could be due to increases in afferent input to the cortex. Several EEG (electroencephalography) studies in healthy individuals have shown that significant sensorimotor processing is present during active pedaling (Jain, Gourab, Schindler-Ivens & Schmit, 2013) and that high-cadence training promotes neural efficiency as defined with EEG spectral power analysis (Ludyga, Gronwald & Hottenrott, 2016). This indicates that activation of proprioceptors with a high frequency but variable pattern may be important for symptom improvements in PD.

The use of the UPDRS Motor III scale for examining the effects of exercise interventions on motor function in PD revealed significant improvements in the scores in four of the analyzed studies (Ridgel et al., 2015; Stuckenschneider et al., 2015; Wilson, 2013; Laupheimer et al., 2011). Although it is a subjective scale that does not provide information about the quality or frequency of movement, it has universal acceptance as a rating scale for PD patients and it has been shown to be reliable and valid (Richards, Marder, Cote & Mayeux, 1994). The studies assessed many scores from this scale: total score, scores for each primary symptom (tremor, bradykinesia) and scores for upper and lower extremity posture and rigidity.

Of six studies which reviewed assessed tremor in PD patients, two of them presented significant improvements in the tremor tests performed (Ridgel et al., 2015; Stuckenschneider et al., 2015). Although mild to moderate tremor generally did not result in functional disability, the presence of tremor during an action could contribute significantly to bradykinesia in PD (Carboncini, Manzoni, Strambi, Bonuccelli, Pavese, Andre & Rossi, 2001). Bradykinesia can have dramatic effects on fine and macroscopic motor control during daily activities (Berardelli, Rothwell, Thompson & Hallett, 2001).

Bradykinesia, one of the most central cardinal symptoms of PD, may have significant origins in the alteration of scale perception as it relates to movement and may point to a possible underlying dysfunction in sensorimotor integration (Berardelli et al., 2001). Our review suggests that the cycling MOTOmed® therapy improves bradykinesia, in two studies significant differences were found for this symptom (Wilson, 2013; Fickes, 2012). The idea that cycling could invoke the retuning and integration of kinesthesia, as it relates to motor programing, is compelling. Naito, Nakashima, Kito, Aramaki, Okada & Sadato (2007) have shown that kinesthetic input illusion activates the primary motor cortex, as well as other related motor areas, including the cingulate motor area and supplementary motor area, in healthy individuals. They also suggested that sensorimotor integration could occur directly in these motor regions. Thus, exploration of this mechanism by studying sensory changes in individuals with PD through the course of the adaptive cycling intervention has a high likelihood of yielding illuminating results regarding mechanisms of improved motor function.

It is already known that there is muscle activity during passive leg cycling in healthy individuals (Nobrega, Williamson, Friedman, Araujo & Mitchell, 1994; Krzeminski, Kruk, Nazar, Ziemba, Cybulski & Niewiadomski, 2000). This activity is believed to be due to reflexes evoked by spindle receptors that measure muscle stretch. Signals generated from muscle spindle receptors during passive movement provide afferent input, which affects corticomotor excitability (Cheng, Brooke, Misiaszek & Staines, 1995). Christensen, Johannsen, Sinkjaer, Petersen, Pyndt

& Nielsen (2000) proposed that cerebral activation during passive cycling in healthy adults was caused by sensory feedback evoked from the moving limb. Individuals with PD often have deficits in proprioceptive regulation. Specifically, long-latency stretch reflexes are enhanced in PD and are correlated with the degree of rigidity of the elbow (Rothwell, Obeso, Traub & Marsden, 1983). These abnormal stretch reflexes could also contribute to bradykinesia by initiated activity in an antagonist muscle during an active contraction of the agonist (Berardelli et al., 2001). Although this interaction has not been documented experimentally, alterations in proprioceptive input to the cortex during passive cycling may play a role in the improvements in tremor and bradykinesia (Ridgel et al., 2011).

The Kinesia® device was used in four studies (Ridgel et al., 2015; Stuckenschneider et al., 2015; Wilson, 2013; Fickes, 2012) to provide objective scores of tremor using developed algorithms, which have been tested and validated against clinical UPDRS scores (Giuffrida, Riley, Maddux & Heldman, 2009), despite observing a trend towards improvement in tremor results after therapy with the MOTOmed® system, only in the study of Stuckenschneider et al. (2015) these results were they significant. The measurements performed with this system are based on linear acceleration and angular velocity data recorded by the Kinesia® provided additional information on movement quality during each of the tests. In addition, speed, and amplitude features of bradykinesia, as measured with Kinesia®, are highly correlated to the MBRS (Modified Bradykinesia Rating Scale) scores (Heldman, Giuffrida, Chen, Payne, Mazzella, Duker & Espay, 2011). These types of quantitative assessments are important in order to detect subtle variability in movement that could have significant implications on the activities of daily living. Furthermore, this type of technology could be useful for the remote assessment of intervention therapies in PD or other movement disorders (Mostile, Giuffrida, Adam, Davidson & Jankovic, 2010).

Regarding the quality of life evaluated in three studies through the PQD questionnaire, one study suggests movement therapy has an anti-depressive effect and improves overall well-being (Laupheimer et al., 2011), which is a fact that has already been presented in other studies (Blumenthal, Babyak, Moore, Craighead, Herman, Khatri & Doraiswamy, 1999; Dunn, Trivedi, Kampert, Clark & Chambliss, 2005).

With these results we can reflect with findings that are already well known in the rehabilitative treatment of the patient PD, as we can mention, muscle weakness is often present in individuals with Parkinson's disease (Latt, Lord, Morris & Fung, 2009). The combination of central nervous system and peripheral muscle deficiencies may result in progression to immobility (Dibble, Hale, Marcus, Droge, Gerber & Lastayo, 2006). According to Davies (2000) the nervous system learns by doing. Granted, one can learn by observation, but this has never been as effective as learning actively. The body needs to 'get in on the act', so to speak, and go through the process of an activity before permanent memory engrams are laid down." MOTOmed® movement therapy provides passive activity and active pedaling; even patients lacking muscle can train. This approach is in line with the Davies concept, suggesting that the MOTOmed® system can improve patients' lower extremity functional recovery and walking ability. Motor training leads to a higher expression of dopamine – which is positive for PD patients as they suffer from degeneration of dopamine-producing cells – and an increase of excitability in the motor cortex due to higher sensory input in the muscle spindles (Muller & Muhlack, 2007).

From a more physiological point of view, we consider it important to emphasize that motor improvement after cycling is not driven by purely cardiovascular or metabolic mechanisms (Alberts, Linder, Penko, Lowe 6 Phillips, 2011). The complex and variable sensory input during dynamic cycling increases sensory feedback from the periphery and subsequent activation of the basal ganglia circuits. Activation of these circuits could enhance central motor processing. Accurate voluntary movement requires somatosensory input from the periphery. Peripheral receptors, such as joint receptors, Golgi tendon organs, muscle spindles, and cutaneous receptors, send information from the limbs to the cortex. Several studies have identified proprioceptive impairment in PD, specifically in muscle spindle responses, load sensitivity and kinesthesia (Berardelli et al., 2001; Adamovich, Berkinblit, Hening, Sage & Poizner, 2001; Zia, Cody & O´Boyle, 2002). This suggests that deficits in peripheral afferent input or sensorimotor integration likely contribute to abnormal motor output in individuals with PD.

The reorganization of cortical function is aided by mandatory, repetitive, and patterned modes of exercise. Traditional "hands-on" interventions can improve motor function to some degree, but therapists may not be able to deliver highly intensive, targeted, and repetitive training due to repetitive strain injuries and excessive fatigue (Zhang, Hu & Xu, 2012). Rehabilitation robots have obvious advantages for this patterned mode of exercises. MOTOmed® movement therapy has achieved good clinical rehabilitation effects because of its intelligent technology and good visual feedback system (Ridgel et al., 2015; Peacock et al., 2014; Ridgel et al., 2011; Laupheimer et al., 2011; Stuckenschneider et al., 2015; Wilson, 2013; Fickes, 2012). Use of the system enhances muscle tone, endurance, and joint pliability, which contribute maximally to the improvement of mobility, balance, and activities of daily living (Damiano, Arnold, Steele & Delp, 2010).

These effects have been confirmed in other patients, such as children with cerebral palsy (Zhang, Tang & Xiong, 2014) and hemiplegic patients. For example, Cheng, Guo & Feng (2017) found that the use of MOTOmed® movement therapy combined with core muscle strength exercises effectively improved motor function and balance ability, with the MOTOmed® system having greater effects than the strength exercises.

Study Limitations

This systematic review had several limitations. Firstly, most of the study population was American, and language and selective biases may exist. Secondly, the experimental designs of the included studies were not described comprehensively. Thus, study quality was not high. The stage H&Y (1967) of PD patients differed among studies, and the intervention durations (1, 4, 8, 10 and 12 weeks) and session frequency (1–5 times per week) were not uniform. Another limitation is that the number of studies using the MOTOmed® therapy is small, and the variables analyzed are very varied, which made our desired development of a meta-analysis an impossibility. Finally, as only published studies written in English, Spanish and Portuguese were retrieved, the literature review may have been incomplete; certainly, relevant gray literature, such as unpublished data and special academic reports, was not included. However, all included studies showed that MOTOmed® movement therapy promoted motor function in patients with PD more effectively than did traditional rehabilitation training. When interpreting the results of this study, however, one must consider that the positive therapeutic effects may not only be explained by MOTOmed® system use; this training was conducted within the scope of patients in rehabilitation, and only combinations of different therapeutic interventions led to the desired progress.

Based on these limitations, we make the following recommendations for future studies: (1) To improve methodological and design quality, researchers should correctly apply random distribution, allocation, and blinding to the greatest degree possible to reduce selectivity, implementation, measurement, and other biases. (2) Training programs should be standardized to determine the best duration and frequency of MOTOmed® movement therapy, the best combinations with other treatment methods, and the cost effectiveness of MOTOmed® system use, and to reduce conflicts of interest related, for example, to funding. (3) Sample sizes should be correctly estimated for the use of large-scale samples, multicenter designs, unified measurement tools, and unified indicators in randomized controlled trials.

Conclusion

The use of this type of therapy is recent and there is the necessity for a consensus on the appropriate use of this technology, in this study we present data that show information that may be relevant and be of help to rehabilitation professionals working in the field of disability. According to the main results and review of the analyzed studies, we can conclude MOTOmed® movement therapy alone or combined with standard rehabilitation improves motor function and main symptoms in patients with Parkinson's disease. We also consider that the performance of intense and forced exercise for PD patients with the MOTOmed® system can be considered safe, since patients are not exposed to an activity where there may be a risk of falling.

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