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REVIEW ARTICLE

Effect of therapeutic exercise on pain intensity in individuals with diseases of the central nervous system: integrative review

Efeito do exercício terapêutico na intensidade de dor em indivíduos com doenças do sistema nervoso central: revisão integrativa

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ABSTRACT

BACKGROUND AND OBJECTIVES: Pain is a common condition in people with diseases of the central nervous system and affects up to two thirds of patients with spinal cord injury, amyotrophic lateral sclerosis, cerebral palsy and, less frequently, stroke. The search for therapeutic methods, such as physical exercise, that can identify and mitigate pain in this population is essential. In order to integrate therapeutic planning and, consequently, improve treatment, the aim of this study was to analyze the effectiveness of physical exercise in reducing pain in people with diseases of the central nervous system.

METHODS: The search was carried out by a reviewer in the databases: Cochrane Library, Google Scholar (first 100 results), LILACS, PeDro, Pubmed Scielo, Scopus and Web of Science. Clinical trials published up to September 2023 were included, with no language restrictions. Selection of studies and data extraction were carried out by a reviewer using a spreadsheet with the relevant variables for preparing the review.

RESULTS: After analysis, 16 articles were eligible. The studies in this review recruited 966 individuals. Most of them showed a significant reduction in pain intensity when global muscle training (strengthening and stretching) was carried out compared to control groups.

CONCLUSION: Various modalities of physical exercise can be an effective intervention method for the treatment of pain in patients with central nervous system diseases. However, studies investigating this outcome are currently still limited.

KEYWORDS: Central nervous system diseases, Pain, Physical exercise.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A dor é uma condição comum em pessoas com doenças do sistema nervoso central e atinge até dois terços dos pacientes com lesão medular, esclerose lateral amiotrófica, paralisia cerebral e, menos frequentemente, acidente vascular cerebral. Torna-se fundamental a busca por métodos terapêuticos, como o exercício físico, que possam identificar e atenuar a dor nessa população. Visando integrar o planejamento terapêutico e, consequentemente, aprimorar o tratamento, o objetivo deste estudo foi analisar a eficácia do exercício físico na redução da dor em pessoas com doenças do sistema nervoso central.

MÉTODOS: A busca foi feita por um revisor nas bases de dados: *Cochrane Library*, Google Acadêmico (100 primeiros resultados), LILACS, PeDro, Pubmed Scielo, Scopus e *Web of Science*. Foram incluídos ensaios clínicos publicados até setembro de 2023, sem restrição de idiomas. Assim como a seleção dos estudos, a extração dos dados também foi feita por um revisor, por meio de uma planilha com as variáveis relevantes para a elaboração da revisão.

RESULTADOS: Após análise, 16 artigos foram elegíveis. Os estudos desta revisão recrutaram 966 indivíduos. A maioria deles apontou redução significativa da intensidade de dor quando realizado o treinamento muscular global (fortalecimento e alongamento) em comparação a grupos controle.

CONCLUSÃO: Constatou-se que o exercício físico de diversas modalidades pode ser um método de intervenção eficaz para o tratamento da dor em pacientes com doenças do sistema nervoso central. No entanto, os estudos que pesquisam esse desfecho ainda são atualmente limitados.

DESCRITORES: Doenças do sistema nervoso central, Dor, Exercício físico.

HIGHLIGHTS

- Pain is a common condition in people with central nervous system diseases and affects up to two thirds of individuals with spinal cord injury, amyotrophic lateral sclerosis, cerebral palsy and, less frequently, stroke
- The search for a resolution to the pain, often neglected, even though is frequent, is essential, especially in people with neurological diseases
- Physical exercise can be an effective intervention method for the treatment of pain in patients with central nervous system diseases

INTRODUCTION

Comprehension about the concept of pain, as defined by the International Association for the Study of Pain (IASP), has led to a number of educational, scientific and clinical advances over the last four decades. A better understanding of pain, allowing different aspects to be covered, has made this symptom even more remarkable[1,2]. Nevertheless, despite considerable progress, the search for strategies to identify and manage pain in special populations, such as patients with neurological diseases, is constantly evolving.

Pain is a common condition in individuals with central nervous system (CNS) diseases. The prevalence of this symptom affects up to two thirds of individuals with spinal cord injury, amyotrophic lateral sclerosis (ALS) and cerebral palsy[3-5]. This condition is also common after a cardiovascular accident (CVA), although it is still under-recognized in these patients[6] and, even when noticed, it may not be treated properly[7]. Taking these data into account, the search for methods that can identify and mitigate pain in this population has become fundamental, with the aim of integrating therapeutic planning and, consequently, improving treatment.

Intense pain is associated with a greater risk of activities and sleep being affected. However, despite being a very relevant symptom, it is possible that pain is underreported and undertreated in individuals with communication difficulties, a condition that is prevalent in patients with neurological disorders[5]. Thus, the professionals who monitor these patients should be more careful when identifying these cases, and have a broad knowledge of the different pain assessment tools and treatment modalities, since the correct management can be resolutive not only for the pain in isolation, but also for the evolution of the treatment involving several issues.

Among the non-pharmacological treatments used to manage pain, therapeutic exercise stands out. Studies carried out on human beings indicate that a higher level of physical activity is related to equal or reduced pain sensitivity in a large number of analyseses[8]. This statement is supported by a systematic review and meta-analysis study[9], which showed that physical exercise of various modalities (resistance training, aerobic exercise, global stretching, group exercises, Pilates-based exercises) can be effective in attenuating pain sensitivity when compared to non-exercise interventions. However, the study reports that it is not clear which appropriate prescription should be used to achieve this goal. In addition, the results obtained had a low quality of evidence.

Regarding the therapeutic approach with exercise in the neurological population, another review study[10] evaluated the use of exercise for pain control in Parkinson's disease (PD). According to this article, which included only two studies, clinical trials exploring the effect of exercise on pain are insufficient to conclude on its effectiveness in relieving pain. This is because one of the studies cited in this article showed that an exercise protocol in a group of PD patients consisting of strengthening, stretching and aerobic exercise showed no improvement in pain intensity. On the other hand, the other study analyzed showed lower pain intensity in PD patients who performed relaxation, flexibility or walking exercises. Another point worth highlighting in this study concerns the absence of pain as the main outcome in both studies, proving the scarcity of articles that have this outcome as the main focus of analysis in these patients.

This context highlights the growing debate about pain in neurological patients. Although this is positive, it is necessary to intensify the search for a solution to this condition which, although frequent, is often neglected, especially in this population. The use of therapeutic exercise in neurological rehabilitation to treat functional outcomes is widely known, but its use as a non-pharmacological strategy to control pain in these patients is not discussed enough.

Considering the need to know what is currently known in the scientific literature about the use of therapeutic exercise to treat neurological patients' pain, the present study's objective was to analyze the effects of therapeutic intervention with exercise on pain intensity in individuals with CNS diseases.

CONTENTS

An integrative literature review was carried out to find out the state of the art in the scientific literature on the subject. The first stage of this integrative review consisted of formulating the question: "What is the effect of treatment with exercise on pain intensity in patients with CNS diseases"? After defining the study's guiding question, the following steps were carried out.

Databases and search

The electronic search was carried out in September 2023 in the Cochrane Library, Google Scholar (first 100 results), LILACS, PeDro, Pubmed Scielo, Scopus and Web of Science databases. For the search, the terms used were "Exercise", "Pain" and "Central Nervous System Diseases". These descriptors were combined as follows: "Exercise AND Pain AND Central Nervous System Diseases". For the search in the Pubmed database, the "randomized control trial" filter was used.

Studies selection

The search for scientific papers compatible with the pre-established question was carried out by a reviewer who first analyzed the titles and abstracts. Next, the eligibility of the studies was determined by reading the articles in full. The inclusion criteria comprised only controlled clinical trials (randomized or non-randomized) that addressed therapeutic intervention using physical exercise (regardless of the type and performed in isolation - without combining it with another therapy) and the measurement of the "pain intensity" outcome (as a primary or secondary variable), published up to September 2023, with no language restrictions. The exclusion criteria included other methodological types of study, such as observational studies, review studies, case studies and case series, as well as studies on patients who did not have a diagnosis of any neurological disease or studies which only assessed functional outcomes, without measuring pain intensity.

Data extraction

Data extraction was also carried out by a reviewer using a spreadsheet with the variables relevant to the preparation of the review. Information on the author, year, objective, sample, variables assessed, evaluation instruments, intervention and main results was extracted.

RESULTS

A total of 954 studies were found in the databases. After reading the titles and abstracts, 23 articles were selected to be fully evaluated, and the others were excluded because they did not meet the criteria regarding the type of study (clinical trial) and/or did not describe the measurement of the "pain intensity" outcome. After full reading, 16 studies were considered eligible. The others were excluded because they did not meet the pre-established criteria, such as quasi-experimental studies (n=2), studies which represented the outcome pain only in the description of the study sample, others that did not represent this variable in comparison before and after the exercise intervention (n=3), and studies which carried out specific interventions focused on vestibular rehabilitation combined with exercise therapy (Figure 1).

The studies brought herein recruited 966 individuals. However, some were not present until the end of the study (n=26). Patients with CVA (n=387), PD (n=332), spinal cord injury (n=166), tropical spastic paraparesis (n=56) and ALS (n=25) were included (Table 1).

The pain assessment tools were heterogeneous. However, despite their variability, most of the studies showed specificity for pain analysis. Among the resources, the Visual Analog Scale (VAS) stands out, which was used in six articles. In addition to pain, other functional variables, not considered as analysis outcomes in this review, were represented in the studies, including gait, balance, quality of life, muscle strength, and others (Table 1).

As well as the assessment tools, the interventions also differed. The articles presented various exercise modalities, such as aquatic therapy, global muscle strengthening, global stretching, yoga, treadmill training, Tai Chi and video-guided exercises. The protocols for performing these modalities varied in terms of frequency (number of sessions per week), duration of training (time spent performing the exercise at each session), duration of treatment (period of exposure to the proposed training), location (outpatient or home-based) and mode of supervision (with or without face-to-face monitoring by a specialist) (Table 1).

Effectiveness of the intervention

The main results of the exercise intervention in patients with CNS diseases are shown in Table 1. Most of the studies showed a significant reduction in pain intensity (11-20), as evidenced by different assessment instruments, VAS, Numerical Pain Scale (NPS), Turkish version of the Nottingham profile, wheelchair user shoulder pain index, Brief Pain Inventory (BPI), joint angle measures associated with self-perceived pain, 3-item functional pain measure, Fugl-Meyer assessment of the upper extremity, as well as SF-36 items.

When considering the effect of therapeutic exercise according to the neurological disease treated, a study involving individuals diagnosed with ALS who underwent a global exercise program showed that there was a worsening of pain in the patients evaluated, identified by an increase in pain classified by the VAS[12]. Another study showed no statistically significant changes in the pain intensity variable: in patients with tropical spastic paraparesis who underwent a home exercise program, only clinical changes were observed[16].

In patients with PD, it was shown that treadmill training[11], trunk mobility exercises[13] and the practice of aquatic Ai Chi[20] led to a reduction in pain. In individuals with stroke sequelae, it was noted that aquatic Ai Chi[19,26], yoga[21], upper limb aerobic exercises[22] and exercises to increase global range of motion were effective in reducing the intensity of pain. For pain management after spinal cord injury, the use of an upper limb exercise bike in a clinical environment and partial weight bearing[14], as well as strength training[15,17] and upper limb stretching[17] are recommended.

As for the type of exercise, most studies showed that global muscle training (strengthening and stretching) was effective in reducing pain intensity compared to control groups (no exercise).

In the aforementioned studies in which there was an increase in pain intensity or no difference in the measures assessed, the type of exercise used also included global training guided by professional in patients with ALS[12] or by videos in patients with PD[24], exercises performed with a cycle ergometer in a home environment with individuals after spinal cord injury[18] and Tai Chi adapted for wheelchairs in patients with stroke sequelae[25].

Three articles[18,24,25] showed no significant differences in terms of pain reduction and used different evaluation measures (5-point scale, wheelchair user shoulder pain index and Fugl-Meyer evaluation of the upper extremity). It is worth noting that the studies included in this review did not demonstrate the superiority of one type of therapeutic exercise over another for pain management in the neurological population.

DISCUSSION

This review sought to analyze the effectiveness of exercise interventions on pain intensity in individuals with CNS diseases. Through the selected studies, it was possible to observe positive results in the attenuation of pain. The modalities and forms of prescription varied, as did the pain assessment instruments in this population, which gave the studies great heterogeneity.

Three studies included in the review analyzed the effects of aquatic Ai Chi treatment on pain, as well as other variables. The article[20] evaluated individuals with PD, divided into two groups (aquatic Ai Chi and floor therapy). In both groups, significant differences were found in the reduction of pain intensity. However, in the control group, the improvement was less significant. The other two articles evaluated individuals diagnosed with stroke divided into three groups (aquatic Ai Chi, floor therapy and combined therapy). In both cases, the aquatic Ai Chi and combined therapy groups showed significant improvements in the VAS, demonstrating superiority over therapy on the ground[19,26].

Table 1. Characteristics of included studies.

Authors	Objectives	Sample	Variables	Evaluation tools	Intervention	Main results
Atan et al.[11]	Evaluate the effects of different percentages of treadmill training with body weight support on gait, balance, quality of life and fatigue in PD.	30 patients divided into 3 groups: conventional treadmill training (n=10), treadmill training with 10% support (n=10) and with 20% support (n=10).	Gait: assessment of PD, balance; quality of life (including the pain variable); fatigue.	6-minute walking test: Berg balance scale; UPDRS I, II and III; Turkish version of the Nottingham health profile (including items referring to pain); fatigue impact scale; fatigue severity scale.	All participants received 30 min of conventional rehabilitation, including ROM, stretching, strengthening and balance exercises, followed by 30 min of treadmill training with body weight support, 5 days/week, for 6 weeks.	UPDRS III scores were significantly lower in the groups with 10% to 20% body weight support. Nottingham Health Profile pain scores at week 6 increased significantly in the group with no support (p=0.019), while they decreased in the 10% and 20% supported groups (p=0.003 and p=0.002, respectively) compared to baseline.
Drory et al.[12]	To determine the effect of moderate regular exercise under guidance on parameters of motor deficit, disability, fatigue, musculoskeletal pain and perceived QoL.	25 patients with ALS or probability of ALS, divided into two groups: one was instructed to exercise (n=14) and the other was instructed not to perform any physical activity beyond the usual needs of daily life (n=11).	Muscle strength; spasticity; disability; fatigue; pain; QoL.	Manual muscle strength test; Ashworth spasticity scale; functional classification scale; fatigue severity scale; VAS; SF-36. The evaluation was carried out at the beginning and after 3, 6, 9 and 12 months.	Exercise Group: list of exercises involving most of the muscle groups of the 4 limbs and trunks. The program was developed for each patient individually, considering their general state of health and level of fitness, lasting 15 minutes, 2x/day at home.	All patients in both groups presented a marked worsening during the follow-up period and the drop-out rate was high, hindering statistical analysis. In patients in both groups, reported pain intensity increased over time. There was no effect of exercise on pain complaints.
Gandolfi et al.[13]	Main: compare the effects of a trunk rehabilitation program on the severity of forward trunk flexion in patients with PD. Secondary: compare the effects of training on the Unified Classification of PD. · Motor subscale of the scale (UPDRS III), dynamic and static balance, pain, falls and QoL.	37 patients randomly assigned to the experimental group - EG (n = 19) or control group - CG (n=18). Two patients in the EG and one in the CG discontinued the interventions.	Change in degrees of forward trunk flexion, changes in UPDRS III, static and dynamic balance, pain and QoL; assessed before treatment (T0), two days after completion (T1) and one month after completion (T2).	Measurement of degrees of forward trunk flexion; UPDRS III; Numerical Pain Scale (NPS); number of falls; Parkinson's Disease Questionnaire-8 (PDQ-8); Single-axis electronic platform; Mini BESTest.	EG: active self-correction exercises with visual exercises, proprioceptive feedback and no feedback; trunk stabilization exercises and functional tasks. CG: joint mobilization, muscle strengthening and stretching, gait and balance exercises (duration 4 weeks, 60 min/day, 2x/week). Three sessions were carried out as "self-practice" at the patients' homes and monitored by the physiotherapist via phone calls.	The reduction in forward trunk flexion and improvement in dynamic and static balance were significantly greater in the EG than in the CG. Overall, both groups showed a significant reduction in pain from T0 to T2 (EG: p=0.001; CG: p<0.001).
Gee et al.[14]	Main: compare the effects of an exercise bike for the upper limbs and treadmill training with body weight support on QoL and intermediate variables in individuals with spinal cord injury. Secondary: examine correlations between initial measurements and changes in physical activity, QoL and intermediate variables.	28 participants divided into two groups. Group 1: exercise bike for upper limbs (UL) Group 2: treadmill training with body weight support.	Quality of life; physical activity during leisure-time; pain; affect; self-efficacy to perform aerobic exercise; independence to manage self-care, respiratory and sphincter needs and mobility; participation and autonomy.	LISAT-9; SWLS; LTPAQ-SCI; SF-36 2-item pain subscale; PANAS; 10-item questionnaire; SCIM version III, IPAQ.	Participants were randomized to one of the groups and took part in 3 exercise sessions a week for 6 months, for a total of 72 sessions. All exercise sessions were carried out in hospital research institutes or in a university exercise program. Participants completed either 30 min/session of moderate to vigorous intensity UL cycling or 60 min/session of body weight supported treadmill training, in which participants were suspended above a treadmill using a body weight support system and volunteers assisted with passive locomotion. The 2 protocols were matched for exercise volume, calculated as the product of the duration of each session and the perceived exertion ratings of the session.	There was a significant interaction effect for the pain subscale, in which pain was significantly lower in the UL bicycle exercise group throughout the intervention compared to treadmill training with body weight support (p = 0.022). The analysis showed that after 72 sessions with the UL exercise bike, pain was significantly lower compared to baseline (p = 0.092).

PD: Parkinson's disease; QoL: quality of life; ALS: amyotrophic lateral sclerosis; VAS: Visual Analogue Scale; NSAIDs: non-steroidal anti-inflammatory drugs; LL: lower limbs; UL: upper limbs; CVA: cerebral vascular accident; ADL: activities of daily living; LISAT-9: Life-Satisfaction Questionnaire-9; SWLS: Satisfaction with Life Scale; LTPAQ-SCI: Leisure Time Physical Activity Questionnaire for People with Spinal Cord Injury; SF-36: Medical Outcomes Short-Form 36-Item Health Survey; PANAS: Positive and Negative Affects Scale; SCIM: Spinal Cord Independence Measure version III; IPAQ: Impact on Participation and Autonomy Questionnaire; UPDRS: Unified Parkinson's Disease Rating Scale; ROM: range of motion; IG: intervention group; CG: control group; FTSTS: 5x sit and stand test; TGUG: Timed Get Up and Go test; WUSPI: Wheelchair User's Shoulder Pain Index; ESES: exercise self-efficacy scale; FSS: exercise self-efficacy scale; PEG: Patient-Reported Experience of Cancer Pain; CRPS: Complex Regional Pain Syndrome; PDQ-8: Parkinson's Disease Questionnaire; FES-I: Falls Efficacy Scale International Version; PDSS-2: Parkinson's Disease Sleep Scale; PHQ-4: short version of the Patient Health Questionnaire.

Table 1. Continued...

Authors	Objectives	Sample	Variables	Evaluation tools	Intervention	Main results
Hicks et al.[15]	Examine the effects of 9 months of physical training on strength, arm ergometry performance and indices of psychological well-being and QoL in people with spinal cord injury.	34 individuals with traumatic spinal cord injury (C4 - L1; ASIA A - D) from 1 to 24 years of age were randomized into exercise (n=21) and control (n=13) groups. 23 subjects, 11 in the exercise group (EG) and 12 in the control group (CG), completed the 9-month study.	Arm ergometry performance; muscle strength; perceived stress; depression; physical self-concept; pain; perceived health; QoL.	Workloads on an arm ergometer; Maximum load that could be lifted in one repetition (1RM) on both limbs for the bench press, elbow flexion and shoulder flexion maneuvers; Perceived stress scale; Center for Epidemiological Studies Depression Scale; Body Satisfaction Questionnaire; SF-36 2-item pain subscale; SF-36 self-reported health transition subscale; Perceived Quality of Life Scale.	EG: supervised progressive training, including a warm-up and gentle stretching of the UL and resistance training, using pulley exercises on the wall, free weights and a weight machine (twice a week, lasting 90 to 120 minutes). CG: a bimonthly education session (together with the EG) on topics such as exercise physiology for people with spinal cord injury, osteoporosis after spinal cord injury and relaxation techniques.	The participants in the EG reported significantly less pain (p<0.01), stress and depression after training, and scored higher than the CG in the indices of satisfaction with physical function, level of perceived health and general QoL (p<0.05).
Macêdo et al.[16]	Evaluate the impact of a home exercise program on pain intensity and QoL in individuals with tropical spastic paraparesis.	56 people with tropical spastic paraparesis classified as definite or probable. 49 completed the 24 weeks of the study (Supervised Group = 15, Unsupervised Group = 10 and Control Group = 11).	Pain and quality of life.	SF-36 and BPI.	Supervised Group: exercise protocol, supervised by a physiotherapist (2x/ week, 45 to 50 min, for 12 weeks). Unsupervised Group: clarification from the physiotherapist on how to carry out the exercise protocol and practice the exercises every other day independently, guided by a booklet (24 weeks, at home); Control Group: maintenance of usual care (diet, pharmacological treatment, physiotherapy treatment) without changes during the study period.	Although no significant changes were shown after the exercise program, when the expression "worst pain experienced in the last 24 hours" was analyzed by the BPI, the Supervised Group showed increased intensity between the first and second evaluations (p=0.25), while the Control Group showed worsening pain between the second and third evaluations (p=0.12) and the Non-Supervised Group maintained the value in all three evaluations (p=0.43). There was also no significant differences in the "average pain" of inflammatory bowel disease between the three groups. From a clinical point of view, however, a 33% difference in pain improvement was observed between the Non-Supervised Group (p=0.69) and the Control Group (p=0.58), while the Supervised Group (p=0.78) showed only a 20% reduction in pain.
Mulroy et al.[17]	Main: investigate the effect of a home exercise program + instructions to optimize the performance of UL tasks on shoulder pain in people with spinal cord injury. Secondary: determine the impact of the intervention on physical activity and participation and to identify whether the improvement in pain or function was maintained 4 weeks after the end of the intervention.	80 individuals with paraplegia due to spinal cord injury and shoulder pain, divided into two groups. Group 1 (n=40): movement/exercise optimization. Group 2 (n=40): attention control intervention.	Shoulder pain, muscle strength (ability to generate force), activity and quality of life.	Wheelchair user shoulder pain index; VAS; dynamometer; propulsion speed over a distance of 25 meters; physical activity scale for individuals with physical disabilities; social interaction inventory; QoL questionnaire, SF-36 and QoL scale.	Home-based program of shoulder strengthening and stretching exercises, with recommendations on how to optimize the movement technique of transfers, lifts and wheelchair propulsion (12-week duration). The attention Control Group watched a 1-hour educational video emphasizing shoulder anatomy, injury mechanisms and general concepts of shoulder pain management.	Shoulder pain intensity was reduced in the immediate post-intervention assessment in Group 1 to approximately one third of the baseline values (from 51.2±33.0 to 14.9±14.0, p<.001), but remained unchanged in the Control Group (from 45.4±38.8 to 45.6±38.2). According to the VAS, shoulder pain intensity was also reduced to a third of baseline values in Group 1 (from 5.1±2.8 to 1.4±1.6, p<.001), but was not significantly reduced in the Control Group (from 4.7±2.7 to 4.2±27).

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Table 1. Continued...

Authors	Objectives	Sample	Variables	Evaluation tools	Intervention	Main results
Nightingale et al.[18]	Assess the influence of a home exercise intervention on health-related QoL in people with spinal cord injuries.	24 individuals with chronic (>1 year) spinal cord injury below the second thoracic level, divided into two groups: Control Group (n=8) and Exercise Group (n=16).	Physical QoL; emotional QoL; number of years with QoL; fatigue severity; global fatigue; shoulder pain; exercise self-efficacy.	SF-36 physical and mental index; Quality of Life Adjusted in Years (QALY); Fatigue Severity Scale (FSS); Wheelchair User's Shoulder Pain Index (WUSPI); Exercise Self-Efficacy Scale (ESES).	IG: moderate-intensity exercise on a portable tabletop ergometer set up in their own home (4x/week for 6 weeks). CG: instructed to maintain their usual physical activity behavior.	The intervention improved health-related quality of life scores in individuals with spinal cord injury. Although there was a small negative effect of the intervention on shoulder pain, there was no significant interaction (p= 0.386) and the mechanistic inference was unclear, suggesting that the intervention had no significant effect on pain perceptions.
Pérez-de la Cruz[19]	To apply 2 physiotherapy protocols to test the effect on the intensity of pain in the lower limbs (LL), balance and quality of life in patients with PD.	30 individuals diagnosed with PD, divided into 2 groups: Experimental Group (n=15) and Control Group (n=15).	Pain intensity, balance, gait and PD assessment.	VAS; BERG: Berg Balance Scale; FTSTS: 5x sit and stand test; Tinetti scale; TGUG: Timed Get Up and Go test; UPDRS: Unified PD Rating Scale.	Ground therapy (Control Group): supervised group training; aquatic Ai Chi: group intervention carried out by a physiotherapist specializing in clinical Ai Chi. Twenty sessions were held 2x/week for 10 weeks.	EG: significant differences in the reduction of post-treatment pain intensity (p<0.001), as well as in the variables related to static and dynamic balance, with the exception of FTSTS. CG: improvements were observed only in the reduction of pain intensity, and were less significant than the changes found in the Experimental Group (p=0.006).
Pérez-de la Cruz[20]	Determine the 12-week effect of 3 treatment proposals on pain, gait and balance in patients with chronic stroke.	40 patients diagnosed with CVA, divided into 3 groups: ground therapy (n=14), aquatic therapy (n=13) and combined therapy (n=13).	Pain intensity, balance, gait and LL strength.	VAS; Tinetti test; 360° turn test; balance test in unipodal support; sit and stand test for 30 seconds.	Ground therapy (Control Group): supervised group training, lasting 45 minutes, twice a week, for a period of 12 weeks; aquatic Ai Chi (Experimental Group): therapy carried out by a physiotherapist with experience in neurological rehabilitation and certified in Ai Chi, lasting 45 minutes, twice a week, for a period of 12 weeks; Combined therapy: alternating joint sessions of floor therapy (Monday and Wednesday, totaling 12 sessions) and aquatic Ai Chi therapy (Tuesday and Thursday, totaling 12 sessions).	The aquatic therapy and combined therapy groups showed significant improvements at the end of treatment in the variables of pain, balance, gait and LL strength (p<0.001), and these improvements were maintained over time in the VAS (reduction in mean score), Tinetti scale (increase in mean score), 360° turn test (reduction in mean score) and the 30-second sit and stand test (increase in mean score). No differences were found between the values obtained in the Control Group (ground therapy) throughout the measurements.
Pérez-de la Cruz[19]	Evaluate the effects of 12 weeks of treatment with aquatic Ai Chi sessions, dry therapy or combined therapy (aquatic therapy and dry therapy) on pain, depression and quality of life in people diagnosed with CVA.	41 CVA patients, divided into 3 groups: ground therapy (n=15), aquatic therapy (n=13) and combined therapy (n=13).	Pain, resilience and QoL.	VAS; Resilience Scale; SF-36 Quality of Life Scale.	Ground therapy (Control Group): sessions lasting 45 minutes, twice a week, for a period of 12 weeks; aquatic Ai Chi (Experimental Group): therapy carried out by a physiotherapist specializing in clinical Ai Chi, with the same number of sessions as the Control Group and lasting 45 minutes; combined therapy: ground physiotherapy sessions and aquatic Ai Chi were alternated under the same conditions as the participants in the other groups, thus receiving the sum of the therapies from the other two groups.	In the Experimental Group, significant differences were found in terms of reduced pain intensity on the VAS scale and higher scores on the resilience scale (p < 0.001). A greater variation was observed in the groups that received aquatic interventions (Ai Chi and combined therapy). These changes were more significant in the post-intervention measures.

PD: Parkinson's disease; QoL: quality of life; ALS: amyotrophic lateral sclerosis; VAS: Visual Analogue Scale; NSAIDs: non-steroidal anti-inflammatory drugs; LL: lower limbs; UL: upper limbs; CVA: cerebral vascular accident; ADL: activities of daily living; LISAT-9: Life-Satisfaction Questionnaire-9; SWLS: Satisfaction with Life Scale; LTPAQ-SCI: Leisure Time Physical Activity Questionnaire for People with Spinal Cord Injury; SF-36: Medical Outcomes Short-Form 36-Item Health Survey; PANAS: Positive and Negative Affects Scale; SCIM: Spinal Cord Independence Measure version III; IPAQ: Impact on Participation and Autonomy Questionnaire; UPDRS: Unified Parkinson's Disease Rating Scale; ROM: range of motion; IG: intervention group; CG: control group; FTSTS: 5x sit and stand test; TGUG: Timed Get Up and Go test; WUSPI: Wheelchair User's Shoulder Pain Index; ESES: exercise self-efficacy scale; FSS: exercise self-efficacy scale; PEG: Patient-Reported Experience of Cancer Pain; CRPS: Complex Regional Pain Syndrome; PDQ-8: Parkinson's Disease Questionnaire; FES-I: Falls Efficacy Scale International Version; PDSS-2: Parkinson's Disease Sleep Scale; PHQ-4: short version of the Patient Health Questionnaire.

Table 1. Continued...

Authors	Objectives	Sample	Variables	Evaluation tools	Intervention	Main results
Schmid et al.[21]	Evaluate the change in physical functioning after 8 weeks of yoga-therapy in people with chronic stroke.	People with chronic CVA (n=47) randomized to yoga therapy (n=37) or control care care in a 2:1 ratio (n=10).	Pain; ROM; strength; endurance.	PEG (3-item functional pain measure), derived from the BPI; Goniometer; Arm flexion test; Sit and stand test for 30 sec; 6 min walk (Senior Fitness Test item); Modified 2 min step test.	The therapeutic yoga sessions were held in a group of no more than 10 people, lasting 1 hour, twice a week, for 8 weeks (16 sessions). A standardized and progressive protocol was developed which included modified yoga postures, breathing, and relaxation in the sitting, standing and supine positions. Participants in the waiting list Control Group received no intervention.	Individuals randomized to yoga had a significant improvement in multiple variables (bilateral neck ROM, passive hamstring ROM, UL strength and increased distance walked in 6 min). Pain improved significantly after 8 weeks of yoga (12.2 vs. 8.9, p = 0.004).
Topcuoglu et al.[22]	Investigate the clinical, functional and psychosocial effects of upper extremity aerobic exercise (arm ergometry) and to compare the effect of aerobic exercise with that of conventional physiotherapy in patients with complex regional pain syndrome type 1 after CVA.	40 patients with hemiplegia associated with a cerebrovascular event that occurred at least 1 month and 6 months before the study, as well as a diagnosis of complex regional pain syndrome on the hemiplegic side.	Motor level; spasticity; pain; level of independence; depressive mood.	Brunnstrom staging; modified Ashworth scale; VAS; Functional Independence Measure (FIM); Nottingham Health Profile (NHP); Beck Depression Scale.	TENS (100 Hz, 20 min/day, cold compress (20 min/day), retrograde massage and contrast baths. Medical treatment involved standard NSAIDs drugs. 20 of the 40 patients received only the standard conventional physiotherapy program. The other 20, in addition to this program, also performed exercises accompanied by arm ergometry (5 days/week, 30 min/day, for 4 weeks). A physiotherapy program for AVE consisting of therapeutic, neurophysiological, postural, balance and coordination and ADL was applied to all patients.	In the Upper Limb Aerobic Exercise Group, patients reported significant pain relief (89.9%) and a significant decline in CRPS signs and symptoms. The mean change between the groups with regard to a reduction in shoulder pain, hand pain, as well as in the NHP scores and Beck depression scale scores, which indicated a reduction in pain, fatigue and depression were statistically significant (p<0.05).
Tseng et al.[23]	Evaluate the effect of a ROM exercise program aimed at improving joint flexibility, activity function, pain perception and depressive symptoms in a sample of stroke survivors.	59 patients with hemiplegia for 6 months or more since the CVA, divided into 3 groups: Special Care Group (n=17), Intervention Group I (n=21) and Intervention Group II (n=21).	Functional independence, joint angle, self-reported pain and depression.	FIM™ ADL subscale; joint angle measurements in 6 joints + self-perceived pain; Chinese version of the FIM™. Geriatric Depression Scale - Short Form (GDS-15).	G1 intervention: protocol of ROM exercises supervised by a nurse; G2 intervention: same ROM protocol with the presence of a nurse to help them physically achieve maximum ROM; Special Care Group: did not receive any extra ROM exercises beyond the institution's routine. The intervention groups completed the protocol five times per joint (6 in total), 2x/day and 6 days/ week, for 4 weeks, with each session lasting approximately 10 to 20 minutes.	The average pre- and post-intervention scores for pain increased by 5.41 in the usual care group and decreased by an average of 7.62 in Intervention Group I, and decreased by 10.00 in Intervention Group II. Intervention Group I, and decreased by 10.00 in Intervention Group II. A comparison of the changes in pre- and post-intervention scores between the three groups showed a statistically significant difference (p<0.001).

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Table 1. Continued...

Authors	Objectives	Sample	Variables	Evaluation tools	Intervention	Main results
Wagner et al.[24]	Evaluate the effectiveness of physiotherapy using a tablet compared to usual care on QoL and other health-related parameters.	230 patients with idiopathic PD who were taking part in a 3-week multimodal treatment (n=93 for IG and n=137 for CG).	QoL, participation restrictions; fear of falling; sleep disorders; anxiety/ depression; comorbidity; pain; performance capacity; physical activity.	Parkinson's Disease Questionnaire (PDQ-8 German version); IMET; Falls Efficacy Scale International Version (FES-I); German version of the Parkinson's Disease Sleep Scale (PDSS-2); short version of the Patient Health Questionnaire (PHQ-4); modified version of the Sangha comorbidity questionnaire; 5-point scale; Performance capacity in the domains of work, daily life and leisure was quantified using numerical scales from 0 to 10; Physical activity was measured using the instrument used by Mensink in the 1999 Federal Health Survey; Pain assessment: individual items (Questions on pain in the Federal Health Survey 98 questionnaire).	IG: tablet app with verbal instructional videos and explanations for all the exercises taught in the multimodal treatment for Parkinson's. CG: usual therapy services of the multimodal treatment and, after discharge, the usual outpatient treatment. A The actual nine-month intervention began after discharge from the clinic. Patients were asked to train using the program for up to 3x/week, in addition to their usual outpatient therapy. therapy. These exercises are available in different degrees of difficulty and promote endurance, strength and balance.	Both the IG and CG achieved significant improvements at the end of treatment. There were only significant differences in the group comparisons for the variables FES-I, PHQ-4 total score and PHQ depression (scores decreased, p<0.01). With regard to pain, no significant changes were observed. There was a worsening in both groups in almost all the primary and secondary outcome variables in the anamnesis. However, this worsening was less pronounced in theIG than in the CG.
Zhao et al.[25]	develop a seated Tai Chi program for subacute stroke survivors and examine its effects.	160 participants divided into two groups.	Upper limb (UL) function; balance control; sitting balance control; depressive symptoms; shoulder ROM; shoulder pain; activities of daily living (ADL; QoL.	Fugl-Meyer assessment of the upper extremity and Wolf motor function test; Berg balance scale; Trunk Impairment Scale; Geriatric Depression Scale Short Form; Shoulder Q; Modified Barthel Index; CVA-specific quality of life scale.	IG: Wheelchair-adapted Tai Chi series offered for stroke survivors with mild weakness (UL muscle strength: 4 or 5). A registered nurse and a qualified Tai Chi master developed the series to meet the needs of stroke survivors with hemiparesis or hemiplegia UL muscle strength: ≤3). The demonstration of the movements was recorded by the Tai Chi master in video form. Caregivers were involved to ensure the safety of the participants and to supervise the practice. Adherence to the treatment protocol between the 2 sites (home and rehabilitation hospitals) was ensured by adherence to the participant handbook and phone call reminders. CG: UL movements recommended by the hospital.	The results revealed significant improvements in UL function in the domains of execution time and functional capacity of the Wolf motor function test (T2, T3 and T4), depression (T2, T3 and T4), balance control (T3 and T4), sitting balance control (T2, T3 and T4), shoulder extension (T2 and T3), shoulder external rotation (T4), internal rotation (T4), ADL (T2, T3 and T4) and QoL (T2, T3 and T4) in the Intervention Group compared to the Control Group (all P<0.05). No significant differences were found between groups at T3 in UL function (Fugl-Meyer assessment of the upper extremity) shoulder flexion, shoulder abduction and shoulder pain (p>0.05).

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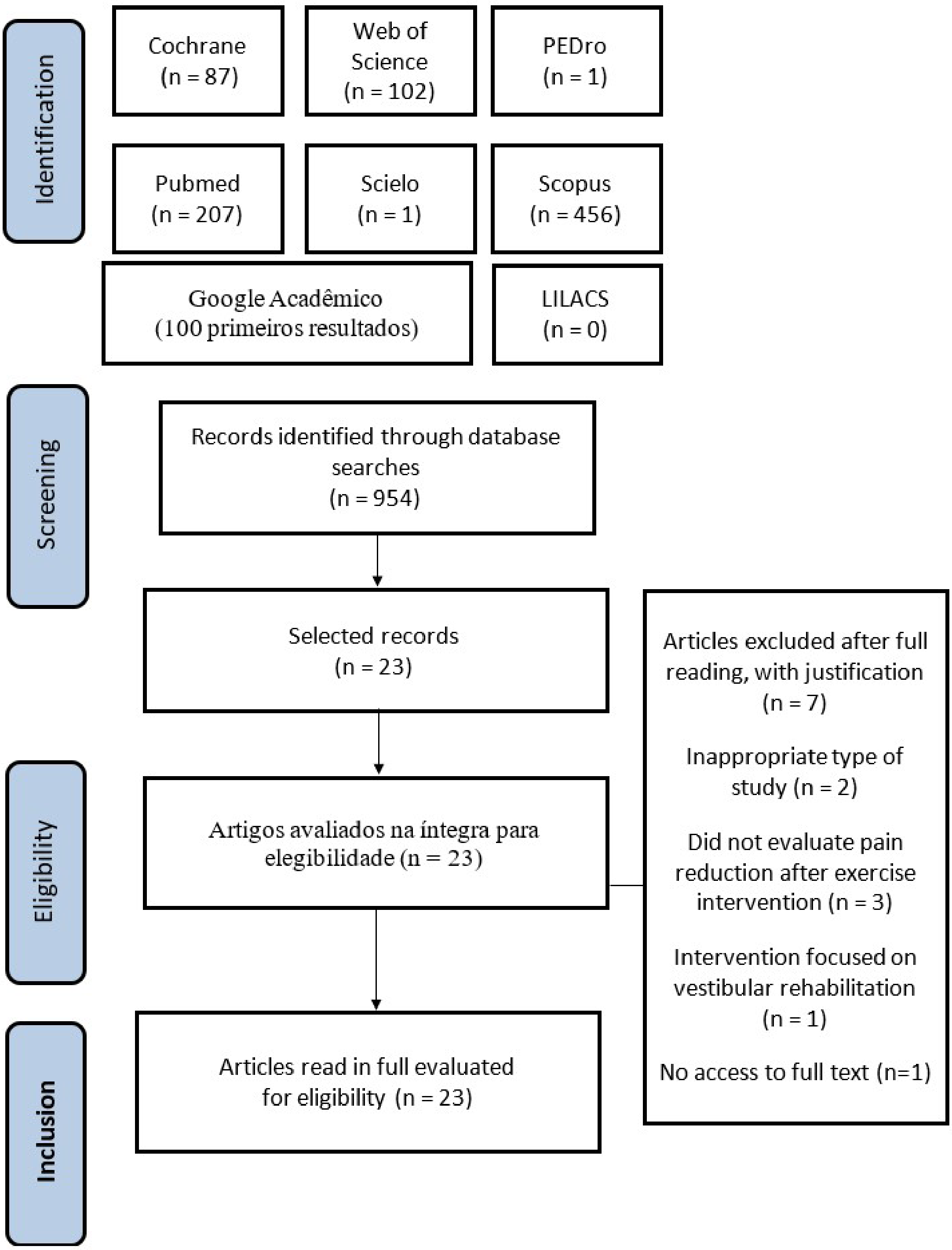

Figure 1. Flowchart of the studies included in the review.

These results contrast with those of a previous systematic review that investigated whether aquatic exercise reduces pain in people with neurological or musculoskeletal diseases, which explains that aquatic exercise and floor exercise have similar effects on pain relief[27]. Thus, even if aquatic therapy does not show superior results when compared to other types of exercise performed on the ground, it is important to consider the use of this modality for the treatment of pain, since it is possible to affirm that aquatic programs improve several variables, in addition to pain, such as quality of life, postural balance, cardiorespiratory conditioning and gait in adults with chronic diseases, including CNS diseases[28].

Exercise has been a widely recommended intervention by health professionals to help control pain[29]. In clinical trials focused on PD, the exercises most commonly used to alleviate pain are aerobic exercises, strengthening exercises, flexibility exercises and aquatic therapy[30]. In this review, three studies that included individuals with PD evaluated the effects of these exercise modalities.

In addition to the approaches already mentioned, other types of exercise were used, such as balance exercises.

The article[13] evaluated PD patients divided into two groups. Both used exercise interventions and showed a significant reduction in pain immediately after treatment and one month afterwards. This improvement in pain can be explained by some mechanisms such as neuroplasticity and neural recovery, attenuation of neuronal apoptosis, dopaminergic analgesic pathway, non-dopaminergic analgesic pathway and inhibition of oxidative stress[30].

The article[11] allocated PD patients into 3 groups. All the participants received an intervention with range-of-motion, strengthening and balance exercises. In addition, they underwent treadmill training without weight support or with weight support, which would be 10% or 20%. The weight-bearing groups showed a reduction in pain compared to baseline. These findings support another study[31] which showed that aerobic exercise reduces pain sensitivity in individuals with PD. However, the group without weight support had the opposite effect and showed an increase in pain in the sixth week of training, which may indicate a need to research the use of weight support during treadmill training in this population.

The study[24] evaluated PD patients who underwent a home exercise program via a tablet app compared to other patients who received usual care from a multimodal treatment. Both groups of patients showed improvement in all parameters, such as quality of life, performance capacity, among others. However, there were no significant differences in relation to pain, which does not shed light on the effects of the intervention in terms of analgesia. As this is a more recent method, no studies were found that used this type of intervention in this specific population. However, considering the positive results obtained with home exercises to reduce pain in other populations[32,33], combining exercise with electronic resources to help with execution seems to have great potential for improving the treatment of neurological patients.

Pain is also prevalent in individuals with spinal cord injury[3]. This review included four studies that evaluated the influence of exercise on pain management in these patients. The reference authors[17] designed a home program for the experimental group with strengthening and stretching exercises for the shoulder, as well as recommendations for transfer techniques. The control group watched an educational video about the shoulder and pain management in this location. After measurement using two scales, only the experimental group showed a significant reduction in the intensity of shoulder pain, and this improvement was associated with an increase in muscle strength and improvements in quality of life.

Studies[15,17] used progressive training with stretching and strengthening exercises for the upper limbs in the experimental group. The control group had a bimonthly education session with the experimental group. After training, the experimental group reported significantly less pain. These results corroborate the systematic review and meta-analysis study[34], which supports active physiotherapy treatment for shoulder pain in people with spinal cord injuries who use manual wheelchairs.

The study[14] compared the effects of upper limb bicycle ergometry and treadmill training with body weight support in individuals with spinal cord injury. The results showed that pain was significantly lower in the upper limb bicycle exercise group over the course of the intervention compared to the other group. On the other hand, the study[18] did not show significant results in relation to pain perception. The participants in the study were divided into two groups, one of which was instructed to perform moderate-intensity exercises with a portable ergometer in their own home, and the other was instructed to maintain their usual physical activity behavior. Despite the non-significant effect found in the aforementioned study, it is known that exercising with a portable ergometer, in addition to improving aerobic capacity, can also strengthen the muscles of the upper limbs[35], which suggests a potential positive effect on pain relief.

The upper limb ergometer was also used in the article[22], which compared the effect of aerobic exercise with that of a program that included transcutaneous electrical nerve stimulation (TENS), cold compress, retrograde massage and contrast bath in patients with complex regional pain syndrome type 1 (CRPS) after CVA. Another comprehensive program consisting of therapeutic exercises was applied to both groups. This program was added to treatment using electrotherapy and thermotherapy resources in one group, as well as treatment using upper limb ergometry in the other group. In the group that used aerobic exercise for the upper limbs, the patients reported significant pain relief, as well as a decline in the signs and symptoms of CRPS, indicating that the combination of aerobic exercises with the physiotherapy program that was established can be a good choice for treatment.

The article[22] also highlighted the use of non-steroidal anti-inflammatory drugs (NSAIDs) in the patients involved in the research. This is an important fact that may have influenced the results found and, although the use of drugs in this category was not mentioned in the other studies, it may be that it is part of the routine treatment of the patients evaluated, since many CVA survivors use drugs to treat pain, with anti-inflammatory drugs being the most common[36]. This research also highlights the need to develop treatments for chronic pain in this population, because even though they seek out various methods of pain relief, many patients perceive them as ineffective.

Three more studies evaluated the effect of exercise interventions on CVA patients by establishing a range-of-motion (ROM) exercise protocol that was carried out in two groups: one supervised by a nurse and the other with the nurse present to help the participants achieve maximum ROM. A third group did not receive any extra ROM exercises beyond the institution's routine. The average pain scores increased in the usual care group and decreased in the groups that performed the exercises, with greater attenuation in the group that received help. These results show that actively assisted exercises seem to be more effective. However, more studies are needed in order to obtain reliable conclusions[23].

Another study[21] evaluated the effect of yoga on CVA patients and included exercises involving modified postures, breathing and relaxation. The control group consisted of fewer participants, who continued their usual treatment. Pain was significantly reduced in the group that did the yoga sessions for eight weeks. This result supports other data found in the literature, such as those shown in the article[37]: the practice of yoga is related to increased pain tolerance and reduced discomfort associated with pain. Taking into account the benefits of the practice and the effects mentioned above, yoga can be considered as a therapeutic intervention option for individuals with chronic pain[38]. However, further studies on the effectiveness of this modality in patients with CNS diseases are needed.

The authors[25] developed a seated Tai Chi program for subacute CVA survivors and did a comparison with a group that performed upper limb movements recommended by the hospital. Tai Chi movements showed significant improvements in upper limb function and other variables assessed. However, no significant differences were found between the groups regarding shoulder pain. The authors stated that although there were no statistical significance in shoulder pain between the two groups, there were some changes in pain intensity at times, and highlighted the small sample size of individuals with shoulder pain in this study, indicating the need for further research.

The study[16] evaluated the impact of a home exercise program on the intensity of pain in individuals with tropical spastic paraparesis. Participants were divided into three groups, one supervised by a physiotherapist, one that received guidance from the professional to perform the exercises at home, and the control group, which was instructed to maintain usual care, including physiotherapy treatment. No significant changes were found after the exercise program when the participants were evaluated. However, the authors report that from a clinical point of view, a more significant reduction in pain was observed in the group that carried out the exercises at home and in the control group, when compared to the reduction observed in the group that carried out the activities under professional supervision. From the information presented in the article, it was not possible to obtain clear information about the exercises used or the results presented. In addition, no articles that discuss the topic in question were found. Therefore, the results on the impact of exercise on this disease are inconclusive.

The effect of exercise has also been evaluated in patients with ALS. The study[12] compared patients who were instructed to perform a list of exercises at home with patients who did no physical activity. The exercises were designed according to each individual's health condition and involved most of the muscle groups. During the follow-up period, all the patients got worse and the intensity of pain increased in both groups. Because of the high drop-out rate, the analysis was hindered. However, even with the difficulty of obtaining a more detailed analysis, it is possible that the worsening may be related to the progressive nature of the disease.

A systematic review with meta-analysis[39] suggested that exercise can improve functional capacity and lung function in ALS patients when compared to no exercise or usual care, and considers exercise to be safe in this population. However, pain was not one of the outcomes analyzed in the study, so it is not possible to draw a conclusion about the effect of exercise on pain in these patients.

The present study had some limitations. Firstly, regarding the quality of the articles: there was no analysis of the risk of bias of the studies included in this review, as it was an integrative literature review which set out to describe the state of the art of scientific literature on the subject. In addition, the qualitative analysis of the studies included made it possible to see the high degree of heterogeneity and variability in terms of the types of exercise and forms of prescription, which makes it possible to identify the modalities that can be used, but also hinders the possibility of a more in-depth analysis for the indication of a therapeutic proposal based on the existing evidence. Despite this problem found in the discrepancy in the therapeutic method of the studies, the presentation of this overview of the scientific literature was considered relevant by the authors of this integrative review as a way of exposing the state of the art and the need to develop studies with clinical impact for the target population of neurological patients.

Another limitation was the fact that some articles did not examine pain as a primary outcome, which may have an impact on the relevance of the choice of assessment tools and approach to this variable by the study investigators. This may also reveal the negligence that exists in the construction of studies by disregarding the pain intensity of neurological patients as a relevant clinical outcome to be addressed with results later applied in clinical practice, something that should be taken into account in future studies on the subject.

It is also worth highlighting the use of pain assessment instruments. Although most of the studies used specific assessment methods for this symptom, some used non-specific resources, but contained items related to pain. This observation leads us to reflect on the relevance of pain in the treatment of these patients, since it is not always seen with the same importance as functional limitations, even though they are directly linked. In addition, some patients with neurological diseases have communication difficulties, as well as cognitive deficits. Thus, there is a clear need to use methods that encompass all these issues and are not just focused on verbal communication, in order to improve the identification of pain in this population.

In short, this integrative review brings to light the panorama of scientific literature on pain management in neurological patients using exercise as a therapeutic strategy. A wide variety of exercise modalities have been studied for this purpose, with positive results for pain reduction, but not supporting the superiority of one type of exercise over another and/or the measurement of pain as a primary outcome in the population of individuals with CNS diseases. Therefore, it is suggested that new systematic reviews be carried out, assessing the risk of bias and the level of evidence of the studies, promoting greater robustness in the elucidations and recommendations generated from the evidence analyzed.

CONCLUSION

Different modalities of physical exercise can be an effective therapeutic intervention method for the treatment of pain in patients with CNS diseases. However, studies researching this outcome are currently still limited and do not allow for in-depth recommendations on the subject. Therefore, new review studies and clinical trials with high methodological rigor, larger samples and well-detailed interventions are needed in order to elucidate the effectiveness of exercise for the reduction of pain of individuals with neurological diseases, as well as to identify the appropriate types of exercise and prescription methods.

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