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André Luiz Silva Santos[1], Mônica Deise dos Santos Rocha[2], Mateus Maciel Santos[2], Josimari Melo DeSantana[1,2]

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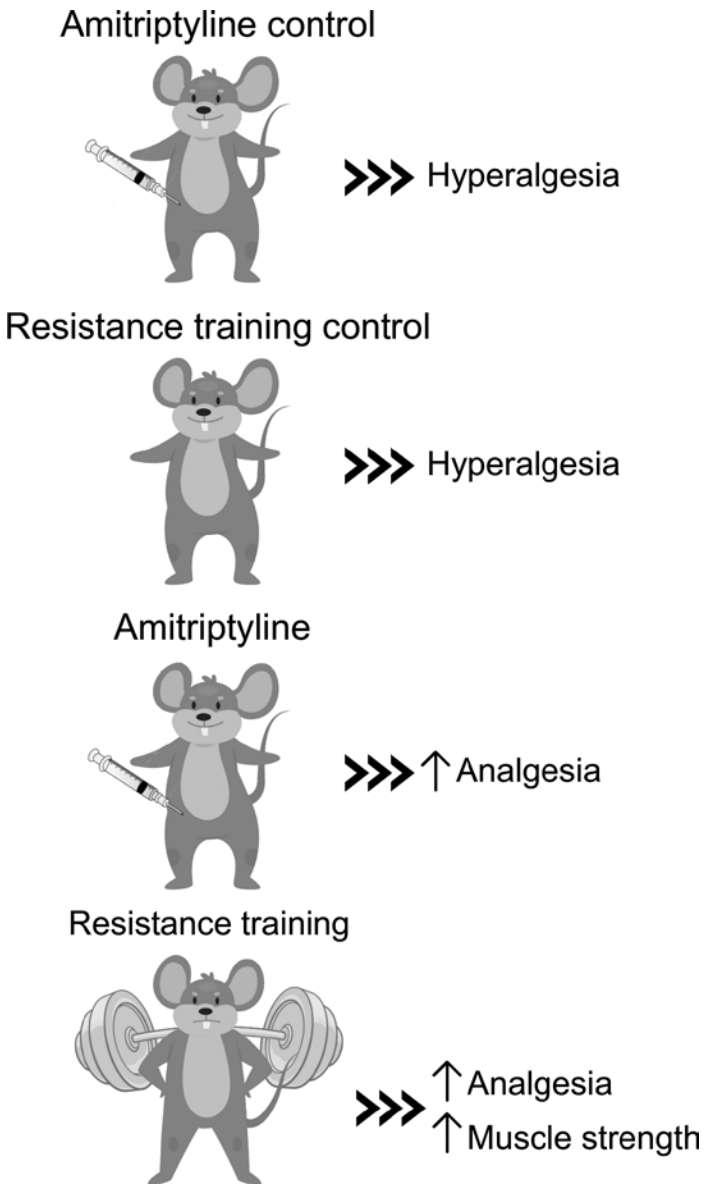
GRAPHICAL ABSTRACT



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ABSTRACT

BACKGROUND AND OBJECTIVES: Fibromyalgia syndrome (FMS) is characterized by different factors, such as chronic diffuse muscle pain (CDMP), fatigue and psycho-emotional changes. Among the animal models that mimic FMS, the acid saline model is consolidated in the development and maintenance of CDMP. Resistance training (RT) has been an effective method for reducing pain in FMS. Thus, the aim of the present study was to evaluate the effects of resistance training on nociceptive and motor responses in an animal model of chronic diffuse muscular pain.
METHODS: Twenty-four male Wistar rats were allocated into four groups: resistance training, RT control, amitriptyline (AMITRIP) and AMITRIP control; all treatment protocols lasted 4 weeks. CDMP was induced in all mice. Then, the animals were treated with low-intensity RT (40% 1 maximum repetition) and AMITRIP (10 mg/kg/day). The mechanical paw withdrawal threshold, locomotor activity and muscle strength were evaluated.
RESULTS: Animals treated with both RT and AMITRIP showed an increase in the mechanical paw withdrawal threshold ($p<0.05$) compared to their controls, suggesting a reduction in mechanical hyperalgesia. There was no improvement in locomotor activity in all groups ($p>0.05$). Animals with CDMP that underwent RT showed an increase in hindlimb muscle strength ($p<0.0001$) compared to the RT control group.
CONCLUSION: Low-intensity resistance training resulted in antihyperalgesic effects and improved muscle strength in animals submitted to the CDMP model.

Keywords: Exercise, Fibromyalgia, Neurosciences, Resistance training.

RESUMO

JUSTIFICATIVA E OBJETIVOS: A síndrome da fibromialgia (SFM) é caracterizada por diferentes fatores, como dor crônica muscular difusa (DCMD), fadiga e alterações psicoemocionais. Dentre os modelos animais que mimetizam a SFM, o modelo de salina ácida é consolidado no desenvolvimento e na manutenção da DCMD. O treinamento resistido (TR) tem sido um método eficaz para redução da dor por SFM. Assim, o objetivo do presente estudo foi avaliar os efeitos do treinamento resistido na resposta nociceptiva e motora em um modelo animal de dor crônica muscular difusa.
MÉTODOS: Vinte e quatro ratos machos Wistar foram alocados em quatro grupos: treinamento resistido, controle do TR, amitriptilina (AMITRIP) e controle da AMITRIP; todos os protocolos de tratamento tiveram duração de 4 semanas. A DCMD foi induzida em todos os ratos. Em seguida, os animais foram tratados com TR de baixa intensidade (40% 1 repetição máxima) e AMITRIP (10 mg/kg/dia). Foram avaliados o limiar mecânico de retirada de pata, a atividade locomotora e a força muscular.
RESULTADOS: Animais tratados tanto com TR quanto com AMITRIP apresentaram aumento do limiar mecânico de retirada de pata ($p<0,05$) em relação aos seus controles, sugerindo redução da hiperalgesia mecânica. Não foi observada melhora da atividade locomotora em todos os grupos ($p>0,05$). Animais com DCMD que realizaram TR obtiveram aumento da força muscular dos membros posteriores ($p<0,0001$) em comparação ao grupo controle do TR.
CONCLUSÃO: O treinamento resistido de baixa intensidade resultou em efeitos anti-hiperalgésicos e melhora da força muscular em animais submetidos ao modelo de DCMD.

Descritores: Exercício físico, Fibromialgia, Neurociências, Treinamento de resistência.

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HIGHLIGHTS
- Strength training attenuates hyperalgesia in rats with chronic diffuse muscle pain.
- Strength exercise induces increased strength in rats with chronic diffuse muscle pain.
- Rats with chronic diffuse muscle pain do not improve locomotion after strength exercise.

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INTRODUCTION

Fibromyalgia syndrome (FMS) is characterized as a syndrome involving various symptoms associated with chronic musculoskeletal pain, such as anxiety, depression, sleep disturbances, intestinal dysfunction, muscle stiffness and increased fatigue[1-4]. This pathological state promotes disorders in the central nervous system by increasing nociceptive stimuli over the long term, resulting in sensitization[3-6].

The etiology of FMS remains unknown, but some pathophysiological mechanisms may be present, such as: medullary summation of ascending pain pathways, hypoactivation of the pain modulator system, sensitization of peripheral and central nociceptors, dysregulation of the neuroendocrine system and autonomic imbalance[3,6-8].

Experimental research has been carried out in order to understand the pathophysiology and mechanisms involved in the treatment of this syndrome[7,9-11]. In this regard, several animal models that mimic FMS have been developed, among which the acid saline model is consolidated in the development and maintenance of chronic diffuse muscle pain (CDMP), as it triggers central sensitization at the level of spinal cord and supraspinal areas[7,9,11].

Even so, in an attempt to minimize the lesions caused by FMS, a range of therapies have been studied, both pharmacological and non-pharmacological[12-15]. The action of pharmacological therapies is aimed at potentiating the release of neurotransmitters (e.g. norepinephrine, serotonin and gamma-aminobutyric acid) involved in inhibiting excitability and reducing neurotransmitters (e.g. glutamate and aspartate) that favor central stimulation[15-17]. However, it should be borne in mind that chronic use of these drugs can promote adverse effects such as drowsiness, xerostomia, sedation, tachycardia, orthostatic hypotension, palpitations and constipation[18-20].

In the search for effective therapeutic alternatives without adverse effects, non-pharmacological therapies (physical activity and exercise) have been called into question, which have favorable outcomes in reducing pain and improving functional performance[12,14,17,21,22]. Regular physical activity is capable of promoting beneficial changes in the central pain inhibitory pathways, as well as acting as a protector of the immune system[21,23].

A preclinical study[24] showed that regular physical activity, using a running wheel, was able to prevent the development of secondary, centrally mediated hyperalgesia in an animal experimental model of chronic non-inflammatory musculoskeletal pain induced by acid saline in mice. Similarly, another study showed that regular physical activity in mice was able to produce an increase in interleukin (IL) IL-10 (anti-inflammatory cytokine) associated with a greater expression of M2-type regulatory macrophages in a model of chronic generalized muscular pain[25].

Furthermore, according to the authors[26], low-intensity aerobic exercise in rats with CDMP resulted in a reduction in mechanical hyperalgesia mediated by opioidergic mechanisms. Nevertheless, chemical mediators such as neurotransmitters, soluble gases, neuromodulators and bioendogenous amines may be involved in the processing of exercise-induced analgesia[23].

Several positive effects are associated with resistance training (RT). This type of physical exercise has gained notoriety due to its benefits, such as analgesia, reduced fatigue, increased baroreflex sensitivity, gains in strength and muscular endurance[12,27,28]. Up until the start of this research, no study had assessed the nociceptive and motor response of animals with CDMP treated with RT. Therefore, the aim of this study was to evaluate the effects of RT in an animal model of chronic diffuse muscle pain.

METHODS

Ethical aspects and animals

This project was carried out in accordance with the ethical aspects of the Brazilian National Council for the Control of Animal Experimentation (*Conselho Nacional de Controle de Experimentação Animal* - CONCEA) and the *Arouca* Law (Brazilian Federal Law 11.794), with approval from the Ethics Committee for the Use of Animals at the Federal University of Sergipe (CEUA UFS no. 1354250619). For this study, 24 male Wistar rats weighing between 250 and 350 g were selected from the Sector Animal Facility of the Neuroscience Research Laboratory at the Federal University of Sergipe. The animals were housed in boxes attached to a ventilated shelf (Alesco®, Monte Mor, SP, Brazil) with food and water *ad libitum* and kept on a 12:12 hour light/dark cycle at an ambient temperature of 71,6ºF.

Design

This is an experimental, randomized, blinded and controlled research. This study was carried out in accordance with the recommendations of the Animal Research: Reporting of *In Vivo* Experiments (ARRIVE). The animals were allocated into four groups (6 animals per group), divided into: 1) RT; 2) RT Control (RTC); 3) Amitriptyline (AMITRIP); and 4) AMITRIP Control (AMC). The animals were allocated to their respective groups using sealed opaque envelopes bearing the letters A, B, C and D, relatively proportional to the 4 study groups. The envelopes were opened immediately before allocation to intervention by a blinded evaluator. As for the study experiments, two previously trained operators were responsible for carrying out the intervention protocol in all groups, while a third operator was responsible for collecting the evaluation variables.

Induction of the chronic diffuse muscle pain model

To induce CDMP, two injections of acidic saline (pH 4.0; 100 μL per injection) were given five days apart, unilaterally, intramuscularly, in the left gastrocnemius muscle. However, it should be noted that, at the time of induction, the animal was anesthetized with isoflurane vaporized at a concentration of 4% (BioChimico®, Itatiaia, RJ, Brazil)[9,11].

Drug administration

The drug amitriptyline hydrochloride, in salt form, was administered daily intraperitoneally, diluted in neutral saline in a volume of 1 mL/kg. After the CDMP model induction, the

animals assigned to AMITRIP group underwent 26 days of treatment with AMITRIP (10 mg/kg/day - *Pharma manipulações*®, Lagarto, Sergipe, Brazil). The animals in AMC group received neutral saline during the same treatment period as the AMITRIP group[29,30].

Resistance training protocol

The animals in the RT and RTC groups underwent 5 days of acclimatization for 10 minutes a day, in a resting position, on the RT apparatus proposed by the study[31]. The animals were stimulated to perform the exercise using an electrode placed on the tail and connected to an electrical stimulator (IBRAMED®, Amparo, SP, Brazil). The electrostimulation parameters were 20V, lasting 0.3s at 3s intervals[32,33]. The RT and RTC groups were subjected to a One Repetition Maximum (1RM) Test, which consists of determining the maximum weight lifted by the rat on the apparatus. The 1RM test was repeated every two weeks to maintain training intensity and record muscle strength progression. The animals were exercised 3 times a week, on alternate days, for 4 weeks. The RT protocol consisted of 3 sets of 10 repetitions with a 90-second interval between sets, using 40% of the intensity established by the 1RM test[34]. The RTC group underwent tail electro-stimulation at a similar intensity and interval to the RT group, but without physical effort.

Mechanical paw withdrawal threshold

The mechanical paw withdrawal threshold was measured using a digital analgesimeter (von Frey) (Insight®, Ribeirão Preto, SP, Brazil). Initially, the animals were acclimatized to the mechanical sensory threshold test for 5 days, for 30 minutes. For evaluation, the stimulus was applied three times to the hind legs of each animal until it made the movement of withdrawing the paw upon stimulation. The average value of the three repetitions was defined as the mechanical paw withdrawal threshold, which was interpreted as mechanical hyperalgesia[9].

Locomotor activity

The distance covered and average speed were assessed using the activity monitor; the data was recorded using the Insight® software (Ribeirão Preto, SP, Brazil). The structure of the equipment consisted of a platform with infrared light sensors on the sides (Activity Monitor, Insight®, Ribeirão Preto, SP, Brazil), as well as an acrylic cube (34.5 cm high x 45 cm deep x 45 cm wide, EP 149, Insight®, Ribeirão Preto, SP, Brazil), which prevented the animals from leaving the instrument. Thus, each animal was placed individually in the equipment, where they remained for a period of 5 minutes and their movements were recorded and analyzed[35].

Statistical analysis

Values are expressed as mean ± standard error. The Shapiro-Wilk test was used to assess the normality of the sample for each variable. The t-test for independent samples was used to assess the mechanical paw withdrawal threshold and locomotor activity at pre-induction and post-induction times. The ANOVA variance test for repeated measures and Tukey's post-test were used to evaluate the moments before, during and after treatment. One-way ANOVA was used to analyze muscle strength. Values were considered statistically significant when $p<0.05$. The GraphPad Prism statistical program version 8.0 (GraphPad Software®, San Diego-CA, USA) was used for all these procedures. The effect size (d) was calculated according to the formula proposed by Cohen[36].

RESULTS

Chronic diffuse muscle pain model

After a double intramuscular injection of acid saline, there was a significant decrease in the withdrawal threshold of the contralateral paw (figure 1A) and the ipsilateral paw (figure 1B) when the pre-treatment moment was compared with the baseline moment in all the experimental groups ($p<0.0001$). This decrease in the paw withdrawal threshold was interpreted as mechanical hyperalgesia.

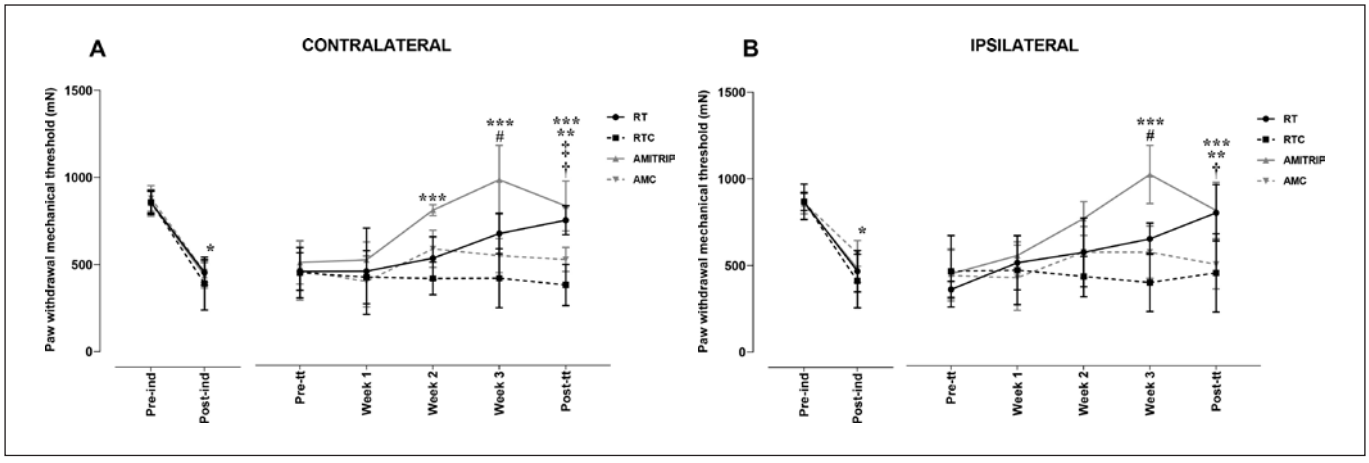

Figure 1. Mechanical withdrawal threshold of the contralateral (A) and ipsilateral (B) paw (in mN) for the animals in the study groups.

RT = Resistance Training; RTC = Resistance Training Control; AMITRIP = Amitriptyline; AMC = Amitriptyline Control; IND = induction; TTO = treatment; *p<0.05 difference between pre- and post-induction of all groups; **p<0.05 in relation to pre-treatment of TR group; ***p<0.05 in relation to pre-treatment of AMITRIP group; †p<0.05 difference between TR and CTR groups; ‡p<0.05 difference between AMITRIP and AMC group; #p<0.05 difference between TR and AMITRIP group. Data are presented as mean ± standard error of the mean. RT, TRC, AMITRIP AMC at pre-induction (before the first acid saline injection), pro-induction (after DCMD induction), pre-treatment, every week of treatment and post-treatment. At pre- and post-induction (independent samples t-test) and pre-treatment, weeks and post-treatment (two-way ANOVA for repeated measures, followed by Tukey's post hoc).

Mechanical hyperalgesia

In the analysis between the groups, a higher mechanical withdrawal threshold was observed in the contralateral paw (p=0.0011) and ipsilateral paw (p=0.0271) in RT group compared to the RTC group after treatment. A higher mechanical threshold was also observed post-treatment in the AMITRIP group compared to the AMC in the contralateral paw (p=0.0206), but not in the ipsilateral paw (p=0.0879). However, there was no post-treatment difference between the RT and AMITRIP groups in both paws (p>0.05). Only in the third week did the AMITRIP group show a higher mechanical withdrawal threshold in the contralateral paw (p=0.0190) and ipsilateral paw (p=0.0112), when compared to the RT group.

Comparing pre- and post-treatment, there was a significant increase in the withdrawal threshold of the contralateral paw (p=0.0345) and the ipsilateral paw (p=0.0006) in the RT group and AMITRIP group for the contralateral (p=0.0098) and ipsilateral paws (p=0.0140). In addition, there was an increase in the mechanical withdrawal threshold of the contralateral paw in the second (p=0.0270) and third (p<0.0001) weeks and the ipsilateral paw only in the third week (p<0.0001) when compared to pre-treatment in AMITRIP group.

The RTC and AMC groups showed no significant difference in the intragroup and intergroup analyses. The reference values for the contralateral paw were: Interaction: F (12, 100) = 3.617, p=0.0002. Time factor: F (4, 100) = 11.05, p<0.0001. Group factor: F (3, 100) = 28.86, p<0.0001. The reference values for the ipsilateral paw were Interaction: F (12, 100) = 3.539, p=0.0002; Time factor: F (4, 100) = 9.897, p<0.0001; Group factor: F (3, 100) = 17.66, p<0.0001. In the intergroup analysis of the effect size at the post-treatment moment, when the RT and RTC groups were compared, a value of 3.14 was obtained in the contralateral paw, while 1.53 was obtained in the ipsilateral paw, values classified as "very large". Similarly, the effect size values were classified as "very large" when AMITRIP and AMC groups were compared, both in the contralateral paw (4.44) and in the ipsilateral paw (2.18).

Motor movement

Distance covered

After induction of the CDMP model, there was a decrease in the distance walked in all groups when comparing post-induction with pre-induction (p<0.0001 - figure 2A). In the analysis between groups, there was no difference between the groups evaluated at any of the measurement times (p>0.05). In the intra-group analysis, no significant difference was observed when comparing pre-treatment in the weeks 1, 2, 3 and post-treatment (p>0.05). Interaction factor: F (12, 100) = 0.6678; p=0.7783. Time factor: F (4, 100) = 1.694; p=0.1573. Group factor: F (3, 100) = 1.717; p=0.1683.

Average speed

As with the distance traveled, a reduction in average speed was observed (p<0.0001) in all groups 24 hours after the second acid saline injection when compared to pre-induction (figure 2B). In the analysis between the groups for the pre-treatment (week 1, week 2, week 3) and post-treatment moments, no significant difference could be observed in the average speed (p>0.05). In the analysis between the groups for the pre-treatment (week 1, week 2, week 3) and post-treatment moments, no significant difference could be observed in the average speed (p>0.05). Similarly, in the intra-group analysis, there was no significant difference when all the moments were compared (p>0.05). Interaction factor: F (12, 100) = 0.6371; p=0.8059. Time factor: F (4, 100) = 1.449; p=0.2236. Group factor: F (3, 100) = 1.727; p=0.1664.

Muscle strength

A significant difference in muscle strength was observed between RT and RTC groups during (p=0.0002) and after treatment (p=0.0004 - figure 3). In the intra-group analysis, a statistically significant increase in strength was noted in TR group both during the treatment period (p<0.0001) and post-treatment (p<0.0001), when compared to pre-treatment. In addition, a significant increase in strength was observed during treatment compared to the pre-treatment measure in RT group (p=0.0024). The effect size values in the intergroup analysis at the post-treatment time point were classified as "very large" (2.78).

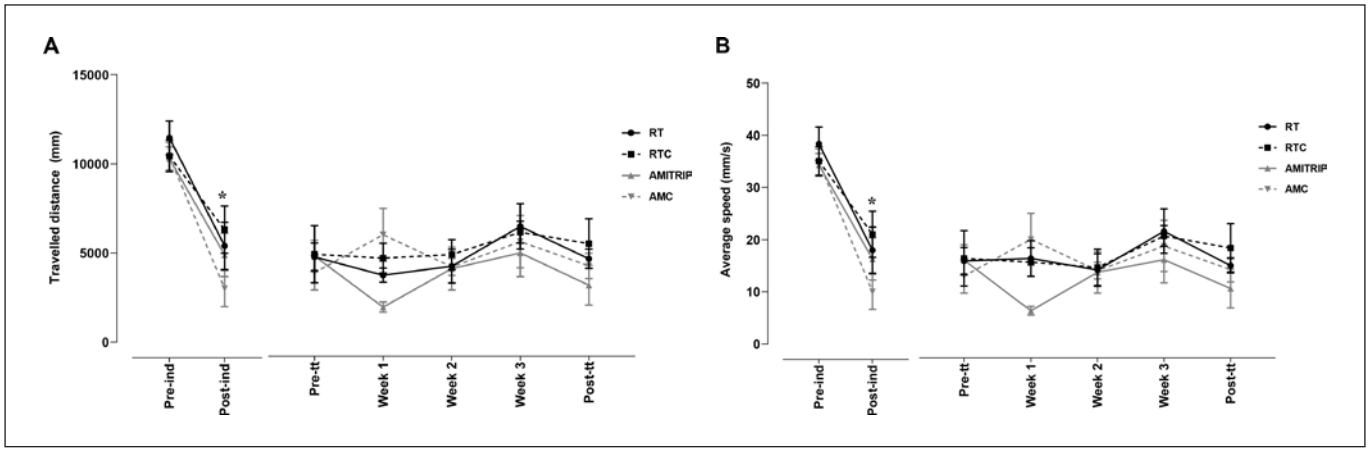

Figure 2. Locomotor activity in terms of distance traveled (A) (mm) and average speed (B) (mm/s) for the animals in the study groups.

RT = Resistance Training; RTC = Resistance Training Control; AMITRIP = Amitriptyline; AMC = Amitriptyline Control; IND = induction; TTO = treatment; *p<0.0001 difference between pre- and post-induction. Data are presented as mean ± standard error of the mean. RT, TRC, AMITRIP AMC at pre-induction (before the first acid saline injection), pro-induction (after DCMD induction), pre-treatment, every week of treatment and post-treatment. At pre- and post-induction (independent samples t-test) and pre-treatment, weeks and post-treatment (two-way ANOVA for repeated measures, followed by Tukey's post hoc).

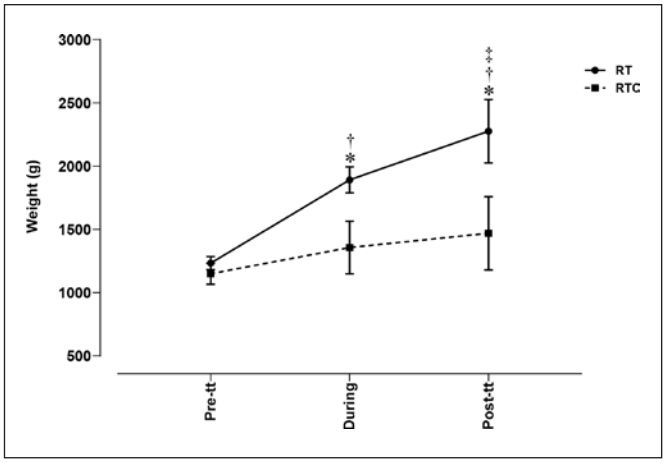

Figure 3. Muscle strength of the hind limbs of the animals in the groups studied.

RT = Resistance Training; RTC = Resistance Training Control; AMITRIP = Amitriptyline; AMC = Amitriptyline Control; IND = induction; TTO = treatment; *p<0.0001 difference between pre- and post-induction; *p<0.05 difference between TR and CTR groups, †p<0.05 in relation to pre-treatment in the TR group, ‡p<0.05 in relation to during in the TR group. Data are presented as mean ± standard error of the mean. Data are presented as mean ± standard error of the mean. RT and CTR at pre--treatment (after DCMD induction), during treatment (two weeks after starting treatment-D21) and post-treatment (after long-term treatment). One-way ANOVA for intra-group analysis and independent samples t-test to evaluate between groups.

DISCUSSION

This study showed that low-intensity resistance training, performed at 40% of the maximum load three times a week for four weeks, reduced mechanical hyperalgesia and increased muscle strength in rats submitted to the CDMP model. Studies evaluating the effects of physical training in the CDMP model are still scarce. This was the first experimental study to investigate the effects of RT as a treatment tool on mechanical hyperalgesia in animals with CDMP.

After 4 subsequent weeks of RT, there was an increase in the mechanical paw withdrawal threshold in the exercised group. In contrast, the animals allocated to RTC group remained with a low amount of physical activity throughout the protocol, as they did not move against resistance generated by an external load, but only received electrostimulation. Thus, the animals in the RTC group showed mechanical hyperalgesia, which was maintained until the end of the protocol, suggesting that there was no antinociceptive effect.

Physical inactivity can be a predictor of the chronic pain development. According study[37], sedentary animals are more likely to develop mechanical hyperalgesia when compared to animals that perform physical activity on running wheels. These authors suggested that increased expression of the serotonin transporter (SERT) affects sedentary animals and is associated with an increased likelihood of developing chronic pain. On the other hand, physically active animals express less SERT protein.

As was found in the RT group, a reduction in mechanical hyperalgesia was also seen in the group that used the tricyclic drug amitriptyline. In previous studies, long-term use of amitriptyline was able to attenuate mechanical hyperalgesia in animal models of neuropathic pain[29,30]. In clinical practice, amitriptyline is a drug prescribed to reduce pain and symptoms associated with fibromyalgia[19,38]. However, it is important to note that its chronic use can lead to adverse effects such as drowsiness, constipation and palpitations[20].

Thus, it is worth pointing out that the benefits of RT observed in people with fibromyalgia are already consolidated in scientific literature[12]. However, experimental research needs to be carried out in order to investigate the mechanisms by which RT promotes these adaptations in the model that mimics fibromyalgia. In this sense, this study initially investigated whether RT resulted in an improvement in hyperalgesia and motor responses in animals with CDMP.

In aerobic training, the authors[26] showed that the opioidergic pathway is involved in reducing mechanical hyperalgesia in the CDMP model. In addition, another study[39] showed that moderate-intensity aerobic exercise reduced mechanical hyperalgesia in the CDMP model, associated with an increase in neutrophin-3 levels in the gastrocnemius muscle after 3 weeks of training. The increase in endogenous opioids and neurotrophin-3 may be associated with the treatment and prevention of the development of mechanical hyperalgesia in this model[26,39].

It is suggested that the activation of opioid receptors, as well as the increase in neutrophin-3 levels, may be involved in the mechanisms that reduce the mechanical hyperalgesia observed in the RT protocol in question. Even though they are exercise modalities with different characteristics, such as movement execution and energy pathway, aerobic exercise and RT promote antinociceptive effects, helping in the treatment of CDMP.

The RT model used in this study uses electrostimulation as a stimulus to produce movement through negative reinforcement behavior[40]. In turn, this can cause neurobiological changes due to exposure to stress, resulting in aversive effects on animals [39,43]. In the present study, this resource was used in both the RT and RTC groups. It was observed that the effects of RT were greater than the stress caused by electrostimulation.

In addition to reducing mechanical hyperalgesia, this study showed that low-intensity RT was able to increase muscle strength in rats with CDMP. Similarly, previous studies using the same RT method observed both an increase in muscle strength and hypertrophy of the animals' hind limbs[31,41]. It is worth noting that to date no study has evaluated the muscle strength of animals submitted to RT in the CDMP model.

Exercises performed with significant overloads can promote pain exacerbation in people with fibromyalgia[21,22]. Thus, adjusting the intensity can be a crucial factor when prescribing RT for this population, and can optimize the positive effects of this training. In addition, it has been shown that RT promotes neuromuscular adaptations regardless of intensity, but the extent of adaptation is inherent to intensity[42].

Despite the improvements obtained in the muscle strength of the animals with CDMP, it was not possible to observe an improvement in motor displacement. As for the locomotor activity, after a double injection of acid saline, all groups showed a

reduction in distance and speed traveled. Despite the benefits observed in reducing mechanical hyperalgesia and increasing muscle strength, this RT method did not improve the animals' spontaneous activity. It is worth noting that the RT model used in this study resembles a squatting condition commonly used by humans. However, performing movements only with the hind limbs of the animals submitted to this protocol may explain the lack of improvement in locomotor activity.

Nevertheless, the movement that mimics squatting in humans is not functionally similar for the quadruped animal. It is important to note that the test used in this study to assess motor displacement involves functional activity of both the hind limbs and the forelimbs. However, as observed in this study, increasing the isolated muscle strength of the hind limbs in animals with CDMP did not improve functionality.

Therefore, it is suggested that experimental RT studies involving both the anterior and posterior limbs, such as the stair climbing model, should be used in order to assess, in addition to hyperalgesia and muscle strength, the functional capacity of animals with CDMP[39]. In addition, combining RT with aerobic exercise could maximize the beneficial effects in the CDMP model, since the anti-hyperalgesic effects of aerobic exercise on the skin and muscles in the CDMP model have already been consolidated in the literature[39].

RT prescription has been an important tool in the treatment of fibromyalgia[12]. However, research into the physiological mechanisms associated with resistance training in this pain model is still needed, with the aim of correlating the main pain modulation pathways and possible neurotransmitters involved in the spinal and supraspinal areas activated by RT.

As seen in this study, the use of RT and amitriptyline showed beneficial adjustments for the treatment of the dysfunctions present in the experimental CDMP model. However, a limitation of this study was the lack of a group that associated RT with the use of amitriptyline, since comparing this group with the groups that only underwent one of the treatments could provide information on the possible maximization of the antinociceptive effects seen in this pain model. Another limitation of this study was the absence of relative strength, which could reinforce the efficiency of RT.

As future perspectives, this research suggests evaluating different models and intensities of RT and investigating the descending inhibitory pain pathways that can elucidate the mechanism of action of the CDMP treatment through RT. A possible target is the investigation of opioidergic and serotoninergic mechanisms.

CONCLUSION

Low-intensity RT had anti-hyperalgesic effects and improved muscle strength in animals submitted to the CDMP model. On the other hand, there was no improvement in the animals' functional capacity. This study suggests that investigating other exercise modalities and intensities could also be beneficial in this model. Moreover, it is also important to emphasize the importance of developing experimental research into the mechanisms by which RT improves symptoms in this model, with the aim of providing a solid base of physiological knowledge and identifying doses of exercise that allow for a targeted chronic diffuse muscle pain treatment.

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AUTHORS' CONTRIBUTIONS

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Statistical Analysis, Data Collection, Resource Management, Project Management, Research, Methodology, Writing - Preparation of the Original, Writing - Review and Editing
Mônica Deise dos Santos Rocha
Data Collection
Mateus Maciel Santos
Data Collection
Josimari Melo DeSantana
Resource Management, Project Management, Research, Methodology, Writing - Review and Editing, Supervision

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