Swimming training and functional assessment of sciatic nociception in rats

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ABSTRACT

Introduction: The protective effect of exercise on individuals with peripheral neuropathy is controversial. Objective: To assess the influence of physical training of moderate and progressive intensity on nociception of rats in an experimental sciatica model. Materials and Methods: The study assessed 18 rats divided into the following three groups: control group (CG); low-intensity swimming group (LISG); progressive-time swimming group (PTSG). To meet the physical training protocol, the animals were placed in a water tank for six weeks, three alternate days per week. In LISG group, the animals swam ten minutes per session, and, in PTSG group, the animals began swimming for ten minutes, and had a ten-minute increase per week. In CG group, the animals swam less than one minute per day, only to get used to the water environment. After finishing the swimming training, the experimental sciatica model protocol was started with constrictive ligature of the sciatic nerve with chromic catgut. Nociception was assessed using the functional disability test, which measures, in a one-minute interval, the time during which the animal holds its hind paw (THHP) in a guarded position. Assessments were performed preoperatively, and on the third, sixth, and tenth post-operative (PO) days. Results: All groups showed a significant increase in THHP on third, sixth, and tenth PO days, as compared to preoperative values. In CG, no significant change was observed in PO assessments, unlike what happened in LISG and PTSG groups. Conclusion: Exercise produced greater hyperalgesia.

Keywords: exercise, pain measurement, swimming.
fractures due to compression, lumbar stenosis and degenerative diseases, which may cause sciatic pain. Sciatic pain is most commonly caused by disc hernia with nerve root compression, but other possible causes include lumbar or foraminal stenosis; tumors or cysts; osteophytes; hematoma; prolonged external pressure; and piriformis syndrome. The following can be considered predictive factors for sciatic pain: heavy labor tasks; obesity; smoking; little leisure physical activity; low back pain; and cervical spine pain.

Bigos et al., in a systematic review, have reported that only interventions consisting in exercise practice were effective for preventing episodes of low back pain, while others, such as psychological support, insoles, orthoses, ergonomic education, and weight reduction, had no success in preventing those episodes. The authors have reported that the reasons for exercise success are not clear, but general benefits may exist, in addition to the specific ones, such as the increase in strength, resistance, and flexibility. Kuphal, Fibuch, and Taylor have reported that swimming training reduced neuropathic nociception in animals, but showed no preventive effect on it. However, according to Claydon, there are no adequate randomized clinical trials showing that either exercise or physical activity are beneficial for peripheral neuropathy. Several effects of physical exercise on low back pain have been reported in literature. However, reports on the effects of physical exercise on sciatic pain are still lacking. Therefore, the aim of this study was to evaluate the influence of moderate and progressive physical training on nociception in rats subjected to an experimental sciatica model.

MATERIALS AND METHODS

Sample and experimental groups
This study assessed 18 Wistar rats (mean weight, 412.60 ± 49.27 g) from the central vivarium of the Universidade Estadual do Oeste do Paraná (Unioeste), maintained in polypropylene cages, with free access to water and food, and controlled 12-hour light/dark cycle and room temperature (24 ± 1°C). The study was conducted according to the international ethical guiding for animal experimentation, and approved by the Animal Experimentation Ethics Committee of Unioeste.

The animals were randomly divided into the following three groups:

- Control group (CG, n = 6): animals undergoing swimming training (less than one minute per session) and an experimental sciatica model protocol;
- Low-intensity swimming group (LISG, n = 6): animals undergoing swimming training (ten minutes per session) and an experimental sciatica model protocol;
- Progressive-time swimming group (PTSG, n = 6): animals undergoing swimming training with progressive time increase and an experimental sciatica model protocol.

Swimming training protocol
For swimming training protocol, the animals were placed in a water tank of 200-L capacity, 60-cm depth, and water temperature between 30°C and 32°C. All animals underwent swimming training for six weeks, three alternate days per week. In LISG, the animals swam ten minutes per session. In PTSG, the animals began swimming for ten minutes, had a ten-minute increase per week, and ended up swimming for 60 minutes by the sixth week. In CG, the animals swam less than one minute per day, only to get used to the water environment.

Experimental sciatica model protocol
One day after finishing the swimming training, the experimental sciatica model protocol was started. The animals were anesthetized with xylazine (12 mg/kg) and ketamine (95 mg/kg). After local epilation, an incision was performed into the middle third of the right thigh parallel to the fibers of the femoral biceps muscle of animals, exposing the sciatic nerve. Constrictive ligature of the sciatic nerve was performed using chromic catgut 4.0 thread in four distinct points, at an approximate 1-mm distance, according to the experimental model originally described by Bennett and Xie.

Nociception assessment
The test of functional disability comprised a computer program and a moving metallic cylinder of 30-cm diameter, covered with a stainless steel net, with connection to a metallic boot adapted to the animal’s hind paw, originally described by Tonussi and Ferreira. The animals walked over the cylinder, which performed three rotations per minute powered by an electric motor. The hind paws received metallic boots. The right metallic boot conducted information from the right paw, through a wire, to a computer. The computer ran a program that measured the time during which the animal held its hind paw (THHP) in a guarded position when walking over the cylinder for one minute. The left metallic boot provided no input to the computer.

At the end of the swimming phase, the animals underwent adaptation to the metallic cylinder. On the following day, their time for normal walking was measured. Then, constrictive
ligature of sciatic nerve was performed, and all animals had their THHP measured on the third, sixth, and tenth post-operative (PO) days. Usually, animals with no changes hold their hind paws in a guarded position for approximately ten seconds, and those with reduced nociceptive threshold due to sciatic compression hold them longer.20-22 All animals of the three groups were assessed on the same days.

Analysis of results

The results were assessed by use of repeated-measures and unidirectional analysis of variance (ANOVA) for intra- and intergroup analyses, respectively. The 5% significance level was adopted for both tests.

RESULTS

The CG group showed a significant increase in THHP on the third, sixth, and tenth PO days when compared with the preoperative values (Figure 1A), but no significant difference between the values on the third, sixth, and tenth PO days was seen.

The LISG group, similarly to the CG, showed a significant increase in THHP at all measurements after surgery. However, when comparing the PO measurements between themselves, a significant increase was observed in THHP of the sixth and tenth PO days as compared to that of the third PO day. However, the THHP of the tenth PO day showed a significant decrease as compared to that of the sixth PO day (Figure 1B).
The PTSG group had results similar to those found in LISG group (Figure 1C).

When comparing the groups, a significant difference could only be observed on the sixth PO day between CG and LISG, whose values were higher. No other significant differences were observed.

**DISCUSSION**

In the athletic population, most cases of low back pain have a mechanical origin, and it is believed to be related to muscle strains or injury to the spinal ligament structures. However, disc hernia, compression fracture, lumbar stenosis, and degenerative diseases can occur in older athletes, while spondylolysis is common in younger athletes. Such lesions are more severe and can produce pain along the sciatic nerve path.

Several physical activities, such as gymnastics, ballet, water sports, weight lifting, running, golf, and baseball, can predispose to lesions in the vertebral disc, being, thus, possible causes of sciatic pain. Ong, Anderson and Roche have assessed the prevalence of lumbar disc degeneration in elite athletes during the 2000 Olympic Games. The authors reported that the athletes showed, on magnetic resonance imaging, a progressive reduction in the intensity of the disc signal towards the caudal segment, in addition to significant degenerative changes in L5-S1, of which, disc protrusion and hernia were the most prevalent. When comparing with changes seen in a non-athletic population, elite athletes have a higher prevalence and intensity of lumbar disc degeneration. Thus, analyzing the effect of physical exercise on one symptom of disc hernia (sciatic pain) is important. The present study aimed at assessing whether physical activity influences nociception resulting from sciatic nerve compression.

Lumbosacral radicular syndrome, also called sciatica, is characterized by irradiating pain in one or more dermatomes, which can be accompanied by phenomena such as nerve root tension and neurologic deficits. There is evidence that the pain is inflammatory, due to the presence of phospholipase, arachidonic acid, and cytokines, mainly TNF-α. Thus, activities that increase or reduce the release of inflammatory mediators, such as physical exercise, may influence the pain originating from sciatic nerve compression.

According to Bennett and Xie, the pain in the experimental model of sciatic nerve compression with chromic catgut thread begins on the second PO day and reaches its maximum from the tenth to the 14th PO days, disappearing after the second month, and remaining only as hypoesthesia. This experimental model simulates nerve compression, similar to what occurs in disc hernia. Thus, the present study assessed nociception in a functional way on the third, sixth, and tenth PO days, corresponding to the period the animal experiences pain.

After performing nerve compression, the animals experience hyperalgesia, evidenced by changes in their gait and prolonged THHP (over ten seconds). This was observed in the present study because, prior to nerve injury, the THHP measurements were close to ten seconds, but increased significantly in all assessments after that.

Neuropathic pain, i.e., pain induced by an injury to the nervous system, may occur due to abnormal ectopic excitability on or near the site of nerve injury, or to nerve sprouting with abnormal discharge and excitability. The possible mechanisms include the unusual distribution of Na⁺ channels, abnormal responses to cytokines and other inflammatory mediators, in addition to attenuation of central inhibitory mechanisms of pain.

THHP assessment showed that the animals that underwent swimming training had a significant increase in nociception on the sixth and tenth PO days, which was not observed in CG. The exercised muscle can release IL-6, which is paradoxical: although it is associated with glucose regulation, stimulates the proliferation of myoblasts and satellite cells, and promotes angiogenesis, IL-6 is also elevated in the presence of muscle hypertrophy. This is also seen with IL-1 and TNF-α, despite controversies regarding the increase in IL-6 after exercise. However, it is worth noting that, in the present study, the animals underwent physical exercise before lesion induction, but not during the PO period, thus, the above-cited influences were probably not felt.

Moreover, according to Pedersen, the exercised muscle releases cytokines, called myokines, which play a role in protection against diseases of inactivity. However, the IL-6 produced by muscle contraction is not related to the activation of pro-inflammatory paths, but acts as sensor of energy (glycogen content). Thus, physical exercise would act as an anti-inflammatory agent, as it does not increase TNF-α and IL1-β (pro-inflammatory), but anti-inflammatory cytokines and inhibitors of other pro-inflammatory cytokines.

Kuphal, Fibuch and Taylor, assessing the nociceptive threshold after injuring the sciatic nerve of rodents, have reported that physical training with swimming caused a reduction of alldynia and hyperalgesia in animals. However, exercising seven days before the injury has not prevented the reduction in the nociceptive threshold originating from nerve injury. In
the present study, after the moment of greatest nociception (sixth PO day), the groups that exercised showed a significant reduction in nociception on the tenth PO day, whose values, however, were significantly higher than those on the third PO day. This shows the worse evolution of the groups trained as compared to that of the CG, even in the absence of a significant difference between the groups, except for that between the CG and LIGS on the sixth PO day.

One limitation of this study was the lack of assessment of inflammatory markers, which can be the subject of further studies.

CONCLUSION
In conclusion, in the experimental sciatica model, physical exercise had a negative influence on nociception, that is, it produced more hyperalgesia than in CG.
REFERENCES


