J Korean Soc Phys Med, 2020; 15(1): 43-54
https://doi.org/10.13066/kspm.2020.15.1.43

Online ISSN: 2287-7215
Print ISSN: 1975-311X

Research Article

Open Access

Effects of High-Intensity Interval Training on Motor Skills Recovery in Sciatic Nerve Crush-Induced Rats

Ki-Hyun Kim, PT, PhD · Hyung-Soo Shin PT, PhD · Nam-Jin Jung PT, PhD · Gak Hwangbo, PT, PhD[1†]

Department of Physical Therapy, Kyungwoon University
[1]Department of Physical Therapy, Daegu University

Received: November 26, 2019 / Revised: December 2, 2019 / Accepted: January 3, 2020

| Abstract |

PURPOSE: This study examined the effects of mild-intensity exercise (MIE) and high-intensity interval exercise (HIIE) on the recovery of the motor function over time in sciatic nerve crush injury rats.

METHODS: The MIE group ran on a treadmill at a speed of 8.3 m/min to perform low-intensity training with maximum oxygen uptakes ranging from 40 to 50%. The HIIE group ran on the treadmill at a speed of 25 m/min to perform high-intensity training with a maximum oxygen uptake of 80%. The interval training was performed based on a 1:1 work-to-rest ratio. The effects of each form of exercise on the rats' walking abilities following their recovery from the peripheral nerve injuries were evaluated based on the results of behavior tests performed at one and 14 days.

RESULTS: According to the test results, the MIE group showed significant improvements in the rats' ankle angle in the initial stance phase, and in the ankle and knee angles in the toe-off phase ($p<.05$). The HIIE group exhibited significant improvements in the ankle and knee angles in the initial stance phase, SFI($p<.05$).

CONCLUSION: The state of such patients can be improved by applying the results of this study in that MIE and HIIE on a treadmill can contribute to the recovery of the peripheral nerve and motor skill. In particular, MIE is used as a walking functional training in the toe-off stance phase, while HIIE is suitable in the initial stance stage.

Key Words: Sciatic nerve injury, High-intensity interval training, Motor skills recovery

Ⅰ. Introduction

Peripheral nerve injuries can result in serious health problems, as well as causing physical disability for life and social problems by diminishing the productivity of working age adults [1,2]. Peripheral nerve injures are common clinically and are caused by a range of factors, such as traumatic injuries, penetrating injury, crush, metabolism diseases, infection, and tumors. In the arms, these injuries generally manifest as damage to the radial

본 논문은 김기현(2018)의 박사 학위 논문의 요약본임.

†Corresponding Author : Gak HwangBo
hbgak@daegu.ac.kr, https://orcid.org/0000-0001-9762-1820

nerve, ulnar nerve, or median nerve. In the leg, acetabular fractures and dislocation injuries are typically associated with many sciatic, femoral, and peroneal nerve injuries [3].

A sciatic nerve injury is caused by lengthening or crushing. Most traumatic neuropathy can occur at work, traffic accidents, and even at home. This happens frequently in young men after traffic accidents [4-6]. In addition, such an injury can occur by inattention in medical intervention. In this case, iatrogenic trauma occurs by a total hip arthroplasty or surgery. Traumatic neuropathy is also caused by piriformis syndrome or a fracture of the femur, hip joint, or cotyloid joint [9].

Peripheral nerve injures cause damage to the muscle that is dominated by the distal nerve of the damaged area and atrophy of the muscle and fibrous tissue [10]. The recovery process of the cell body, proximal stump, and distal stump is complicated, depending on the degree of neurological damage. In cases of light damage, reproduction and recovery occur immediately after the injury [11].

The treatment of peripheral nerve injures can be divided into two types: invasive and noninvasive therapy. The former includes surgery, injection, and nerve block. Among them, surgery, such as direct repair, nerve transfer, and nerve grafting, is commonly used [12,13]. Direct repair can result in neuropathy and infection. In addition, the procedure has difficulty in reproducing the alignment of a small bunch. Nerve transfer has a restriction on the number and length of the provider's nerve but has a low effect on morbidity. Nerve grafting makes it difficult to reconstruct a nerve through a fibrin clot [14].

Noninvasive therapy includes drug treatment, electrotherapy [15], treadmill exercise [16], and hydrogymnastics [17]. The treadmill exercise for experimental animals with a sciatic nerve injury increases the reinnervation of the muscle and reproduces the axon with myelin [18]. Controlling intensity and time is important for effective treatment. According to a previous study, high-intensity exercise after axonotmesis has a better effect than low-intensity exercise, even in a shorter time [19].

High-intensity interval exercise (HIIE) means intermittent, anaerobic exercise. Compared to continuous exercise, HIIE has a greater impact on the autonomic nervous system [20,21].

Mild-intensity exercise (MIE), as an aerobic exercise, is recommended to stroke patients as an exercise to improve mobility, aerobic capacity, and cardiovascular system. On the other hand, HIIE is effective in nerve development, proprioceptive neuromuscular improvement, and the capacity related to gait speed [22]. HIIE also is effective in muscle strengthening and performance [23].

Studies focusing on the effects of HIIE in stroke, obesity, and diabetes have already been conducted, most of which focused on nerve development and muscle strengthening. In addition, many studies on the recovery of the peripheral nerve function in terms of intensity and time have already been done. Therefore, this study focused mainly on how HIIE assists in the recovery of injures to the peripheral nerves, particularly on motor skills.

Ⅱ. Methods

1. Experimental subjects and periods

In this study, six eight-week-old Sprague-Dawley white rats, weighing 250 to 300 grams, were used. During the experiment period, a temperature and relative humidity of 23±°C and 55±10%, respectively, were applied. The light and night cycles ranged from 8 a.m. to 8 p.m. and from 8 p.m. to 8 a.m, respectively. To minimize the impact of environmental changes, the rats were given one week of adjustment; breeding and experiments were conducted in the same environment. For breeding, cattle cake (Cargill Agri Purina Inc., Seongnam, Korea) and water were provided to the rats ad libitum. Using random sampling, the subjects that had an intentional injury to the sciatic nerve were divided into two groups through treadmill

Table 1. Numbers of Each Subject Group and Experimental Design (n=6)

Groups	N	Resting	Training
MIEG	3	3 days	2 weeks
HIIEG	3	3 days	2 weeks

MIEG: Mild-Intensity exercise group
HIIEG: High-Intensity Interval exercise group

intervention: mild-intensity exercise group (MIEG, n=3) and high-intensity exercise group (HIIEG, n=3). Before the intervention, the damage was checked thoroughly for three days. As the intervention, the MIEG conducted treadmill exercise for 30 min, once a day for two weeks, whereas the HIIEG performed the exercise for 10 min (Table 1).

2. Materials and Methods

1) Surgery for Sciatic nerve crush

When causing the sciatic nerve injures, a general anestheti, 1mg of tribromoethanol per 1kg, was injected into the abdominal cavity. After checking for anesthesia through an avoidance reaction to pain, the animal was fixed to the operating table. The right femur and the knee joint were shaved to analyze the sciatic nerve damage and gait. The muscle and fascia surrounding the sciatic nerve were separated from the sciatic nerve by making a 2cm long cut to the skin on the hip joint. The area was then pressed continuously for 30 seconds using hemostatic forceps (Crile) before ramifying into the tibial nerve and fibular nerve. The part was crushed after sterilization by alcohol and the hemostatic forceps was covered with soft plastic to prevent additional damage by the sharp forceps during the crush. The hemostatic forceps have three levels of strength control; the third level of pressure was applied during the crush.

A suture for the experimental animals was used; the area was disinfected to prevent infection. Three of each were separated into two standard plastic cages (290x 430x180mm) before the intervention. The environment of the breeding room was the same.

2) Dartfish program

A kinematic behavior test was conducted in a quiet room during the light cycle. Both the MIEG and HIIEG groups were tested using the Dartfish program (Pro Suite, Dfkorea, Korea) before and after the intervention (one and 14 days) to analyze the kinematic gate motion. The Dartfish program is software that can trace the motion of the subjects after recording their movement. Before recording, the greater trochanter of the hip joint, lateral epicondyle of the knee joint, and metatarsophalangeal joint of the little toe of the rats were marked with a black marker for video analysis after disinfecting the hip joint area of all subject rats using 70% alcohol and shaving. After marking, a recording was made as the rats walked through a transparent passage that was 10cm high, 100cm long, and 8cm wide. The rats were guided to reach a dark room that was placed at the end of passage. The result was measured by an average value after recording three attempts for each rat. The object distance was one meter, which recorded the sagittal plane with a 60Hz digital camera. The rats measured the angle of the knee joint and ankle joint of the sciatic nerve injures in the initial stance phase and the toe-off stance phase through the program. Only the video that shows the perfect gait cycle was used as the measured value. The intraclass correlation coefficient (ICC) of Dartfish had a reliability of more than 0.9 [24].

3) Sciatic functional index (SFI)

The SFI was measured in both groups of experimental animal rats on days 1 and 14 to determine the behavior of MIEG and HIIEG after the sciatic nerve crush. After wetting the soles of the experimental animals with ink, the foot was measured by placing it on white paper in a dark passage 10cm high, 50cm long, and 8cm wide. At the end of the experiment, the dark room was made to proceed in the straight direction. Each experimental animal performed the test three times, and the results were obtained as an average value. The following were measured for SFI analysis: the distance to the third toe (print length, PL), the distance between the first and fifth toes (toe spread, TS), and the distance between the second and fourth toes (intermediary toe spread, IT). The data were calculated using the arch nerve function index. Normal rats are close to zero and -100 in severely damaged rats [5]. The reliability of SFI was 0.82 at ICC [25].

SFI= (-38.3× PLF) + (109.5× TSF) + (13.3× ITF) - 8.8

PLF (print length factor)=(EPL−NPL)/NPL

TSF (toe spread factor)=(ETS−NTS)/NTS

ITF (intermediary toe spread facor)=(EIT−NIT)/NIT

E: experimental side

N: normal side

PL: distance from the heel to the third toe, the print length

TS: distance from the first to the fifth toe, the toe spread

IT: distance from the second to the fourth toe, the intermediary toe spread

3. Experimental managements

1) Treadmill exercise

A small treadmill for animals (JD-A-09 type, JEUNGDO Bio & Plant Co., Ltd., Korea) was used for the intervention in the current research, both the MIEG and HIIEG. The treadmill exercise was set to allow both groups to work the same amount, 250 meters. The MIEG performed exercise at 8.3 m per minute at a gradient of 0% for low-intensity exercise with a maximum oxygen uptake of 40-45%. The exercise time was 30 minutes per time to give a total exercise of 250 m. HIIEG performed exercise at 25 m per minute at a gradient of 0% for high-intensity exercise with a maximum oxygen uptake of 80%. For the same workout as the MIEG, the exercise was carried out for a total of 250 m-long exercise for ten minutes. The HIIG performed exercise using a one-minute workout and a one-minute break. The total amount of exercise and break was 20 minutes [26,27](Table 2).

The MIEG and HIIEG were given a one-day break after the crush damage on the sciatic nerve to check the degree of damage; the rats had an adaptation period of 15 minutes at a gradient of 0% with the speed of 8 m per minute for two days. The intervention period was limited to less than 30 minutes to minimize the adverse effects of stress and was conducted in the dark cycle, in which the rats were very active. The experiment was designed to give an electric stimulation of 10 volts to the bottom of the treadmill belt to induce continuous movement if the

Table 2. Experimental MIEG and HIIEG and the CG of the Intervention Program

Variable \ Groups	MIEG(n=3)	HIIEG(n=3)
Duration(weeks)	2	2
Gradient(%)	0	0
Intervention Time(min)	30	10
Speed (m/min)	8.3m/min	25m/min

MIEG: Mild-Intensity exercise group
HIIEG: High-Intensity Interval exercise group

Table 3. Results of the Pre Homogeneity Test (unit: °)

Variable \ Groups	MIEG	HIIEG	t	p
IC-A	65.75±1.81	64.73±2.73	.536	.621
IC-K	98.86±2.60	107.767±6.36	-2.240	.089
TO-A	57.58±2.67	62.68±4.96	-1.568	.192
TO-K	73.75±5.05	71.56±1.50	.718	.513
SFI	-87.24±16.83	-76.88±4.76	-1.026	.363

MIEG: Mild-Intensity exercise group
HIIEG: High-Intensity Interval exercise group
*: p<.05

Table 4. Results of Statistical Analysis of the Ankle Angle in Initial Contact (unit: °)

Ankle Angle in Initial Contact	1day	14day	t	p
MIEG	65.75±1.81	68.66±1.62	-5.559	.031*
HIIEG	64.73±2.73	73.36±.73	-4.846	.040*
t	.536	-4.560		
p	.621	.010*		

MIEG: Mild-Intensity exercise group
HIIEG: High-Intensity Interval exercise group
*: p<.05

experimental animal stopped working out during the intervention.

4. Statistical analysis

This study used SPSS for Windows (version 20.0) to analyze the data. An independent t-test was used to compare the results of the two groups, and a paired t-test was used to compare the effects between one day and 14 days after the intervention. The statistical significance level was set to α=.05.

Ⅲ. Results

1. Result of the pre homogeneity test

Six healthy male of Sprague-Dawley (eight weeks old, 250-300 g) were used as the experimental animals in this stud. The homogeneity test of the MIEG and HIIEG revealed, there was no significant difference in any of the variables (p>.05)(Table 3).

.

2. Statistical analysis of the ankle angle in the initial contact

The results before and after the MIEG intervention showed a significant increase from 65.75±1.81 to 68.66±1.62 (p<.05). The results before and after the HIIEG intervention showed a significant increase from 64.73±2.73 to 73.36±.73 (p<.05). No significant difference in the kinematic measurements was observed between the groups before and after the intervention (p>.05)(Table 4).

3. Statistical analysis of the knee angle in the initial contact

The results before and after MIEG intervention showed a decrease from 98.86±2.60 to 95.63±2.89, but the

Table 5. Result of Statistical Analysis of the Knee angle in the Initial Contact (unit: °)

knee Angle in Initial Contact	1day	14day	t	p
MIEG	98.86±2.60	95.633±2.89	1.551	.261
HIIEG	107.767±6.36	99.333±5.98	12.603	.006*
t	-2.240	-.965		
p	.089	.389		

MIEG: Mild-Intensity exercise group
HIIEG: High-Intensity Interval exercise group
*: p<.05

Table 6. Comparison of the Ankle Angle in Toe Off (unit: °)

Ankle Angle in Toe Off	1day	14day	t	p
MIEG	57.58±2.67	83.53±4.15	-6.600	.022*
HIIEG	62.68±4.96	65.23±2.72	-.689	.562
t	-1.568	6.377		
p	.192	.003*		

MIEG: Mild-Intensity exercise group
HIIEG: High-Intensity Interval exercise group
*: p<.05

difference was not significant (p>.05). The results before and after HIIEG intervention decreased significantly from 107.76±6.36 to 99.33±5.98 (p<.05). No significant difference in the kinematic measurements was observed between the groups before and after the intervention (p>.05)(Table 5).

4. Comparison of the ankle angle in toe off

The results before and after MIEG intervention showed a significant increase from 57.58±2.67 to 83.53±4.15 (p<.05). The results before and after HIIEG intervention showed an increase from 62.68±4.96 to 65.23±2.72, but the difference was not significant (p>05). No significant difference in the kinematic measurements was observed between the groups before and after the intervention (p>.05)(Table 6).

5. Result of statistical analysis of the knee angle in toe off

The results before and after the MIEG intervention showed a significant increase from 73.75±5.05 to 87.66±3.02 (p<.05). The results before and after the HIIEG intervention showed an increase from 71.56±1.50 to 79.70±3.50, but the difference was not significant (p>05). A significant difference in the kinematic measurements was observed between the groups 14 days after the intervention (p<.05)(Table 7).

6. Statistical analysis of SFI

The results before and after MIEG intervention showed a decrease from -87.24±16.83 to -49.67±9.16, but the difference was not significant (p>.05). The results before and after HIIEG intervention showed a significant decrease from -76.88±4.76 to -48.62±5.22 (p<05). No significant difference in the SFI measurements was observed between

Table 7. Statistical Analysis of Knee Angle in Toe Off (unit: °)

Knee Angle in Toe Off	1day	14day	t	p
MIEG	73.75±5.05	87.66±3.02	-9.957	.010*
HIIEG	71.56±1.50	79.70±3.50	-3.790	.063
t	.718	2.983		
p	.513	.041*		

MIEG: Mild-Intensity exercise group
HIIEG: High-Intensity Interval exercise group
*: p<.05

Table 8. Result of Statistical Analysis of SFI (unit: score)

SFI	1day	14day	t	p
MIEG	-87.24±16.83	-49.67±9.16	-2.711	.113
HIIEG	-76.88±4.76	-48.62±5.22	-6.564	.022*
t	-1.026	-.173		
p	.363	.871		

MIEG: Mild-Intensity exercise group
HIIEG: High-Intensity Interval exercise group
*: p<.05

the groups before and after the intervention (p>.05)(Table 8).

Ⅳ. Discussion

This study examined the effects of MIE and HIIE over time on the recovery of the motor skills of rats with sciatic nerve injury. The research evaluated how each exercise improved the gate function by the recovery of the peripheral nerves through a neurologic motor behavior test at the first and fourteenth day after damage from a sciatic nerve crush.

Treadmill exercise is a method used widely to recover the peripheral nerves, and according to the maximal oxygen uptake, low intensity (40-45% of the maximal oxygen uptake), medium intensity (65-70% of the maximal oxygen uptake), and high intensity (80% of the maximal oxygen uptake) are used to indicate the amount of exercise. Measurements of the maximum oxygen uptake of rats using the metabolic rate meter revealed 82% a maximum oxygen uptake at a speed of 28.5m/min and 16m/min of 82% and 67%, respectively [28]. In Bedford's study, the treadmill speed was 40-45%, 65-70%, and 80% of the maximum oxygen intake at 8m/min, 16m/min, and 24m/min, respectively [29]. High-intensity exercise is an exercise that is equal to or higher than the maximum oxygen uptake. This is a time-efficient method to improve the cardiopulmonary health of healthy people [30]. In addition, high-intensity exercise after axon cutting may be effective in a shorter time than low-intensity exercise [19].

Large damaged fibers are affected more by motor paralysis, proprioception, and tactile loss than small fibers. A favorable prognosis of the nerve function and remyelination is possible, even after a few days or weeks if there is no nerve block and axonal degeneration on the further area [31,32].

Three recovery mechanisms occur after peripheral nerve damage: remyelination, side-germination from a preserved axial fiber, and reconstruction of the damaged area [33]. From 24 to 36 hours after the damage, regenerative germination of the axon begins from the body nerve stumps and penetrates the area of damage. Recovery could vary according to the extent of the damage, cicatrization, the close degree of both damaged areas, and the patient's age [34]. The damage of the peripheral nerve block results in ischemia and demyelination. Demyelination results in a leak in the flow to the next Ranvier node, which extends the Ranvier node slowing the speed of stimulus conduction [35]. This is not because the conduction of demyelinated nerves is reduced like unmyelinated normal nerves, but because there are fewer sodium channels between the branches of those nerves with myelin [34]. Reinnervation of the target organ may take months, depending on the distance from the damage. Reconstruction of the connection with the nerve root depends on the response between the basic composition of the muscle fiber and the axon being regenerated [31].

The functional recovery of nerve regeneration plays an important role in the recovery of the neuromere, far from the damaged area and reinnervation. For regenerative germination of an axon, the ability of nerve regeneration should be strengthened through external stimulation. Retrogressive degeneration, the damage of the cyton and incorrect reinnervation, adversely affect the recovery of the peripheral nerve, which restricts delicate motor regulation [36,37]. In this study, the angles of the ankle and knee increased between the first and fourteenth days, which means that appropriate therapy needs to be applied for neurotization, reinnervation, and functional recovery of complicated peripheral nerve. In addition, this research is in line with a previous study in which the axon is effectively connected by external stimulation [38]. Therefore, functional recovery is possible by promoting neuronal recovery through treadmill exercise.

According to the exercise methods of respective groups, the result of the angle of ankle and knee in the initial stance phase and the toe-off stance phase showed a larger increase in the angles of the ankle and knee of the HIIEG in the initial stance phase than those of the MIEG. In contrast the angle of ankle and knee of the MIEG increased more in the toe-off stance phase than those of the HIIEG. This showed that MIE is effective in recovering the walking function in the initial phase; HIIE is effective in the toe-off stance phase. This is because, under the observation of muscular activation in the gait cycle, it could be related to many muscular contractions at the tibialis anterior muscle in the initial phase and those at the soleus muscle in the toe-off stance phase [39]. The type I and II muscle form prevails in the soleus muscle and tibialis anterior muscle, respectively [40]. Therefore, continuous MIE is effective in walking function training in the toe-off stance phase; HIIE is effective in the initial stance phase. This is consistent with the results of a previous study in which the exercise intensity affects the recovery depending on the form of the muscle fiber, in the case of HIIE, the activity of PGC-1α increases in the fast twitch muscle [41]. HIIE, which repeats exercise and breaks during recovery, was reported to affect the facilitating proprioceptive neuro muscle and nerve development and improve the gait speed and functions [22]. HIIE is believed to be effective in increasing muscular strength and performance [23].

Muscles under distal nerve domination in the early stages of a peripheral nerve injury are injured, and fibrous tissue and muscle atrophy appear to reduce the joint angle [10]. In particular, damage to the tibial nerve, the common peroneal nerve, etc., due to the damage to the hips, resulted in atrophy in the muscles of the hamstring muscle, adductor magnus muscle, lower legs, and feet. This results in weakness of the hip extensor, foot drop, inversion, and eversion [42]. In the motor function, the stance phase and swing phase movement patterns are changed, and the range of motion of the knee and ankle joints is decreased [43,44]. In addition, owing to the weakening of the muscles around the knee and ankle joint, the angle could be reduced due to an insufficient rotational force. In general, a peripheral nerve injury is believed to result in abnormal gait patterns caused by neurological pain symptoms, such as spontaneous pain and hyperalgesia [15]. In addition, muscle changes appear to be the result of a nerve block injury, which is believed to have decreased joint angle at the beginning of the injury because temporary blockage can cause insoluble atrophy [33].

The exercise intensity also affects the recovery of the muscle fibers. High-intensity exercise increased the PGC-1 α activity in the fast twitch muscles [41]. HIIE is a repetition of exercise and rest during the recovery period. This is effective in promoting neurodevelopment and facilitating proprioceptive neuromuscular or anaerobic exercise, walking speed, and walking-related functions [22]. In addition, HIIE is effective in strengthening the muscle performance [23]. HIIE had a greater effect on the autonomic nervous system compared to continuous exercise, and cardiovascular autonomic adjustment was shorter than aerobic exercise [45]. HIIE resulted in the faster adaptation of a gradual load than high intensity non-interval exercise [27].

The SFI measurements increased gradually with increasing measurement time of each group, which was different from the previous study, which reported a decrease in the score up to four days [46]. The decrease in SFI score after sciatic nerve crush injury appears to be due to the progression of degeneration due to a peripheral nerve injury [47]. Although this study differs from the method of exercise, it is consistent with the recovery of function by the voluntary contraction of axons in recovery due to aquatic stimulation [48].

In this study, MIE and HIIE were effective in recovering the motor function of the sciatic nerve-damaged rats and in relieving pain according to a kinematic examination on the gait. In particular, MIE and HIIE could be employed for the gait functional training in the toe-off stance phase and the initial stance phase, respectively.

On the other hand, it can be challenging to apply this treatment immediately to clinical patients because the subjects were not humans, but white rats. The intensity and interval need to be set again to make this treatment suitable for patients. In addition, there was difficulty in clarifying the effects of the interval exercise itself due to the comparison between MIE and HIIE. A future study will need to assess the method of treadmill exercise in relation to the intensity and interval adjustment.

Ⅴ. Conclusion

This study examined the effects of MIE and HIIE over time on the recovery of the motor function of white rats with crush damage on the sciatic nerve. Treadmill exercise helped recover the damaged peripheral nerve because both MIE and HIIE were effective in recovering the motor function. In addition, damaged motor function related to gait was recovered effectively. Proper stimulation is essential for recovering the nerve. Overall, treadmill exercise can be used to help stimulate recovery. Specifically, MIE was much more effective in the angle of ankle and knee in the toe-off stance stage than HIIE because, in the toe-off stance phase, there is high activation of the soleus muscle, in which the type Ⅰ muscle form prevails. Therefore, MIE was suitable for walking function training in the toe-off stance phase.

On the other hand, HIIE was far more effective in improving the angle of ankle and knee in the initial stance stage than MIE because, in the initial stance stage, there is a high level of activation of the tibialis anterior muscle, in which the type Ⅱ muscle form prevails. Therefore, HIIE was considered suitable for walking function training in the initial stance phase.

A patient whose peripheral nerve is damaged usually suffers muscular atrophy caused by pain and nerve damage. MIE and HIIE on the treadmill can improve the peripheral nerve and motor skills. In particular, MIE can be used as walking functional training in the toe-off stance phase, while HIIE can be used in the initial stance stage.

References

[1] Li M, Zhang P, Guo W, et al. Protein expression profiling during wallerian degeneration after rat sciatic nerve injury. Muscle Nerve. 2014;50(1):73-8.

[2] Braga Silva J, Marchese GM, Cauduro CG, et al. Nerve conduits for treating peripheral nerve injuries: A systematic literature review. In Hand Surgery and Rehabilitation. 2017;36(2):71-85.

[3] Matthew TH, Alexander YS. Management and Complications of Traumatic Peripheral Nerve Injuries. In Hand Clinics. 2015;31(2):151-63.

[4] Ciaramitaro P, Mondelli M, Logullo F, et al. Traumatic peripheral nerve injuries: epidemiological findings, neuropathic pain and quality of life in 158 patients. J ouranal of the peripheral nervous systemt. 2010; 15(2):120-7.

[5] Badri O, Shahabi P, Abdolalizadeh J, et al. Combination therapy using evening primrose oil and electrical stimulation to improve nerve function following a crush injury of sciatic nerve in male rats. Neural Regeneration Research, 2017;12(3):458-63.

[6] Emamhadi M, Saberi A, Andalib S. Sciatic nerve injuries following femoral shaft fractures: Does the time interval from injury to surgery matter?. In Clinical Neurology and Neurosurgery, 2016;147:6-10.

[7] Ruiz-Arranz JL, Alfonso-Venzala I, Villalon-Ogayar J. Piriformis muscle syndrome. Diagnosis and treatment. Presentation of 14 cases. Revista Española de Cirugía Ortopédica y Traumatología(English Edition). 2008; 52(6):359-65.

[8] Natsis K, Totlis T, Konstantinidis GA, et al. Anatomical variations between the sciatic nerve and the piriformis muscle: a contribution to surgical anatomy in piriformis syndrome. Surg. Radiol. Anat. 2014;36:273-80.

[9] Dina E, Puigdemasa A, Navarro X. Passive and active exercise improve regeneration and muscle reinnervation after peripheralnerve injury in the rat. Muscle & Nerve, 2011;43(4):500-9.

[10] Jill E Shea, Jared W Garlick, Mohamed E Salama, et al. Side-to-side nerve bridges reduce muscle atrophy after peripheral nerve injury in a rodent model. In Journal of Surgical Research. 2014;187(1):350-8.

[11] Burnett MG, Zager EL. Pathophysiology of peripheral nerve injury: a brief review. Neurosurg Focus. 2004; 16:1-7.

[12] Sia S, Lepri A, Ponzecchi P. Axillary brachialplexus block using peripheralnerve stimulator:a comparison between double and triple-injection techniques. Regional Anesthesia and Pain Medicine. 2001;26(6):499-503.

[13] Calum RK Grant, Pavan Kumar BC Raju. Lower limb nerve blocks, In Anaesthesia & Intensive Care Medicine. 2016;17(4):182-6.

[14] Chen MM, Qin J, Chen SJ, et al. Quercetin promotes motor and sensory function recovery following sciatic nerve-crush injury in C57BL/6J mice. In The Journal of Nutritional Biochemistry. 2017;46:57-67.

[15] Udina E, Cobianchi S, Allodi I, et al. Effects of activity-dependent strategies on regeneration and plasticity after peripheral nerve injuries. Ann. Anat. 2011;193:347-53.

[16] Cobianchi S, Casals-Diaz L, Jaramillo J, et al. Differential effects of activity dependent treatments on axonal regeneration and neuropathic pain after peripheral nerve injury. Exp. Neurol. 2013;240:157-67.

[17] Gutmann E, Jakoubek B. Effect of increased motor activity on regeneration of the peripheral nerve in young rats. Physiol Bohemoslov. 1963;12:463-8.

[15] Asensio-Pinilla E, Udina E, Jaramillo J, et al. Electrical stimulation combined with exercise increase axonal regeneration after peripheral nerve injury. Exp Neurol. 2009;219:258-65.

[19] Arbat-Plana A, Torres-Espı´n E, Navarro X, et al. Activity dependent therapies modulate the spinal changes that motoneurons suffer after a peripheral nerve injury. Exp Neurol. 2015;263:293-305.

[20] Boutcher sh. High-intensity inermittent exercise and fat loss. Jouranl of obesity. 2011;10.

[21] Trapp EG, Chisholm DJ, Boutcher SH. Metabolic response of trained and untrained women during high-intensity inermittent cycle exercise. American Joural of physiology-Regulatory, integrative and comparative physiology. 2007;293:R2370-75.

[22] Boyne P, Dunning K, Carl D, et al. High-Intensity Interval Training and Moderate-Intensity Continuous Training in Ambulatory Chronic Stroke: Feasibility Study. Phys Ther. 2016;96(10):1533-44.

[23] Nytrøen K, Rustad LA, Aukrust P, et al. High-intensity interval training improves peak oxygen uptake and muscular exercise capacity in heart transplant recipients. Am J Transplant. 2012;12(11):3134-42.

[24] Paul SS, Lester ME, Foreman KB, et al. Validity and reliability of two-dimensional motion analysis for quantifying postural deficits in adults with and without neurological impairment. The anatomical record. 2016;299:1165-73.

[25] Vanessa VMR, Claudio HB, Nilton M. Sciatic functional index in smashing injuries of rat's siatic nerves. Evaluation of method reproducibility among examiners. Acta ortop bras. 2006;14(3).

[26] brooks GA, White TP. Determination of metabolic and heart rate responses of rats to treadmill exercise. journal of applied physiology, 1978;45(6):1009-15.

[27] NG, DeLorey DS. A prospective evaluation of non-interval- and interval-based exercise training progressions in rodents. Appl Physiol Nutr Metab. 2011;(5):723-9.

[28] Shepherd RE, Gollnick PD. Oxygen uptake of rats at different work intensities. P flugers Arch. 1976;362(2): 219-22.

[29] Bedford TG, Tipton CM, Wilson NC, et al. Maximum oxygen consumption of rats and its changes with various experimental procedures. J Appl Physiol Respir Environ Exerc Physiol. 1979;47(6):1278-83.

[30] Gillen JB, Gibala MJ. Is high-intensity interval training a time-efficient exercise strategy to improve health and fitness?. Appl Physiol Nutr Metab. 2014;39(3):409-12.

[31] Campbell WW. Evaluation and management of peripheral nerve injury. Clin Neurophysiol. 2008;119:1951-65.

[32] Grant GA, Goodkin R, Kliot M. Evaluation and surgical management of peripheral nerve problems. Neurosurgery. 1999;44:825-40.

[33] Zochodne DW, Levy D. Nitric oxide in damage, disease and repair of the peripheral nervous system. Cell Mol Biol(Noisy-le-grand). 2005;51:255-67.

[34] Lawrence R. Robinson MD. Traumatic injury to peripheral nerves. Muscle Nerve. 2000;23:863-73.

[35] Rasminsky M, Sears TA. Internodal conduction in undissected demyelinated nerve fibres. J Physiol. 1972; 227:323-50.

[36] Fu SY, Gordon T. The cellular and molecular basis of peripheral nerve regeneration. Mol Neurobiol. 1997; 14:67-116.

[37] Navarro X. Chapter 27 neuralplasticity after nerve injury and regeneration. International Review of Neurobiology, 2009;87:483-505.

[38] Sobral LL, Oliveira LS, Takeda SYM, et al. Immediate versus later exercises for rat sciatic nerve regeneration after axonotmesis: histomorphometric and functional analyses. Brazilian Journal of Physical Therapy. 2008; 12(4):311-6.

[39] Joseph E. Muscolino DC. Kinesiology: The Skeletal System and Muscle Function, 2e. Philadelphia, PA : Mosby Publish. 2010.

[40] Nielsen AR, Mounier R, Plomgard P, et al. Expression of interleukin-15 in human skeletal muscle effect of exercise and muscle fibre type composition. Physiol. 2007;584(1):305-12.

[41] Godin R, Ascah A, Daussin FN. Intensity-dependent activation of intracellular signalling pathways in skeletal muscle: role of fibre type recruitment during exercise. J Physiol. 2010;1:588.

[42] Patricia HV, Ruth-Mary d, David C. Peripheral nerve lesions. Neurosurgery. Surgery. 2015;33(8).

[43] Bain J, Mackinnon S, Hunter D. Functionalevaluation of complete sciatic, peroneal, and posterior tibial nerve lesions in the rat. Plasticand Reconstructive Surgery. 1989;83(1):129-38.

[44] Garnier C, Falempin M, Canu MH. A 3D analysisofforeand hindlimb motion during locomotion : comparison ofoverground and ladder walking in rats. Behavioural Brain Research. 2008;186(1):57-65.

[45] Heydari M, Boutcher YN, Boutcher SH. The effects of high-intensity intermittent exercise training on cardiovascular response to mental and physical challenge. International Journal of Psychophysiology. 2013;87(2): 141-6.

[46] De Koning P, Brakkee JH, Gispen WH. Methods for producing a reproducible crush in the sciatic and tibia1 nerve of the rat and rapid precise testing of return of sensory function. Beneficial effects of melanocortins. J Neurol Sci. 1986;74:237-46.

[47] Fawcett JW, Keynes RJ. Peripheral nerve regeneration. Annual of Review Neuroscience. 1990;13:43-60.[48] Sarikcioglu L. Oguz N. Exercise training and axonal regeneration after sciatic nerve injury. Int. J. Neurosci. 2001;109(3):173-7.