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# *Oscillating Electric Field on Motor Function Recovery and Axon Regeneration in Gray Rabbits with Spinal Cord Injury*

**Milo Masson**

*The University of Manchester, UK*

***Keywords:*** Oscillating Electric Field, Spinal Cord Injury, Motor Function, Axon Regeneration

***Abstract:*** Spinal cord injury is a common multiple disease, belongs to the central nervous injury disease, this kind of disease will be extremely destructive to the human body, has a high disability rate, has a serious impact on the quality of life of patients. Therefore, it is of great significance to explore the scientific treatment of spinal cord injury and promote the continuous improvement of treatment effect. The purpose of this paper is to explore the effect of oscillating electric field on the recovery of motor function and axon regeneration in gray rabbits with spinal cord injury, so as to provide theoretical support for the clinical treatment of spinal cord injury and promote the continuous improvement of the actual therapeutic effect of spinal cord injury. Firstly, the concept, pathological development and main manifestations of spinal cord injury were discussed in detail, and then the common treatment methods of spinal cord injury were introduced. Then, the influence of oscillating electric field on motor function recovery and axon regeneration of gray rabbits with spinal cord injury was investigated through the establishment of spinal cord injury model. The experimental results showed that compared with no interference electric field, the motor function and axonal regeneration ability of gray rabbits with spinal cord injury under the intervention of oscillating electric field were significantly improved, with about 19% increase in axonal regeneration ability, about 19% increase in injury recovery speed, and about 17% increase in overall recovery effect. In summary, the oscillating electric field can promote the effective recovery of spinal cord motor function in gray rabbits with spinal cord injury, but the intervention time of oscillating electric field should last more than 6 weeks.

## 1. Introduction

Spinal cord injury is a common traumatic disease, and its incidence is also increasing under the influence of comprehensive factors. Young adults account for a large proportion of spinal cord injury patients, which brings a serious burden to the society and the family. Therefore, the research and treatment of spinal cord injury has attracted much attention. The key to the treatment of spinal cord injury lies in the regeneration of dead neurons and the reconstruction of nerve connections, and finally the restoration of axon conduction function. At present, some achievements have been made in this field, but the effect is not obvious in the clinical treatment of spinal cord injury due to the insufficient research in this field. With the progress of medical concept and technology, some scholars proposed to realize the recovery and regeneration of motor function of spinal cord injury by means of oscillating electric field, and the existing research has preliminarily proved the feasibility of this treatment method.

Due to the harmfulness and high incidence of spinal cord injury, scholars at home and abroad have been paying close attention to it, and a series of studies have been conducted on it in the medical field, and relevant research results have been obtained [1]. In literature [2], the author demonstrated the relationship between the external electric field of cells and axon regeneration through in vitro experiments. The experimental results showed that the nerve fibers in the growing state would react to the electric field, and continuously extend along the direction of voltage gradient. In literature [3], based on the characteristics of different electrodes of the oscillating electric field and the specific principle that the regeneration direction of axons is constantly toward the cathode, the author proves that the oscillating electric field can realize the simultaneous two-way repair of the damaged cephalic and ctrailing sides. In literature [4], with the help of rat spinal cord injury model, the author explored the main influencing factors of spinal cord injury from the inside of the body, and proposed specific strategies for prevention and treatment of spinal cord injury. In literature [5], based on the rat spinal cord injury model, the author applied various types of medical observation technologies such as immunofluorescence to explore the role of electronic wire irradiation in the treatment of spinal cord injury, and the results showed that it played an important role in promoting cell activation and proliferation and restoring motor function.

In order to explore the influence of oscillating electric field on the recovery of motor function and axon regeneration of gray rabbits with spinal cord injury, theoretical support is provided for the clinical treatment of spinal cord injury, and the actual therapeutic effect of spinal cord injury is continuously improved [6]. Firstly, the concept, pathological development and main manifestations of spinal cord injury were discussed in detail, and then the common treatment methods of spinal cord injury were introduced. Then, the influence of oscillating electric field on motor function recovery and axon regeneration of gray rabbits with spinal cord injury was investigated through the establishment of spinal cord injury model in gray rabbits with experimental analysis [7]. The study in this paper, on the one hand, promoted the improvement of the therapeutic effect of spinal cord injury, and on the other hand, laid a theoretical foundation for the subsequent studies in related fields [8].

## 2. Treatment of Spinal Cord Injury

### 2.1. Overview of Spinal Cord Injury

Spinal cord injury, or SCI for short, is a disease that can seriously harm the quality of human life. At present, with the constant changes of the society, the development of traffic towards high-speed, the rapid development of extreme sports and violent injuries are the main causes of spinal cord injury [9]. In recent years, the incidence of spinal cord injury has increased globally. Spinal cord injury diseases are characterized by high incidence, high disability rate, high cost and low mortality [10]. High incidence refers to the increasing proportion of patients with spinal cord injury in the world population. In China, for example, according to statistics, there are about 137,000 people with spinal cord injury out of an average population of 1 million. High disability rate refers to the high disability probability caused by spinal cord injury. According to statistics, total paralysis patients account for about 67% of these patients. High cost refers to the high cost of treating such diseases. Low mortality rate refers to the relatively low threat of spinal cord injury to human life safety, with the mortality rate about 5% [11]. Young adults account for a large proportion of patients with spinal cord injury. Since spinal cord injury often causes lifelong disability and brings great pain to patients and their families, in-depth basic research on spinal cord injury is of great significance for the improvement of treatment effect and clinical treatment [12].

At present, scholars generally believe that the pathological evolution of spinal cord injury can be divided into two steps: First, under the action of mechanical external forces, the spinal cord produces primary damage, thereby damaging blood vessels, promoting axonal degeneration and astrocyte death. Secondly, based on the primary spinal cord injury, some secondary spinal cord injuries may occur, resulting in biochemical changes in the blood vessels of the body, necrosis of the injured site, inflammatory reaction, etc., which will seriously affect the patients. Sustained tissue damage is a major feature of spinal cord injury, which is the result of failure to repair during wound recovery. Cases of spinal cord injury changes were experienced three different stages, respectively is chronic, acute, secondary, and display the characteristics of spinal cord injury at different stages are also different: spinal cord injury in the first few hours, the pathological characteristics mainly for the integrity of the nerve and blood vessel structure is broken, and vascular spasm, axons rupture, hemorrhage, and so on. Is the secondary stage of spinal cord injury a few weeks, this stage due to swelling in the spinal cord function, makes the internal pressure is much higher than the pressure inside the vessels of the spinal cord, so local secondary ischemia could be happening, and spinal cord injury of neurons shock makes spinal cord ischemia degree deepens, ischemia can cause lack of organizational support releasing toxic substances, thereby led to further expand, spinal cord injury tissue necrosis and glial cell activation and axonal degeneration phenomenon produces. The months following a spinal cord injury are a period of chronic injury, in which glial scarring, produced by glial cells, occurs in the area of the patient's injury. A large amount of damaged white matter also forms during this period, leading to degeneration of tissue fibers.

After spinal cord injury, a series of relatively important cellular reactions will occur. Astrocytes will divide and proliferate and turn into scar astrocytes, myelin sheath will form fragments under the action of lysis, and microglia and oligodendrocytes will gradually proliferate and migrate to the damaged site. All types of glial cells at the site of injury can inhibit the regeneration of axons, because these glial cells will form Nogo and MAG after maturity, both of which have inhibitory properties. The most complex of these are astrocytes: they promote axonal growth in the undamaged spinal cord or in the immediate period when the injury occurs, but over time they begin to form proteoglycan with inhibitory properties. While microglia promote axon regeneration, they also produce different toxins to kill neurons and damage axons. Due to the failure of repair, only part of the spinal cord is repaired, which can lead to permanent dysfunction. For a long time, scholars have believed that it is difficult for the central nervous system to regenerate once the central nervous system is damaged. However, some recent studies have gradually refuted this theory, and many existing studies have shown that the central nervous system can still regenerate after the injury.

## 2.2. Treatment of Spinal Cord Injury

The treatment of spinal cord injury mainly consists of four parts: early treatment, drug treatment, surgical treatment and complication treatment. First, early treatment. The early treatment of spinal cord injury directly affects the recovery and therapeutic effect of the injury. Early treatment mainly includes field treatment, emergency treatment and early specialist treatment. The evaluation of patients with spinal cord injury can be carried out at the scene of the injury. The presence of spinal cord injury can be determined according to the patient's performance on the scene. Once the patient is determined to have spinal cord injury, it is necessary to pay attention to the orderly rescue and transport, so as to reduce the further damage to nerve tissue caused by this process. Based on the rescue principle of ABC, respiratory patency should be ensured in patients with spinal cord injury to avoid shock and ischemia. Second, medication. Drug therapy is a common method for the treatment of spinal cord injury. The therapeutic task of this method is to avoid the further expansion of the spinal cord injury area and form an effective protection for healthy spinal cord tissue. Drug therapy is the most effective and convenient way to reduce the further expansion of spinal cord injury. To achieve this goal, the key is to achieve spinal cord sequence restoration and promote spinal stability. The commonly used therapeutic drugs for spinal cord injury include corticosteroids, gangliosides, scopolamine and neuroleptics. Third, the treatment of complications. Death occurs in severe cases of spinal cord injury, mostly due to complications. The common complications of early spinal cord injury include cervical spinal cord injury, and the causes of death are persistent high fever, low temperature, respiratory failure or heart failure. In patients with advanced spinal cord injury, pressure ulcers, urinary tract infection, respiratory tract infection, nutritional failure and other types of complications may occur, resulting in progressive death. About 59 percent of spinal cord injuries are estimated to die of complications. Therefore, the treatment of complications of spinal cord injury is very critical, and the prevention and timely treatment of complications can effectively reduce the mortality of patients with spinal cord injury. Fifth, surgical treatment. Surgical treatment is suitable for patients with severe spinal cord injury. These patients need to be corrected and treated by surgical treatment to reduce the harm of spinal cord injury because of severe deformity caused by spinal cord injury. In addition, rehabilitation and treatment of spinal cord injury, and effect on the general recovery of patients with spinal cord injury, rehabilitation treatment including psychotherapy, functional exercise, physical therapy and electronic stimulation, such as a variety of ways, rehabilitation treatment of the comprehensive application of fast recovery in patients with spinal cord injury has a good role in promoting.

## 3. Grey Rabbit Model Experiment

(1) Experimental animals and materials

Gray rabbit in the trials was composed of 90 adult health gray rabbit, the level of the 90 gray rabbit belong to clean level, all are female gray rabbit, weight for 220 + 109 g, gray rabbit experiment has provided a formal experimental animal center, experimental environment is provided by a rehabilitation center laboratory animals and all experiments are done in the test environment. Materials used in the experiment in this paper include anti-gray rabbit GFAP polyclonal antibody, rabbit anti-NF200 monoclonal antibody, goat anti-gray rabbit IgG, goat anti-rabbit IgG, NYu percussion instrument, neuroelectrophysiology instrument, implantable oscillating electric field stimulation, DM2500 optical microscope, DMTJA 4000B fluorescence positive microscope and Image Pro Plus6.0 software.

(2) Experimental method

Will be involved in this paper the experiment of 90 gray rabbit, carried out in accordance with the digital coding way random grouping, average divided into experimental group and control group, each group of 45 only gray rabbit, and USES the modified Allen hit after spinal cord injury model in the form of production, the measure model of success is to observe the hind legs and tail of gray rabbit spinal cord injury whether the condition of spasm and epidural hemorrhage, electrode stimulation at the same time. The experimental group of gray rabbits received oscillating electric field intervention, while the control group of gray rabbits only placed the oscillating electric field stimulator, without oscillation intervention. Based on the gray rabbit awake state, continuous stimulation is given. The intensity of the oscillating electric field is 600V/ MNL, 15mir per minute is the oscillation period, and inductive power supply is the main power supply mode. According to the observation time, the two groups of grey rabbits could be divided into three subgroups, namely, the 2-week subgroup, the 6-week subgroup and the 12-week subgroup, with 15 grey rabbits in each subgroup. In case of sudden death and elimination of grey rabbit, it is necessary to supplement grey rabbit again.

(3) Animal model preparation

According to the standard of 3ml/100g, 10% chloral hydrate was intra - abdominal injected to anesthete the gray rabbit, and the bone marrow at the level of T10 was exposed. The gray rabbit was fixed in NYU percussion platform, and the spinal cord impinged on the gray rabbit with the potential energy of 50GCF. Two different electrodes in the vibrating electric field were sutured layer by layer by non-absorbable suture. The sutured sites were T8 ~ T9, T11 ~ T12 spinous process and bilateral articular process, and the main body of the electric field was placed in vitro. After the operation, the intervention of oscillating electric field can be added to the experimental group of gray rabbits.

(4) Experimental materials and slicing

Successful animal model after 2 weeks, 6 weeks, 12 weeks, respectively in the abdominal cavity position with concentration of 10% chloral hydrate anesthesia injections, sports cause some degree of potential detection, location within your heart perfusion concentration of 4% paraformaldehyde, from gray rabbit body damage will occur at the center of the spinal cord segmental and 1 cm at the head end, and should be fixed in the concentration of 4% paraformaldehyde, fixed time of 12 h, paraffin embedding the injury as the core, and the continuity of coronary slice.

(5) Experimental detection

The experimental detection in this paper mainly includes three parts: behavior detection, electrophysiology detection and histology. First, behavioral detection. 2, 6, and 12 weeks after the completion of the experiment, gray rabbit behavior detection score, or BBB score. The whole movement function of hind limb of grey rabbit was observed. The observation method was single-blind, in which two people observed and scored separately, and the final score was based on the average value of two people. Second, electrophysiological testing (MEP). Two pairs of needle-like stimulation electrodes were placed on the surgical field and in the space between the inferior spines, i.e. R17/8 and L1/2. A negative electrode is placed at the end of the positive electrode with an interval between 0.5-0.8cm. Rectangular pulse is the type of stimulus. The output voltage is constant, the wave width is 0.05ms, and the output intensity of the electric field is 100V-150V. Action potentials (CMAP) corresponding to the muscles were recorded with electrodes at the right calf gastrectomy. The index is the latency and the amplitude difference between the upper and lower damage areas. The smaller the difference between the MEP above the damage area and the MEP below the damage area, the better the recovery of its conduction function. Third, histological examination. The damage of the spinal cord HE dyeing processing, to carefully observe the pathological changes of the local damage, at the same time for routine dewaxing and hydration process, and with the help of the related reagents to rinse of frozen experiment section, respectively to join rabbit monoclonal antibody NF200 GFAP, rabbit polyclonal antibody, and rinse temperature of 4 ℃ for the night, with the help of software, to observe axon count measure.

(6) Statistical analysis of data

The experimental measurement values were expressed in the form of $x \pm s$, and pairwise comparisons were made for the data at different experimental time points. After the completion of the statistics of experimental data, the computer graphics software was used to draw data charts, analyze and integrate the experimental data charts, and on this basis, the experimental conclusions of this paper were drawn.

## 4. Analysis of Experimental Results

### 4.1. Experimental Results

In the whole experiment process of this paper, a total of 8 gray rabbits died, and 5 gray rabbits had subcutaneous local infection at the electrode embedded sites. All the experimental gray rabbits were supplemented according to the experimental requirements. In this paper, the following experimental data are obtained through the grey rabbit model experiment. The specific experimental data are shown in the chart. The data in the chart is the result of the author's experiment.

(1) BBB score results

*Table 1. BBB scores of grey rabbits at different time points*

| Group | Experimental group | | Control group | |
|---|---|---|---|---|
| | Left hindlimb score | Right hindlimb score | Left hindlimb score | Right hindlimb score |
| 1d | 2.4±1.43 | 1.9±1.08 | 2.6±1.50 | 2.1±1.33 |
| 2 weeks | 4.0±2.27 | 3.9±2.41 | 4.9±1.35 | 4.1±1.47 |
| 6 weeks | 7.65±2.51 | 7.72±1.91 | 6.20±1.44 | 6.16±1.82 |
| 12 weeks | 9.50±2.02 | 9.65±2.34 | 6.80±2.11 | 6.74±2.31 |
| *Data came from the experimental results | | | | |

Table 1 as the BBB ratings of the gray rabbit hind limbs function, based on the time factor within the group on gray rabbit experimental data were analyzed, and the experimental data show that in Table 1 as time prolonged, the experimental group the BBB rating of gray rabbit gradually increased, while the control group of gray rabbit in six weeks and 12 weeks when the BBB score differences between the small, has no obvious statistical significance.

(2)MEP detection results

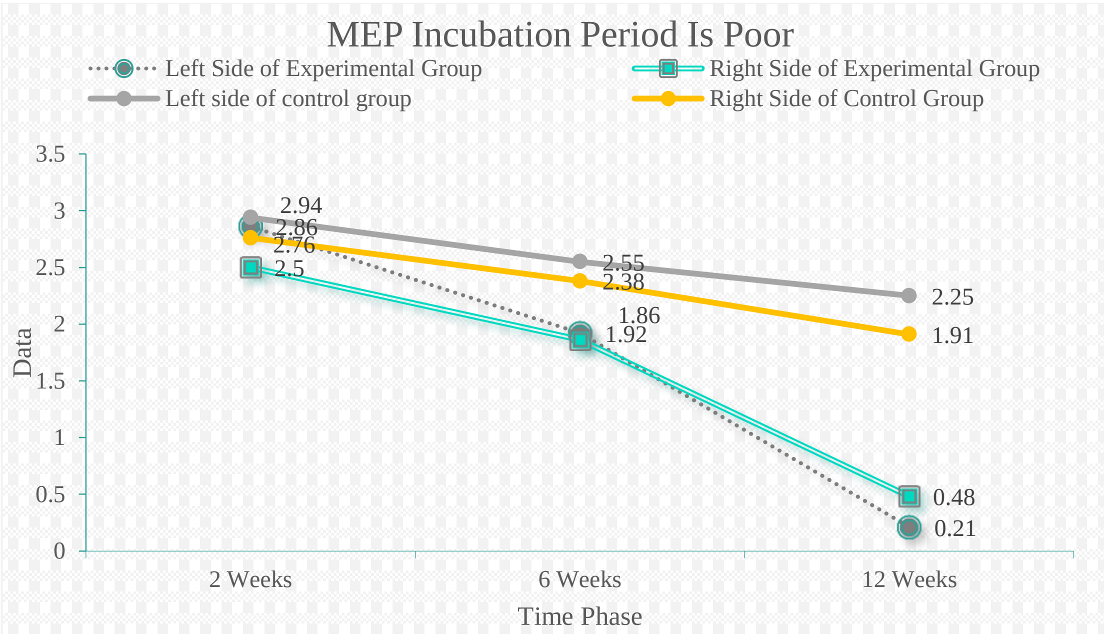


*Figure 1. Latency difference of MEP*

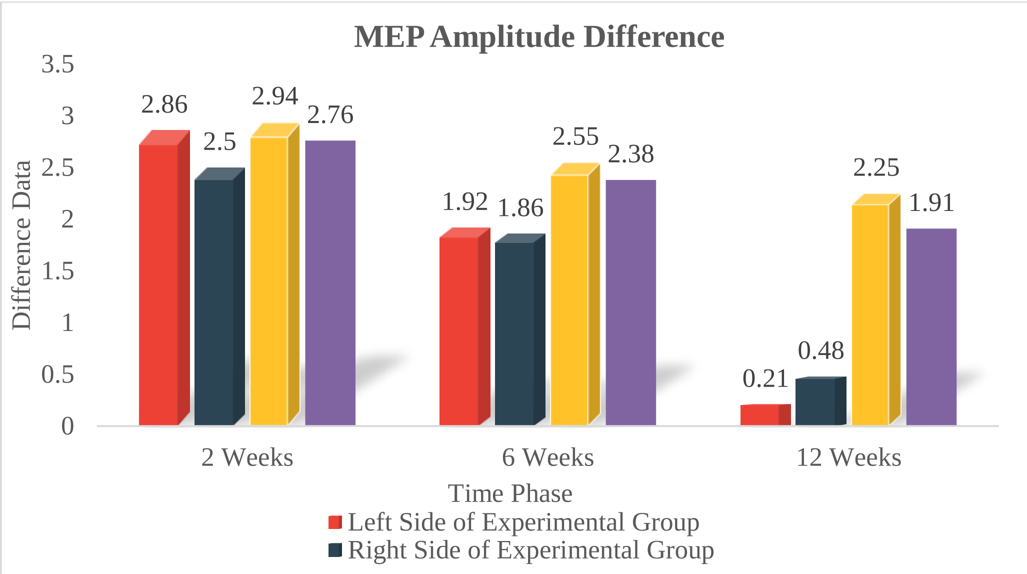


*Figure 2. MEP amplitude difference*

Figure 1 and Figure 2 respectively show the MEP latency and amplitude difference data of gray rabbits in different groups. It can be seen from the data in Figure 1 and Figure 2 that, after 2 weeks of the experiment, the amplitude difference of MEP on the right side of rats in the experimental group was shorter than that in the control group. The amplitude difference on both sides of the 6-week and 12-week groups was shorter than that of the control group, and there was significant difference between the two groups. At two weeks of the experiment, the amplitude difference between different groups was small.

(3) Histological observation results

Through histological examination, we first found that at 2 weeks of the experiment, HE staining results of sections in the control group and the experimental group showed unclear boundaries of the gray matter in the spinal cord. After 6 weeks of the experiment, a spinal cavity was observed and a small amount of white matter remained in the surrounding area. After 12 weeks of the experiment, glial scars were observed at the site of the injury. Immunohistochemical staining of GFAP protein in the two groups was observed. The results showed that in the spinal cord injury area of gray rabbits, glial cell proliferation was observed in both the experimental group and the control group, and the density difference between the two groups was small. However, by measuring the Angle of astrocyte processes, it was found that the Angle of gray rabbits in the experimental group was 34.39±8.51 and that in the control group was 66.32±15.84, which was significantly smaller than that in the control group. Observation of the sagittal section of the spinal cord under an optical microscope revealed that the NF200 positive nerve fibers gradually changed to brownish yellow and brown. At 2 weeks of the experiment, in sections of the control group and the experimental group, scattered brown staining points could be observed in the white matter of the sections. After 6 weeks and 12 weeks of the experiment, more nerve fibers could be observed passing through the damaged area in sections of the experimental group. The specific results are shown in Figure 3. The data in the figure are the results of the author's experiment.

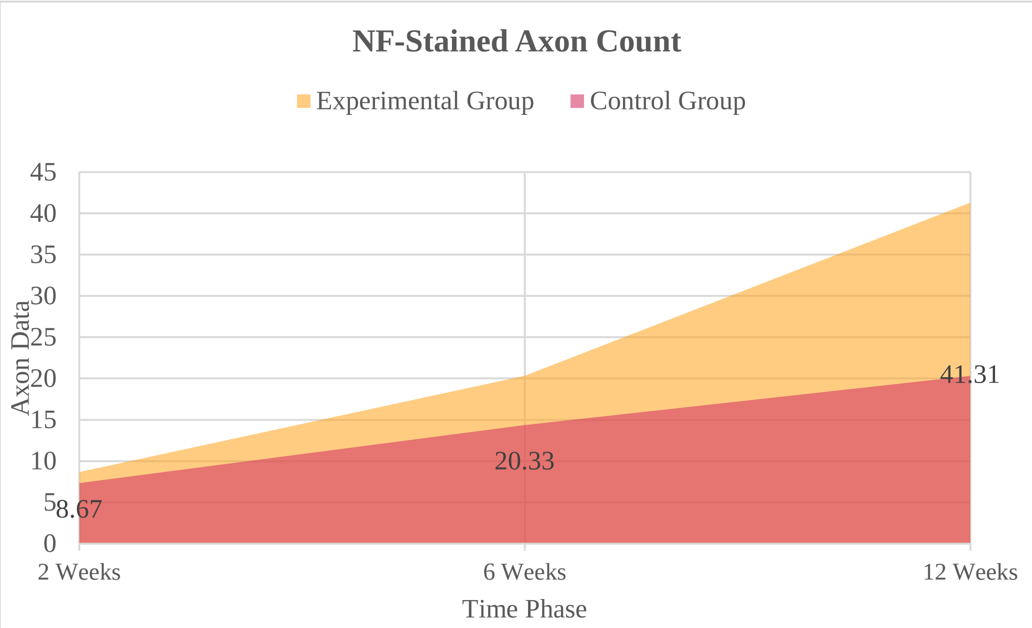


*Figure 3. NF staining axon count*

## 4.2. Impact Analysis

The existing research results show that dc or oscillating electric field has a good promoting effect on the recovery of nerve function in animals with spinal cord injury. Based on a double-blind randomized clinical trial, some scholars conducted a comprehensive evaluation of the effect and biological compatibility of placing oscillating electrodes in the spinal canal in dogs with spinal cord injury. After the placement of the oscillating electric field for 14 weeks, the dogs were able to walk normally. However, some researchers have tried direct current field in rats with acute spinal cord injury, and found that after 8 weeks of direct current field, the rats showed no significant improvement in behavior or electrophysiology. Experiments in this paper, after spinal cord injury in the rabbit rapidly oscillating electric field of the intervention, the control group only placed stimulator is not intervene oscillating electric field, the final BBB score data show that in oscillating electric field intervention in 2 weeks, gray rabbit hind limbs motor function and no obvious improvement, the oscillating fields intervention after 6 weeks of gray rabbit hind limbs motor function to recover gradually. With the extension of time, the recovery of gray rabbits in the control group gradually stopped, which is consistent with the existing research conclusions.

In this study, the MEP detection results after 2 weeks showed that the oscillating electric field had improved the motion conduction function of gray rabbits in the early stage of spinal cord injury. Although gray rabbits with spinal cord injury did not show significant recovery of hind limb movement after 2 weeks of oscillating electric field intervention, MEP detection results showed that the latency of right hind limb MEP of gray rabbits was significantly shortened, which may be related to the absence of glial scar within 2 weeks of spinal cord injury. The early interference of oscillating magnetic field in the spinal cord injury region accelerated the growth rate of axons. Although it promotes the change of electrophysiology to a certain extent, it does not mean that the grey rabbit's motor function is restored. Experiment at 6 weeks and 12 weeks MEP test results suggest after 6 weeks of oscillating electric field stimulation, improve the motor conduction function of gray rabbit spinal cord injury, and present the results of the study area, and in time and gray rabbit hind limbs motor function recovery time corresponding to each other, this suggests that oscillating electrical energy may be based on the improvement of spinal cord nerve conduction function, realize the fast recovery of motor function.

Some researchers have tried to shorten the axons in the dorsal cord of adult pigs, and to add an electric field from the outside to promote the regeneration of the transverse axons. Neoplasms that successfully penetrate the colloid are generally less than 1 m, and proteins that damage nearby regions are the main distribution regions. Experiments in this paper the experimental group and control group in a short time the axon count does not exist significant differences in the gray rabbit, after 12 weeks, but the experiment, the experimental group gray rabbit in regeneration of nerve fibers, and its axon count obviously higher than the control group, and the experimental group gray rabbit MEP testing results show that the group of gray rabbit spinal cord nerve conduction function recover gradually, compared with the control group hind limbs motor function has been improved significantly.

The main reason of inhibiting axon regeneration and nerve function improvement is the production of glial scar. Some scholars believe that electric fields can reduce the possibility of gliosis in the damaged area. In this paper, the 10D value of glial fiber acid protein was measured. The test data showed that there was no significant difference between the two groups of different experimental time points, which may be related to the small sample size. Some scholars also use oscillating electric field to effectively inhibit the extension of astrocytes in spinal cord injury areas and guide them to re-determine the extension direction based on the direction of electric field. In this paper, the experiment measured the area astrocytes of spinal cord injury (sci) the Angle between the adjacent axon size, test results show that the experiment had a significantly higher after 12 weeks of illumination Angle, this suggests that although the glial scar and no obvious relation between oscillating electric field, but the oscillating electric field can realize linear array of astrocytes, which provide specific channels of axon growth.

The author consulted relevant materials and found that weak current field can realize the effective recovery of nerve function and plays an important role in promoting axon regeneration. American researchers took patients with acute spinal cord injury as research objects. The results showed that the application of oscillating electric field in the treatment of acute spinal cord injury could promote the significant improvement of patients' perception and motor function. However, some experimental results showed that although the weak current field could promote the improvement of nerve function, the difference was not obvious from the histological level. It could not guide the proliferation of Schwann cells and ependymal cells and promote the formation of new myelin sheath, but also existed the development of synapses. Other scholars proved that there was no direct correlation between the growth of zebrafish neuron cells cultured in vitro and the applied electric field, and they believed that the oscillating electric field affected the repair of spinal cord injury without sufficient evidence. In this paper, the experimental study shows that, for a period of 6 weeks after intervention, the oscillating electric field experimental gray rabbit axon count and astrocytes linear array obviously better than control group in gray rabbit, and the experiment of MEP test results show that the experimental group is obtained through gray rabbit whole motor conduction function improved, to some extent, also improved the function of hind leg movement. These results also correspond to different time, which also indicates that the oscillating electric field can improve the neural function by improving the regeneration of axons.

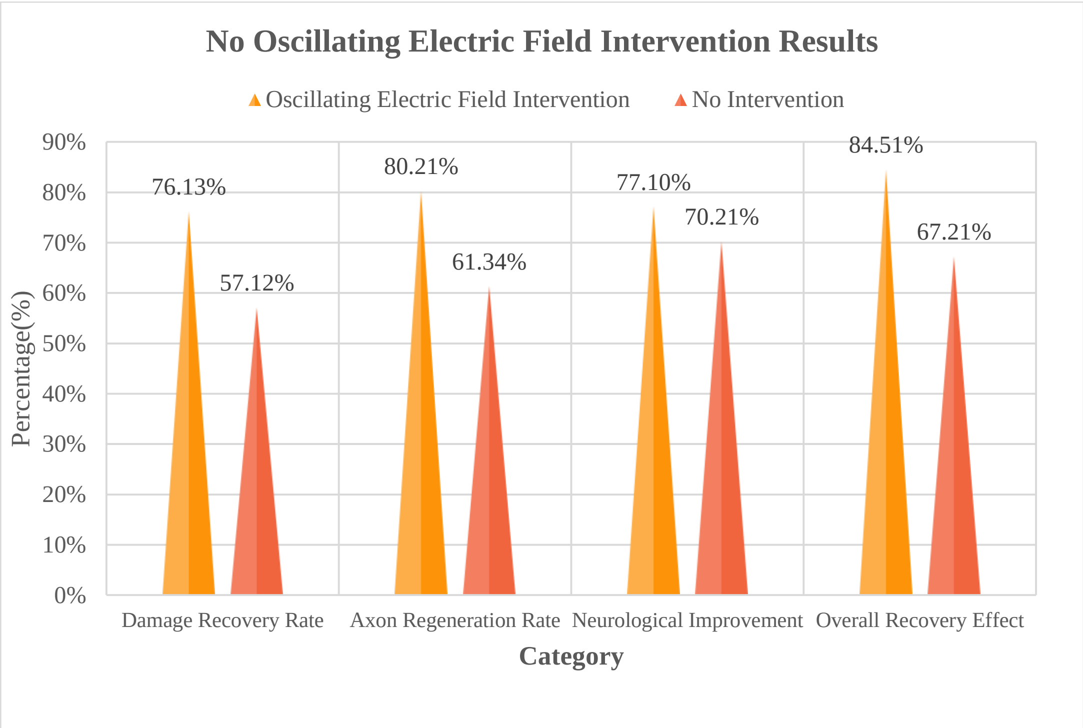


*Figure 4. Intervention results with or without oscillating electric field*

Figure 4 for the presence of oscillating electric field under the intervention of gray rabbit spinal cord injury recover data comparison, from the data can be seen in the figure, compared with no intervention in the electric field, oscillating electric field under the intervention of gray rabbit spinal cord injury movement function and axon regeneration ability were improved significantly, its axon regeneration increased by about 19%, the injury recovery rate increased by about 19%, the overall recovery effect increased 17%. In summary, the oscillating electric field can promote the effective recovery of spinal cord motor function in gray rabbits with spinal cord injury, but the intervention time of oscillating electric field should last more than 6 weeks. The specific mechanism may be to promote axon regeneration, induce its directional growth, promote the linear arrangement of astrocytes, and provide axon growth channels.

## 5. Conclusion

To sum up, spinal cord injury diseases have a serious impact on the quality of life of patients. Therefore, it is of Paramount importance to improve the treatment plan and promote the continuous improvement of treatment effect in the study of spinal cord injury diseases. In this paper, the experimental analysis of spinal cord injury was carried out with the help of the grey rabbit spinal cord injury model, and the author drew the following conclusions:

(1) After spinal cord injury, a series of important cellular responses will occur, which are closely related to the recovery of spinal cord injury; The treatment of spinal cord injury mainly consists of four parts: early treatment, drug treatment, surgical treatment and complication treatment.

(2)The oscillating electric field can promote the effective recovery of spinal cord motor function in gray rabbits with spinal cord injury, but the intervention time of oscillating electric field should last more than 6 weeks. The specific mechanism may be to promote axon regeneration, induce its directional growth, promote the linear arrangement of astrocytes, and provide axon growth channels.

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## Data Availability

Data sharing is not applicable to this article as no new data were created or analysed in this study.

## Conflict of Interest

The author states that this article has no conflict of interest.

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