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Discussion about Comprehensive Impacts in Peripheral Nerves Fibers Regeneration

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Abstract**—** *This paper represented discussion about comprehensive impacts of peripheral nerves fibers regeneration. Not only from cytobiological points of view, but also surgical therapy. In addition, it involved bio-chemistry, bio-physiology analysis, refer to osteopathic, endocrinopathic cases. There are varieties of cell functioned very important role in neuros system regeneration; eliminated metabolites of degenerative myelin sheath; constructed microenvironment for axonal regeneration effectively etc. Locality of microenvironment and reduction of scar would impact significantly as well as surgical stitching technique. In terms of bio-chemistry analysis, growth and inhibitory factors are discussed finally regards to histology and embryology. A complexity theory about the impacts in peripheral nerves fibers base on literature reviews are summarized, experimental data and methodologies are quoted consequently.*

Keywords**—***Peripheral Nerves; Regeneration; Nerves Repair; Schwann Cell; Nerves Fibers.*

I. INTRODUCTION

Peripheral nerves injury, is commonly occurred in clinical circumstances, some of the patients might disabled for life [3] [7] [14] [18] [25] [27] [28] [40] [44] [45]. Following the improvement of mechanized degree and development of transportation system, the incidence of peripheral nerve injury increased significantly [7]. Even though end-to-end suture would be able to perform through surgery, it is not ideal impacts of nerve regeneration [7]. Especially, in the case of short-distance nerve defect, nerve conduit can be used for nerve repair, it provides a suitable microenvironment for nerve fibers to regenerate and reach the distal end [7]. The regeneration of peripheral nerve after injury is a very complex biochemical and cytological process, which is affected by local or even global factors [24] [25] [26].

This paper discusses various impacts of affecting the regeneration of peripheral nerve fibers, bases on biochemistry, cell biology and other disciplines, and cites the specific cases of orthopedics, endocrinology, and other related diseases.

II. MAIN IMPACTS

According to literature reviews and previous experimental analysis, there are six main impacts we would be able to be summarized (Fig 1).

A. Schwann Cells (SCS)

The origin of Schwann cells is embryo of neural crest cells, and they are myelination which are forming peripheral nervous system (PNS), the axons surrounding or wrapping PNS, are forming myelinated or unmyelinated nerve fibers [8] [11].

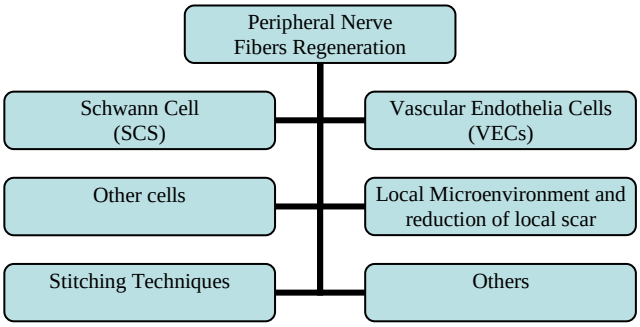

Fig. 1. Impacts of Peripheral Nerve Fibers Regeneration

SCS is not only closely related to PNS within the whole process of development, such as the survival of peripheral neurons and the jumping conduction of mature myelinated fibers, etc., but also reversibly differentiated into immature state after peripheral nerve injury, forming btingner band, secreting neurotrophic factors, promoting the sprouting and regeneration of severed axons, and re-wrapping the regenerated axons to form myelin sheath, which plays an important role in the regeneration and repair of central and peripheral nerve injury [8]. SCS are the myelin forming cells of PNS, which are essential for normal development and function of peripheral nerve [8] [11]. In addition, SCS were found in the nervous system and played an important role in repair of the system, which could remove the metabolites of denatured myelin sheath and secrete nutrients at the same time [8]. Meanwhile, to create a favorable microenvironment for axon regeneration and effected axon regeneration into the bridging conduit [8]. Myelin sheath is an important structure of peripheral nerve and a marker of mature myelinated nerve fibers [9]. Neu gene regulator-1 NRG-1, neurotrophic factor and PO protein regulate the development and regeneration of peripheral nerve [9]. The important factors of myelination are involved in the regulation of different stages of myelination [9]. SCS as glial cells of peripheral nervous system, the main functions of supporting, protecting, separating, nutrition, chemotaxis and promoting the maturation of regenerated nerve fibers [21].

The proliferation of SCS after peripheral nerve injury provides an environment conductive to axonal regeneration, it can be used as a cell substrate for axon growth, secrete many neurotrophic factors, express cell adhesion molecules and

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integrin on the surface, and produce extracellular matrix molecules such as laminin, fibronectin, collagen and proteoglycan, it also secretes a variety of monocyte chemokines to stimulate the recruitment of macrophages into degenerative nerves; the latter can remove axons and myelin sheath fragments, as well as myelin associated glycoprotein (MAG), which inhibits axon growth [38]. The basement membrane, composed of many extracellular matrix components, is an essential growth substrate for peripheral nerve regeneration [38]. After nerve injury, the integrity of the basement membrane far from the injury is the necessary condition for nerve regeneration, in many extracellular matrix molecules, there are not only molecules that promote axon growth, such as laminin, fibronectin and type IV collagen, but also molecules that inhibit axon growth, such as chondroitin sulfate proteoglycans (CSPGs) [38]. The latter also exists in the central nervous system and is an important factor in inhibiting the regeneration of central nervous system after injury, the remodeling of extracellular matrix after peripheral nerve injury is very important for nerve regeneration [38]. Chondroitinase ABC is a Glucosaminoglycan (GAG) specific glycosidase, which can decompose the gag side chain of CSPGs, thus degrading CSPGs, using chondroitinase ABC to degrade CSPGs to promote nerve regeneration and improve functional recovery has been confirmed in many studies of central nervous system injury, but there is little research of its effect on peripheral nerve regeneration [38]. In addition, the effect of chondroitinase ABC treatment on Schwann cells, other components of basement membrane and structural integrity of basement membrane are unknown [38].

The growth of myelinated and unmyelinated nerve fibers indicates that venous cannula, as an important representative of regeneration chamber, can promote peripheral nerve regeneration [11]. The results showed that the experimental group had more myelinated and unmyelinated nerve fibers than the control group, the results showed that the effect of Schwann cells injected into the venous cannula on peripheral nerve regeneration was better than that of intravenous cannula alone, it provides a new method for the repair of peripheral nerve defect [11].

The opening and closing of ion channels and the activity of related cytokines in spinal dorsal horn and dorsal root ganglion can promote or inhibit the nerve injury and repair in patients with diabetic peripheral neuropathy (PDPN) [1]. Nerve growth factor (NGF) can promote peripheral nerve regeneration and improve nerve conduction, it has direct protective effect on neurons by regulating calcium balance and antagonizing free radicals; nimodipine has a direct protective effect on the sciatic nerve of diabetic rats and can increase the blood flow of neurotrophic vessels [12]. FG-NGF membrane can slowly release nerve growth factor and transport it to the cell body and maintain the survival of neurons [13]. Slowly released nerve growth factor (NGF) promotes the proliferation and maturation of Schwann cells by binding to p75 receptor on Schwann's surface, thus inducing the growth of axons and the maturation of myelin sheath [13]. Slow release of nerve growth factor can increase the formation of sciatic nerve end effector organs and promote maturation [13].

After nerve injury, the first step of body repair is the enlargement of neuron cell body, the decomposition of Nissl body, the movement of nucleus to the periphery of cell, and the initiation of protein synthesis [14]. Due to the nutritional disturbance or even interruption of the distal nerve, the cytoplasm coagulates and liquefies, and the axon demyelinating and disintegrating, the characteristic Wallerian degeneration of the peripheral nerve appears, which is mainly manifested by the disintegration and phagocytosis of the myelin sheath at the distal part of the injured part, the withering of the axon, and the similar changes in the proximal part of the injured site [14]. This Wallerian degeneration does not occur immediately after nerve injury, once the Wallerian degeneration process is activated, the axons can be completely disintegrated within a few hours [14]. Then, Schwann cells and macrophages collected in the injured area will phagocytize the axon and myelin fragments, the removal of myelin fragments is very important for nerve repair, because myelin contains inhibitors of axon growth, which may hinder nerve regeneration, after that, the residual basement membrane and its associated Schwann cells (SC) formed a complete intimal tube structure, forming a channel for axon regeneration [14]. Once axons begin to regenerate, the distal nerve stumps form new buds, re-enter the endoneural tube, and then grow towards the target tissue, the axons can still accurately locate the previously associated tissues and re-establish functional synapses [14].

B. Vascular Endothelia Cells (VECs)

Vascular endothelial cells are monolayer flat cells covering the inner surface of blood vessels. They are not only a selective barrier between blood and vascular wall, but also an important part of capillaries [21]. There are abundant blood vessels in the normal nerve tissue, and there is capillary network in the nerve intima, which is the bridge between nerve tissue and nutrients, and ensure the information of nerve fibers and the normal function [21].

C. Other Cells

In the process of peripheral nerve regeneration, the growth, orientation and maturation of regenerated axons are affected by various factors in the microenvironment of peripheral nerve regeneration, including cells, extracellular matrix and diffusion factors [16]. In the early stage of regeneration, there are degenerative axons and myelin sheath debris, including SC, fibroblasts, mast cells and macrophages, after peripheral nerve injury, the distal end of the nerve fiber lost contact with the neuron body, resulting in Wallerian degeneration of the whole length of the nerve fiber, under the light microscope, the axon swelling, irregular shape, fracture and dissolution can be seen [16]. Because of the continuity between the proximal end and the neuronal cell body, the degeneration of one or several nodes of Ranvier appears according to different degrees of trauma, in the process of peripheral nerve regeneration, the regeneration of proximal axons and the growth of distal axons are the necessary conditions of nerve

regeneration and the primary factor of nerve regeneration, and SC is exactly the most important factor in the micro-loop of peripheral nerve regeneration [16].

IL-1 β can aggravate Wallerian degeneration after nerve injury, accelerate the clearance of degenerative tissue, and recover the degree and function of nerve regeneration well, after the monocytes of rats are exhausted by dichloromethylene diphosphate liposome, the clearance of degenerated tissue after nerve injury is delayed and the early nerve regeneration is poor, IL-1 β can increase the synthesis and secretion of local neurotrophic factors (NGF and GDNF) in the early stage of injury, inhibit the proliferation of glial scar, and promote the regeneration of peripheral nerve [36]. The combination of medication in regeneration chamber and local injection of interleukin-1 β can be used as a method and means for the treatment of peripheral nerve injury [36].

D. Local Microenvironment and Reduction of Local Scar

The regeneration of peripheral nerve after repair is affected by many factors, the microenvironment at the anastomotic site and the formation of local vitiligo seriously affect the repair effect after nerve injury [18]. Therefore, improving the local microenvironment and reducing the local scar is conducive to peripheral nerve regeneration and promoting the recovery of nerve function [18]. Amniotic membrane is semi permeable, which can ensure the smooth passage of nutrients, promote the proliferation of Schwann cells, accelerate the growth of nerve axons, inhibit the biological activity of peripheral fibroblasts, limit the invasion of peripheral nerve tissue into nerve stumps, inhibit the formation of peripheral scar, and prevent nerve adhesion and nerve compression [18]. As a kind of biomaterial, human amnion has a good effect on repairing peripheral nerve injury, it can reduce the adhesion between the injured nerve and the surrounding tissue, reduce the scar formation at the nerve anastomosis, promote nerve fiber regeneration, increase the diameter of axon, and thicken the myelin sheath; it can reduce the inflammatory reaction and immune response at the nerve incision [18].

After peripheral nerve injury, a good microenvironment of nerve regeneration is beneficial to protect the injured neurons and promote the effective regeneration of axons, the results showed that the autogenous peripheral nerve tissue plasma catheter could simulate the microenvironment of peripheral nerve regeneration and promote nerve fiber regeneration, but there was still a gap between the two groups [5].

Biological cannula rich in NGF and nerve fragments plays an important role in the regeneration and repair of peripheral nerve injury, the observation results of repairing peripheral nerve injury with small gap of autogenous nerve adventitia and absorbable biological cannula under different factors intervention are obviously superior to the traditional end-to-end direct anastomosis; biological cannula can make up for the deficiency that the autogenous adventitia is easy to collapse and affect the effect of nerve recovery when repairing nerve injury [10]. The combined application of autologous nerve fragments and NGF can significantly improve the repair effect of nerve injury in the microenvironment of peripheral nerve regeneration, which provides a theoretical basis for guiding clinical repair of peripheral nerve injury [10].

Nerve regeneration needs a suitable guiding environment and appropriate biological factors to promote nerve regeneration [28]. According to this, a new type of RGD peptide grafted poly (lactic acid glycolic acid-l-lysine) / polylactic acid / β - tricalcium phosphate / nerve growth factor (PRGD / PDLLA / β - TCP / NGF) was prepared and characterized by cell culture in vitro and animal experiment in vivo to provide theoretical basis for clinical repair of peripheral nerve defect [28].

These factors affect, hinder and interfere with nerve regeneration, it is confirmed that there is tendency and nutrition in the process of peripheral nerve injury and regeneration; the regeneration of human peripheral nerve is also affected by the tendency and nutrition; making full use of the principle of tendency and nutrition for nerve repair can obtain very satisfactory clinical effect [45]. On the basis of these theoretical studies, this theory was introduced into clinical practice, and the systematic research and clinical application research of nerve defect vein bridging, small gap vein bridging nerve anastomosis, the treatment of stump painful neuroma and the application of exogenous nerve growth factor in the repair of peripheral nerve injury were carried out, and satisfactory curative effect was achieved [45]

Long term denervation after peripheral nerve injury can lead to terminal organ atrophy and functional loss [35]. However, the peripheral nerve cannot regenerate through mitosis of neurons after injury, only axon and myelin sheath regeneration can restore nerve function and achieve reinnervation of target tissue, the repair and regeneration of peripheral nerve after injury is a very complex pathophysiological process, and the results are closely related to the recovery of function, the degree of injury and reasonable treatment, the microenvironment and blood supply of the injured area are the main influencing factors [35].

In the repair of peripheral nerve, topical application of sodium hyaluronate gel or local suture with autogenous vein can significantly reduce scar formation, increase nerve conduction velocity and promote peripheral nerve regeneration in [33].

E. Stitching Techniques

Suture technology is one of the most important foundations of nerve regeneration, the epineurium suture method, which has been used in clinic all over the world, because it cannot make thousands of nerve fibers with different properties in the nerve trunk to connect accurately, which greatly affects the effect of nerve repair [3]. Meanwhile, it has been found that the regenerated nerve fibers can selectively grow into the distal nerve of the same nature, that is, the selective regeneration of the peripheral nerve [3]. The traditional epineurium suture method was changed to replace the peripheral nerve suture method which has been used for nearly 100 years [3].

The adhesion of anastomotic stoma after peripheral nerve amputation is the main factor affecting the recovery of nerve function, the application of effective, biodegradable and

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absorbable biomaterials into the anastomotic stoma can promote the growth of nerve fibers, Carboxymethyl chitosan carboxymethyl cellulose membrane can effectively prevent the formation of anastomotic neuroma and promote the regeneration of nerve fibers [6].

Although the end-to-end suture can be carried out by surgical method, the effect of nerve recovery is still not ideal, especially in the case of short-distance nerve defect, nerve conduit can provide a suitable microenvironment for nerve repair, so that nerve fibers can regenerate and reach the distal end smoothly [7].

After increasing the contact area of nerve stump, nerve fiber regeneration was good; increasing the contact area of nerve stump could obtain more effective nerve regeneration; the number of nerve fibers growing into the distal end was related to the contact area of recipient end anastomosis [2].

It is difficult to establish the original precise innervation relationship between nerve regeneration fibers and target tissues after the nerve regeneration fibers pass through the injured segment [8]. Therefore, the discovery of effective induction signals for regeneration and synaptic formation of target tissues after nerve injury is of great significance for the complete functional recovery after injury repair [8]. Nerve regeneration room, also known as nerve guide tube, is a natural or synthetic tube used to bridge nerve defects, venous catheter is one of the representatives of nerve regeneration room, the thin wall of the tube is conducive to the penetration of nutrients, the establishment of new blood supply, the stabilization of microenvironment of nerve regeneration, and the prevention of scar invasion [8]. In addition, autologous vein has the characteristics of wide source, easy sampling, no obvious influence on donor site and good histocompatibility, so it is often used [8]. The combination of Schwann cells and nerve conduits, combined with pulsed electromagnetic fields for real-time stimulation, can build a microenvironment conducive to nerve regeneration and effectively promote the repair of peripheral nerve defects [17].

In the animal experiment of small gap sleeve suture, the protective effect of small gap sleeve suture and cannula on regenerated nerve and preventing nerve from escaping to form neuroma were confirmed; the suitable gap length was found out, and the theory of coexistence of chemical induction and selective regeneration of nerve regeneration in gap was put forward; through the comparative study with epineurium suture group, small gap sleeve suture was confirmed [44]. In order to apply this technique to clinical practice, we independently designed and developed a biological tube bridge suitable for small gap sleeve suture in the world for the first time; in the world, we took the lead in using absorbable biological cannula to carry out systematic research on peripheral nerve regeneration from rats to primates, in addition, we boldly proposed to use small gap sleeve technique to repair peripheral nerve in clinic, instead of the nerve adventitia suture technology which has been used for nearly 100 years [44]. Thus, forming a minimally invasive, simple and significantly improved nerve regeneration effect of the new peripheral nerve suture technology [44].

F. Others Impacts

Nerve growth inhibitory factors (NGFS) prevent nerve regeneration, such as chondroitin sulfate proteoglycans (CSPGs) can inhibit axon growth, it exists not only in the central nervous system, but also in the peripheral nerve, it is widely distributed in the peripheral nerve sheath and neural stroma, and in the peripheral nerve injury, after treatment, its expression was significantly up-regulated and axonal regeneration was inhibited and chondroitinase sulfate ABC (chondroitinase ABC, ChABC) can degrade the Glucosaminoglycan (GAG) side chain of CSPGs, thus degrading CSPGs. Zuo and Tatsuya etc. found that after treatment of acellular nerve scaffold with ChABC, regenerated axons could pass through the anastomotic site of nerve and scaffold, and the number and growth length of regenerated axons in acellular nerve scaffold were significantly increased [26].

Factors that promote nerve growth promote nerve regeneration, after peripheral nerve injury, a series of complex changes will take place in the microenvironment of the local nerve, central nervous system and muscle, and regulate the expression of neurotrophic factors and some peptide substances, such as vascular endothelial growth factor (VEGF), calcitonin gene-related peptide (CGRP) and so on, the expression changes of these nerve growth promoting factors are closely related to the regeneration process after nerve injury [26].

Short term application of immunosuppressive therapy can rapidly reduce the immune rejection after peripheral nerve injury, to improve the microenvironment of regeneration after peripheral nerve injury, improve the speed and quality of nerve regeneration, and achieve the same effect as long-term application of immunosuppressive agents without fatal adverse reactions, which has potential significance for clinical application of immunosuppressants [4].

Brain injury can promote the repair of peripheral nerve injury to a certain extent, craniocerebral injury can reduce the scar healing of sciatic nerve, promote the growth of nerve fiber, accelerate the maturation of myelin sheath, and promote the rapid recovery of nerve morphology and function [19].

At present, with the increasing use of Extract from Rabbit Skin Inflamed by Vaccinia Virus for Injection (ERSVV) in the treatment of nerve repair, the route of administration from muscle injection and intravenous infusion to celiac plexus and subarachnoid space is also expanding [22]. Antiphlogistic and analgesic liquid combined with ERSVV is beneficial to the repair of injured nerve, ERSVV can repair the injured nerve better than intramuscular injection [22].

Polylactic acid biofilm and fibrin glue can effectively prevent nerve adhesion and promote nerve regeneration, methylpre dnisolone has a certain effect on preventing nerve adhesion and promoting nerve regeneration [25].

Yuhong (A Chinese Drug) ointment can promote wound healing and repair, improve the quality of healing: Yuhong ointment can promote the proliferation of fibroblasts and the secretion of collagen fibers in the proliferative phase of skin wound healing; Yuhong ointment can promote the secretion of

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neuropeptide substance P and promote the regeneration of nerve fibers in the process of skin wound healing [31].

The recovery of peripheral nerve function after repair is the result of many factors, including correct anastomosis, nerve fiber regeneration, axoplasmic flow recovery, active substance transportation, and finally the restoration of nerve conduction function [40]. Any defect will affect the effect of nerve repair, in the process of peripheral nerve injury repair, autologous vein wrapping can significantly improve the excellent and good rate of repair, and has no adverse effect on the autologous tissue, the effect is better than that of patients with simple nerve repair in the same period, this method is simple, practical and has good clinical effect [40].

There are many inhibitors of neurite regeneration in the myelin sheath of CNS, such as Nogo, myelin associated glycoprotein (MAG), oligodendrocyte associated glycoprotein (OMgp), this study confirmed the inhibitory effect of CNS white matter membrane protein on neurite growth, and the inhibitory effect was more obvious with the increase of protein concentration; while the neurite growth was inhibited, the mRNA expression of RhoA in neurons was significantly up-regulated, indicating that RhoA participates in the regulation process of neuronal axon growth [32].

Nerve growth factor (NGF) can promote the regeneration of peripheral nerve after injury [41]. However, its clinical application is limited because of its short half-life in aqueous solution and easy to be affected by humidity, pH and other factors [41]. Therefore, it is urgent to find a reasonable and effective route of administration and preparation, we propose: to prepare a NGF sustained-release system, which can delay the release of NGF, and the released NGF has biological activity, it can be applied to the local part of peripheral nerve electrical injury to release active NGF slowly in the local area, which may maintain a long-term role in the process of nerve regeneration and promote peripheral nerve regeneration [41].

Peripheral nerve injury is a kind of clinical disease that causes nerve conduction dysfunction, nerve axon interruption or nerve rupture, which leads to sensory, motor and sympathetic dysfunction of trunk and limbs, it seriously affects the labor force and quality of life of patients [42]. Regeneration and repair after injury has always been one of the focuses of trauma surgery and neuroscience, after the peripheral nerve injury, the myelin sheath and axon of the nerve fiber in the far part of the injury plane and the proximal part of the nerve fiber disintegrated and destroyed, namely Wallerian degeneration [42]. Then the injured proximal axons sprouted and extended into the distal Schwann cell line, which re myelinated the regenerated axons and established contact with the corresponding target organs, in addition, the central nervous system corresponding to the injured peripheral nerve can also be injured and regenerated, tissue repair and regeneration is inseparable from cell proliferation, so this process must involve the role of cell cycle regulatory proteins [42].

Neurotrophic factor (neurotrophic) is the most common neurotrophic factor Factors (NTF) is a kind of soluble protein produced by the body to regulate the survival, growth and differentiation of nerve cells [37]. The deficiency of endogenous neurotrophic factors after peripheral nerve injury is an important cause of nerve regeneration dysfunction and poor functional recovery, combined application of multiple exogenous neurotrophic factors to promote nerve regeneration has gradually become an important way to further improve the curative effect of nerve repair Methods [37].

However, the recovery of peripheral nerve function after repair is the result of many factors, including correct anastomosis, nerve fiber regeneration, axoplasmic flow recovery, active substance transport, and finally the restoration of nerve conduction function, any defect will affect the effect of nerve repair, in the process of peripheral nerve injury repair, autologous vein wrapping can significantly improve the excellent and good rate of repair, and has no adverse effect on the autologous tissue, the effect is better than that of patients with simple nerve repair in the same period, this method is simple, practical and has good clinical effect [40].

III. Conclusion

Peripheral nerve fiber regeneration might be affected by various impacts and functions. Comprehensive discussions about after peripheral nerve injury, tissue repair etc. always is being researched. According to previous contexts we discussed, there are five main factors: Schwann Cells (SCS); Vascular Endothelia Cells (VECs); Other Cells; Local Microenvironment and reduction of local scar; Stitching Techniques. However, many factors would still affect the result of peripheral nerve fibers regenerations. There are more comprehensive evaluations of the literature review, as well as the experimental works, ultimately, concerning of peripheral nerve fiber regeneration would represent at future.

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References

[1] Huang Y Q, Len J H, 2019. Research progress of nerve injury and repair in diabetic peripheral neuropathy (in Chinese). Chinese Journal of Pain Medicine, 25, 456-460.

[2] Jia Y W, Duan W P, Liang B SH, Zhang D F, Chang W K, Qiao H Y, Chen Zh & Li G, 2013. Experimental study on the effect of different anastomosis area on nerve end to side anastomosis (in Chinese). Journal of Practical Orthopedics, 19, 429-431.

[3] Kou Y H, Yin X F, Zhang P X& Jiang B G, 2011. Technique and new material for repairing peripheral nerve with small gap (in Chinese). Journal of Peking University (Medical Edition), 647-651.

[4] Song Y X, Ma Y H, Wang R J, Chen B & Liu J F, 2010. Injury and regeneration of peripheral nerve after short-term immunosuppressive limb transplantation in rats (in Chinese). Tissue engineering research and clinical rehabilitation in China, 14, 5786-5789.

[5] Qin J Zh, Wang P J & Wang Y, 2009. Experimental study on repairing peripheral nerve defect by wrapping myometrial flap with PLGA microfilament in amniotic tube to simulate the microenvironment of peripheral nerve regeneration (in Chinese). Tissue engineering research and clinical rehabilitation in China, 13, 3093-3096.

[6] Xiao H J, Hou Ch L & Xue F, 2009. Effect of carboxymethyl chitosan carboxymethyl cellulose membrane on peripheral nerve adhesion and regeneration (in Chinese). Tissue engineering research and clinical rehabilitation in China, 13, 6680-6684.

[7] Li X Q, Mo X M & Fan Ch Y, 2007. Research and development of nerve conduit (in Chinese). Chinese Journal of Bioengineering, 27, 112-116.

[8] Wang W J & Ding W L, 2006. Phenotypic expression of Schwann cells during development and after peripheral nerve injury and its influencing factors (in Chinese). Chinese Journal of Neuroanatomy, 22, 469-473.
[9] Shi Y M, Li F & Zhang J Y, 2006. Main influencing factors and possible mechanism of peripheral nerve myelination (in Chinese). International Journal of pathology and Clinical Sciences, 26, 169-172.
[10] Xu L J, 2016. Experimental study on repairing nerve injury with biological cannula rich in NGF and nerve fragments (in Chinese). Master, Inner Mongolia Medical University.
[11] Huang G, 2005. Effects of Schwann cells and venous cannula on regeneration of peripheral nerve defect (in Chinese). Master Thesis, China Medical University.
[12] Wang J F, 2015. Comparative study of nerve growth factor and nimodipine in the pretreatment of diabetic peripheral neuropathy (in Chinese). Master Thesis, Zhengzhou University.
[13] Gao Ch Zh, 2011. Study on the mechanism of fg-ngf glue film anastomotic stoma embedding promoting peripheral nerve growth (in Chinese). PhD Thesis, Shandong University.
[14] Zhao L, 2013. Effects of macrophages and surface topology on the expression of NGF and laminin in rsc96 cells (in Chinese). Master Thesis, Southern Medical University.
[15] Peng Y, 2013. Repair of long segment sciatic nerve defects in beagle dogs with highly simulated tissue-engineered nerve repair materials (in Chinese). PhD Thesis, The Fourth Military Medical University.
[16] Wang H B, 2013. Experimental study on Schwann cells of adult mouse sciatic nerve in vitro (in Chinese). PhD Thesis, Southern Medical University.
[17] Liu L, 2015. Activation of Schwann cells by pulsed electromagnetic fields and its application in the repair of peripheral nerve injury (in Chinese). PhD Thesis, The Fourth Military Medical University.
[18] Kou W G, 2015. Experimental study on the effect of fresh amniotic membrane on the repair of peripheral nerve injury (in Chinese). Master Thesis, Hebei Medical University.
[19] Wang W, 2015. Effect of craniocerebral injury on the repair of peripheral nerve injury (in Chinese). Master Thesis, Chengde Medical College.
[20] Yang J, 2010. Experimental study on treatment of sciatic nerve injury with trunk neural crest stem cells chitosan fiber and silicone tube (in Chinese). Master Thesis, Shandong University.
[21] Li Y J, 2011. Experimental study on co culture of Schwann cells and vascular endothelial cells in vitro (in Chinese). Master Thesis, Hebei Medical University.
[22] Zhou Y J, 2009. Effects of anti-inflammatory and analgesic solution combined with extracts from rabbit skin inflamed by vaccinia vaccine in different ways on repair of sciatic nerve injury in rats (in Chinese). Master Thesis, Hebei Medical University.
[23] Hu X Y, 2009. Preparation and application of high-fidelity tissue engineering nerve repair materials (in Chinese). PhD Thesis, The Fourth Military Medical University.
[24] Qing J Zh, 2007. Experimental study on repairing peripheral nerve defect by transposition of adventitia and implantation of PGLA microfilament in amniotic tube (in Chinese). Master, Guangdong Medical College.
[25] Chen B, 2008. Experimental study on the effect of anti-adhesion methods on the repair of peripheral nerve injury (in Chinese). Master Thesis, Department of medicine, Zhejiang University.
[26] Wang Y, 2011. Effect of bone marrow mesenchymal stem cells combined with chondroitinase ABC on the repair of sciatic nerve defect in rats (in Chinese). PhD Thesis, China Medical University.
[27] Meng H, 2011. Application of photochemical technology in tissue engineering repair of sciatic nerve injury in rats (in Chinese). PhD Thesis, The Fourth Military Medical University.
[28] Yan Q J, 2008. Preparation of prgd / PDLLA / β - TCP / NGF composite nerve conduit and its application in peripheral nerve repair (in Chinese). PhD Thesis, Wuhan University of Technology.
[29] Zhang X Q, 2008. Expression of apoptosis and pathological changes of peripheral facial nerve after facial nerve transection in rabbits (in Chinese). Master Thesis, Anhui Medical University.
[30] Feng X F & Wang Sh Sh, 2012. Clinical report of 108 cases of peripheral nerve injury repaired by nerve adventitia micro regeneration chamber (in Chinese). Proceedings of the national peripheral nerve conference of hand surgery branch of Chinese Medical Association and the third academic conference of hand surgery in Northeast China. Shenyang.
[31] Huang Q Y, 2007. Experimental study of Yuhong ointment on neuropeptide substance P and nerve fiber regeneration in the process of skin wound healing and repair in rats (in Chinese). Master Thesis, Chinese Academy of traditional Chinese Medicine.
[32] Deng Q Y, 2006. Design and screening of NgR and nep1-35 binding peptide and its promotion of central nerve regeneration (in Chinese). PhD Thesis, Third Military Medical University.
[33] Wei Y, 2003. Experimental study on the effect of sodium hyaluronate gel and autologous vein on scar formation to promote peripheral nerve regeneration (in Chinese). Master Thesis, Qingdao University.
[34] Xiao Y H, 2005. Experimental study on repairing peripheral nerve defect with tissue engineering artificial nerve (in Chinese). PhD Thesis, Sichuan University.
[35] Zhao Zh H, 2008. Effect of Xiaoyan Zhentong liquid combined with injection of extract from rabbit skin inflamed by vaccinia vaccine on repair and regeneration of sciatic nerve injury (in Chinese). Master Thesis, Hebei Medical University.
[36] Luo Y Ch, 2004. Regulation of Wallerian degeneration and its effect on sciatic nerve regeneration in rats. Master Thesis (in Chinese), Third Military Medical University.
[37] Chen J, 2005. Effect of combined application of neurotrophic factors on peripheral nerve regeneration and its visualization (in Chinese). PhD Thesis, Chongqing University.
[38] Yin Zh G, 2007. Chondroitinase ABC promotes axonal regeneration after autologous nerve transplantation (in Chinese). PhD Thesis, Tianjin Medical University.
[39] Yang W B, 2010. Experimental study on the treatment of brachial plexus injury with end to side neurorrhaphy (in Chinese). PhD Thesis, Fudan University.
[40] Guangrao people's Hospital, 2011. Experimental study and clinical application of autogenous vein wrapping in the repair of peripheral nerve injury (in Chinese).
[41] Xiong H H, 2006. NGF sustained release system promotes regeneration of sciatic nerve after electrical injury in rats (in Chinese). PhD Thesis, School of medicine, Nanchang University
[42] Shi Sh X & Shen Ai G, 2007. Relationship between p27kip1, Skp2 and peripheral nerve injury and regeneration (in Chinese). The 7th Biennial Meeting and the 5th Congress of the Chinese Society for Neuroscience Proceedings. Hangzhou.
[43] Cheng S Y, 2005. Experimental study on the treatment of peripheral nerve injury with genetically engineered neural stem cells combined with tissue engineering materials (in Chinese). PhD Thesis, Third Military Medical University.
[44] Jiang B G, Sun Y Sh & Zhang P X, 2010. Technique and new material for repairing peripheral nerve with small gap (in Chinese). Peking University.
[45] Yi W T, Wang G J, Gao Q G, Cui Sh S, Zhang J, Liu B, Xu zh M, Wei Zh, Zhang J, Li Q L, Zhu Q Y, Wang Y F, Yang J & Li Y, 2001. Animal experiment and clinical study on the tropism of peripheral nerve (in Chinese). Jilin University.

Jian Gao, "Discussion about comprehensive impacts in peripheral nerves fibers regeneration," *International Journal of Multidisciplinary Research and Publications (IJMRAP)*, Volume 3, Issue 6, pp. 74-79, 2020.