Ultrastructural Observation of Axon Complex of Epithelial Cells after Nerve Implantation into Denervated Fingers of Monkey

Haiou Zhang
Lei Wu
Weiyan Zhao
Chunlei Zhu
Lingling Wang

Abstract: The recognition of visual shape in monkeys depends on a multi-layer pathway from primary visual cortex to lower temporal cortex. Visual stimulation is received by retina and then projected to the primary visual cortex VI region through lateral geniculate nucleus. There are a large number of neurons activated by linear stimulation such as short side and line segment. This paper mainly studies the ultrastructural observation of axon complex of epithelial cells after nerve implantation in monkey nerve loss fingers. Through the ultrastructural view of epithelial axon complex, we can master the changes of nerve regeneration function to skin cells and solve the problems caused by nerve defects. this paper mainly studies the method of nerve implantation, uses the neural interface model and the algorithm of nerve electrode, and compares the experiment with the monkey without nerve implantation, and then observe the synaptic ultrastructure under the electron microscope after the experiment to find that nerve implantation can promote the skin sensory organs. The results showed that the repair of sensory cells was faster than that of the skin sensory cells after nerve implantation in the ultrastructures of epithelial axon complex after nerve implantation in monkeys. 90% of the cells implanted with nerve were very fast to repair, which could provide useful information for the study of peripheral nerve regeneration in the nervous system. Nerve implantation regeneration has been a medical research the research focus of the topic,medical researchers hope to find an effective method of nerve implantation for skin cell repair.

Keywords: Nerve Implantation, Epithelial Axon Complex, Skin Sensory Function, Nerve Regeneration
Tob Regul Sci.™ 2021;7(5): 1406-1415
DOI: doi.org/10.18001/TRS.7.5.59

Since 1870, after more than 100 years of microsurgery, Taylor and ham reported the success of the self-implantation of anastomosed blood vessels for the first time in 1976. Since then, the research on nerve implantation with and without blood vessels has been emerging, and the results are different. There are some controversies between the implantation of the ideal soft tissue bed and the non-vascular nerve implantation. Most researchers believe that the effect of vascular nerve implantation is better than that without vascular, while few people's research does not support this view. Among them, the study of setuergren and wood found that the blood flow of the implanted segment without blood vessels was significantly higher than that of

Haiou Zhang Department of Hand and Foot Surgery, Affiliated Hospital of Beihua University, Jilin 132012, Jilin Province, China, Lei Wu Department of Cardiothoracic Surgery, Jilin Central Hospital, Jilin 132001, Jilin Province, China, Weiyan Zhao Department of Hand and Foot Surgery, Affiliated Hospital of Beihua University, Jilin 132012, Jilin Province, China, Chunlei Zhu Department of Hand and Foot Surgery, Affiliated Hospital of Beihua University, Jilin 132012, Jilin Province, China, Lingling Wang Precision Medical Center,Affiliated Hospital of Beihua University,Jilin,132012,P.R.China .Corresponding Author: Lingling Wang 12 Jiefang Road,Jilin,132012,P.R.China 79225834@163.com,* *Acknowledgement: Jilin Provincial Department of Health Research Project (No. 2014Q004), Jilin Provincial Department of Health Research Project (No. 2018J084), Jilin Science and Technology Bureau Medical and Health Key Projects (No. 201830461)，Jilin Science and Technology Bureau Medical and Health Key Projects（201830823）*

the nerve implantation section with blood vessels 4-6 days after operation. It was believed that the nerve implantation in the ideal soft tissue bed was very fast even without the vascular.

The placement order of the autogenous nerve implants can be divided into: anterograde placement and retrograde placement. Nerve implantation is that each segment of the implanted nerve is placed in a smooth way, which seems to be more logical in theory. In the experiment, the treatment effect of the nerve cell defect is also good. The study on which nerve placement is better than retrograde placement is not much at present, and there are less studies on the additional band and no vascular. In view of this design, the experiment is designed. The ultrastructural structure of axon complex of epithelial cells after nerve implantation in monkey nerve loss finger was used to carry out self-nerve implantation by bundle membrane suture. The ideal method was found out by comparing the two methods: placing nerve implantation along the way with blood vessel, placing nerve without blood vessel, retrograde placement with blood vessel and retrograde placement without blood vessel.

Nerve implanted nerve fibers, including quantitative intraepidermal nerve fibers, are considered to be less likely to develop symptoms. Patients with neurofibrosis and neuralgia can provide diagnostic information because of the low degree of neurofibrosis, which can be detected by routine electrophysiological examination. Green J believes that the motor nerve transfer and replantation time had an effect on the regeneration of nerve roots. The bilateral paravertebral muscles were dissected about 3cm from the posterior incision of cervical spine. The bilateral lamina was removed, C5-7 nerve roots were removed from the left side, C6 nerve roots were replanted in the anterior lateral spinal cord, and then the brachial plexus nerve and musculocutaneous nerve were exposed to 3cm away from the incision. The longitudinal branch 1 of the median thoracic nerve and the end branch of the musculocutaneous nerve were synthesized One family, put the monkey of thoracic median nerve in the foster family for 3 months, and then implanted the monkey into the host family one month after operation by the anterior operation. The motor nerve was implanted into the host family in the early stage, which promoted the regeneration of skeletal muscle through the spinal nerve root after replantation, and continued to foster. However, the experimental research lacks specific data [1]. Gonzalezcarpio g believes that the intrinsic movement area in skeletal muscle is the best part of muscle nerve reinnervation. The effect of direct nerve implantation in the denervated area of sternocleidomastoid muscle was cut off from the right SM muscle. The distal end of the severed SM nerve was immediately implanted into the small muscle seam of nmz in the muscle in the end plate of denervation. The effect of DNI nmz reinnervation was evaluated 3 months after operation. Specifically, the degree of functional recovery is measured by muscle force measurement. The nmz in muscle is the ideal part of the reinnervation and function recovery of the endplate nerve. Further research is needed to improve the effect of DNI nmz technology in muscle nerve reinnervation, but there is no necessary experimental data [2]. Weyers L believes that upper respiratory tract stimulation is FDA approved treatment plan, and is suitable for patients with moderate to severe obstructive sleep apnea who cannot persist in continuous positive airway pressure ventilation. UAS can reduce apnea and hypopnea index in the control clinical trials and academic institutions, but there is no content of numerical analysis [3]. Franke s considered that the over activation of the sympathetic nervous system of the heart will increase the severity of heart failure correspondingly and with a worse prognosis. As it is not clear whether there is similar CSN activation in patients with aortic stenosis, the effect of transcatheter aortic valve implantation is significantly reduced. WR of MIBG can be used as a useful indicator of CSN activity and severity in as patients, but some of them are not accurate [4].

The innovation of this paper is to use the method of nerve implantation, the neural interface model and the algorithm of nerve electrode, and the experimental contrast experiment between the implanted nerve and the monkey without nerve implantation, and the observation of synaptic ultrastructure under the

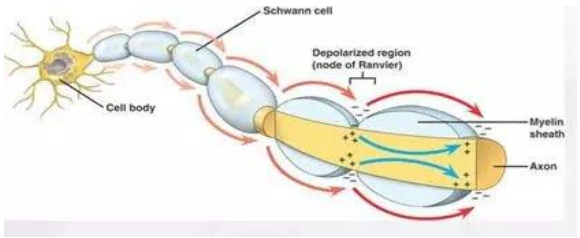
electron microscope after the experiment to find that nerve implantation can promote the repair and regeneration of peripheral nerve defects [5,6]. TNerve implantation quantification of nerve fibers in epidermis can be used for early detection or evaluation of diabetic neuropathy, which has made great progress in clinical traditional Chinese medicine [7].

NERVE IMPLANTATION

Nerve Implantation

After more than 100 years of research, the results of neural implantation are many, but the clinical treatment is not effective [8]. There are still questions about the repair and regeneration of nerve injury [9,10]. How to improve the neurons after peripheral nerve injury to prevent death, create the axons for regeneration, how to guide the graft into the end of the road nerve fibers to target organs, long-term loss of nerve control, can reduce the atrophy and dysfunction of target organs [11]. The results show that the sensory nerve and motor nerve fibers can reach the maximum value of the target organ [12]. The target auto nerve transplantation of organ function recovery results in the loss of donor nerve function. However, the source is limited but no substitute for the auto transplantation has been found. The peripheral nerve defect, defect repair and nerve regeneration are reduced, and the transplantation segment can be preserve [13]. Blood circulation has an important effect on nerve regeneration, and there is no obvious polarity in the head and tail of the nerve transplantation segment. The difference is that the research of artificial neural materials has some enlightenment significance. The blood circulation problem may be an important problem of artificial neural materials, and its effect is not as good as that of autogenous transplantation [14]. The research of artificial neural materials should not only pay attention to the basic structure of the materials, but also the addition of materials, cells, cytokines, etc., and how to construct a good biomaterial blood flow as shown in Figure 1:

Figure 1.
Nerve implanted nerve signal source
（http://alturl.com/idjx9）



Neural Interface Model

Capacitance

When we place the electrode in aqueous solution, the water molecules will be polarized due to the contact potential, and the positive end of hydrogen will be close to the metal side [15,16]. The thickness of the charge layer formed by the specific adsorption is only about a few angstroms [17]. On the outside of the polarized water molecule, there is a layer of hydrated ions wrapped by the polarized water molecule with opposite charge to the met [18]. The solution ions in this layer and the charges in the metal layer are only affected by the long-term electrostatic charges (called non-specific adsorption ions), which are affected by the thermal disturbance of the solution, it is dispersed in a distant three-dimensional region, generally in a few nanometers. The two charge layers and the metal interface with opposite charges form a series capacitor structure:

$$C_{fab} = \frac{\varepsilon_1 \varepsilon_2 D}{b} \quad (1)$$

ε_1 is the permittivity of free space， ε_2 It is the relative permittivity in 25 ° C water environment, and its value is 78.54, which can be as low as 6 in the environment of electric double layer capacitance

$$\frac{C_{fab}}{D} = 5.3 \times \frac{10^{-11}}{b} \quad (2)$$

Suppose B = 5V,C_{fab}的 The value is 11 f [19].

According to Gauss theorem, the capacitance near the electrode can be deduced as follows:

$$C_{bff} = \frac{\varepsilon_1 \varepsilon_2 D}{\lambda} cosh(hv_0/2v_t) \quad (3)$$

Where D is the electrode area, λ is the Debye length, h is the charge number of the ion band, the thermal voltage at room temperature, and the total capacitance is:

$$\frac{I}{C_{fab}} = \frac{I}{C_{ab}} + \frac{I}{C_{bff}} \quad (4)$$

Because in neural networks, the initial value of the hidden layer activation is usually used as the output of the next layer. So, we set up $c_j^{(1)}$ the input value of the activation function of the jth neuron in layer is as follows:

$$c_j^a = \sum_{i=1}^{r_{a-1}} h_{ji}^{a-1} r_i^{a-1} + a_j^{a-1} \quad (5)$$

Input data x= ($X_1, X_2^K \; X_i$) the forward propagation process of multilayer feedforward network.

Resistance

Charge transfer: the interface with charge transfer is generally called Faraday interface, which means that there is electrochemical reaction at the interface, and it exists before reaching the redox threshold. Electrochemical reactions include charge transfer from solution to metal interface and reverse transfer [20]. The current density between the electrode and the solution, which is formed by the electron increasing and electron removing effects of electrochemistry, can be obtained by the Butler Volmer equation:

$$i = i_0 \, exp(\frac{b_b H}{AT}\eta) - i_0 \, exp(\frac{b_c H}{AT}\eta) \quad (6)$$

Where I is the current density, η Voltage applied or called overpotential, b_b, b_c The transfer coefficients reflected by anode and cathode are respectively. From the expression, it can be seen that the total net current is increased, and the load transfer impedance is used to describe the difficulty of charge transfer. When the over potential is very small, the net current equation can be regarded as a linear equation, and the net current can be simplified as follows:

$$i = i_0 \left(\frac{\eta H}{FT}\right) \quad (7)$$

$$H = \frac{HT}{i_0 F} \quad (8)$$

For any electrode, because the ions are affected by the diffusion velocity of solution, there is a saturation current or limit current. The impedance limited by diffusion is called diffusion impedance. Under the condition of sinusoidal voltage excitation, it will drive a spatial distribution of ion concentration. With the increase of frequency, the concentration gradient at the electrode interface will also increase and then the current increases:

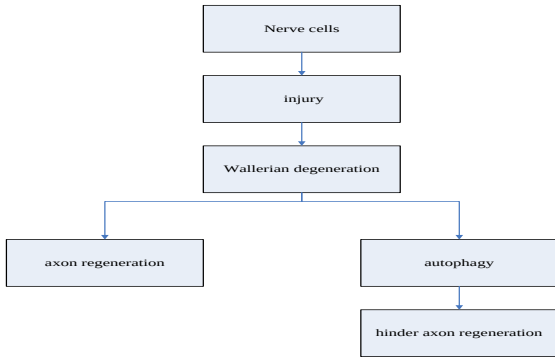
$$|H_b| = \frac{a}{\sqrt{f}} \quad (9)$$

Axonal Regeneration

The cell body and axon of a neuron are a whole. The cell body and axon often need transportation and exchange. The bidirectional axoplasmic transport of axon is not only the premise of material transportation and exchange between cell body and axon, but also plays an important role, On the one hand, anterograde transport transports neurotransmitters and neurotrophic factors from nerve cell body to axon end, stimulates nerve endings and effectors, and maintains the activity and function of innervating effectors, as shown in Figure 2:

Retrograde transport transports neurotrophic factors and nerve inducible factors from nerve endings to cell bodies to maintain physiological functions. In addition, retrograde degeneration may occur in the proximal axons of the injured area after peripheral nerve injury, and the degree of degeneration is related to the location and severity of the lesion. The more serious the lesion is and the closer it is to the cell body, the more likely it will lead to the death of neurons. The cell body of neurons is the premise of axon regeneration. If the cell body of neurons dies, the nerve cannot regenerate.

Figure 2.
Molecular mechanism of axonal regeneration



Nerve Electrode

Where is the frequency of the sinusoidal voltage. The diffusion impedance can be expressed in series or parallel capacitance and resistance models. In the parallel model, Warburg impedance can be expressed as:

$$H = (\frac{1}{R_i} + j2\pi \cdot a \cdot C_i)^{-1} \quad (10)$$

Among them, f is the ion concentration and B is the diffusion coefficient. In salt solution, Warburg impedance is much smaller than charge transfer impedance in the range of 100 Hz-10 kHz, so it is unnecessary to consider in high frequency circuit model:

$$R_i = \frac{1}{2\pi} \cdot f \cdot C_i \quad (11)$$

$$R = 10^6 \frac{V}{qbD\sqrt{\pi f A}} \quad (12)$$

In practical solution, the frequency response characteristics of double-layer electric layer are not directly equivalent to pure capacitance, but slightly or greatly deviated. This phenomenon is called "dispersion effect":

$$Z_Q = \frac{1}{F(ir)^n} \quad (13)$$

In the long-term recording process of implantable electrodes, many factors affect the normal recording of signals. One of the main reasons is hardware failure

$$HRE = 10\,log(\frac{{A_h}^2}{{A_r}^2}) \quad (14)$$

The disturbance current generated by the neural electrode increases the noise amplitude. The magnitude of thermal noise is not related to the applied voltage, but closely related to the impedance

$$A_{ktf} = \sqrt{kTF\Delta h} \quad (15)$$

OBSERVATION EXPERIMENT AFTER NERVE IMPLANTATION OF MONKEY'S DENERVATED FINGERS

The nerve implantation has been proved by clinical and animal experiments to promote the recovery of skin sensory function. In order to understand the changes of sensory terminal after nerve implantation, the ultrastructural changes of axon complex of M Erkel cells were observed after nerve grafting of monkey fingers.

Materials and Methods

Animal group

Nine monkeys were randomly selected, with a weight of 4-6kg. The fingers were randomly divided into three groups: 19 fingers in nerve transplantation group and 15 fingers in non-transplantation group. The normal skin of group B was controlled by 6 fingers.

Experimental methods

The median incision of the finger was performed under acetone radon anesthesia. Two finger nerves were taken, the other was removed from the root of the finger, and the dorsal branch of ulnar nerve and the superficial branch of radial nerve were cut off. The nerve transplantation group implanted the spare nerve under the finger flap. Nerve transplantation group: dorsal nerve removal; normal control group: normal observation of abdominal skin hanging, after observation, from the abdomen of the finger, transmission electron microscopy observation. In the normal control group, m Erkel cells were distributed in basal cell layer, close to basement membrane. The cell body is kidney shaped embedded in the basal cells and forms the bridging grain connection. The nucleus is oval on one side, and there are various neuroendocrine granules and a large number of mitochondria in the cytoplasm.

Observe the Nerve Implantation Group

According to the experiment, we observed the ultrastructures of axon complex of epithelial cells after nerve implantation into the denervated finger of monkey. No nerve fiber regeneration was found in the epidermis and dermis of palmar skin, most of them were m Erkel cells showed that the cell volume decreased, mitochondria and neuroendocrine granules decreased, mitochondria changed from oval to pea shape, and the connection between mitochondria and epidermal basal cells was broken. The axonal membrane of nerve endings outside the cell breaks, the axoplasm overflows, the axial membrane fragments scattered in the cell, and the microfilaments and microtubules in the axonal plasma disappear. The small part of M Erkel cells with crescent shaped space outside the m Erkel cell have the dissolution degeneration as shown in

Table 1:

Table 1.
The original data of nerve implantation in experimental group

Serial number	Left	right
1	567	234
2	563	176
3	523	145
4	543	156
5	524	87

The number of labeled cells increased gradually from 4 to 12 weeks after operation. The number of labeled cells was 58 at 4 weeks after operation, compared with the normal side, there was statistical significance; at 8 weeks, the number of labeled cells on the operation side was significantly higher than that on the normal side, reaching 116.27% of the normal side, which was statistically significant; at 12 weeks, the number of labeled cells on the operation side was significantly higher than that on the normal side, accounting for 131.91% of the normal side. Compared with the normal side, the difference was statistically significant, as shown in Table 2:

Table 2.
Comparison of preoperative bilateral finger swing data in monkeys

Finger	frequency	amplitude
Right	6	46
Lef	7	48
P	0.56	0.76

No Nerve Graft Group

The degenerated Merkel cells were observed in all groups under microscope, and there was no axonal complex structure of regenerated Merkel cells. Compared with the nerve grafts, the process of degeneration was faster. The nerve began to enter the epidermis, mainly near the blood vessels in the dermis, and ran randomly after entering. Merkel cells also migrate along the basement membrane, and the two eventually establish a connection, which may be driven by chemotaxis, as shown in Figure 3:

Skin Sensory Organs

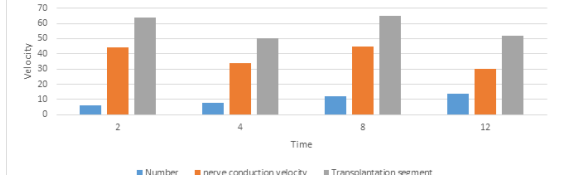
Skin is the largest organ of human body, and it has abundant nerve fibers. After nerve injury, nerve structure and integrity are damaged, may lead to abnormal or missing nerve function, organ degeneration and degeneration. Skin biopsy is a common tool for the diagnosis and treatment of skin diseases, which provides valuable information for the diagnosis, treatment, prognosis and diagnosis of the disease. Because they only reflect the function of nerve fibers, Dulles quantitative sensory test can reveal the sensory dysfunction of diseased nerve fibers, but they rely heavily on the coordination of patients and cannot distinguish peripheral sensory pathway or central sensory pathway. Skin biopsy cannot reveal the etiology of human epidermal and dermal small nerve fiber neuropathy. It can be used for the diagnosis and follow-up of peripheral neuropathy such as diabetes and impaired glucose tolerance. Skin biopsy can also be used for the study of small nerve fiber neuropathy.

ULTRASTRUCTURAL OBSERVATION AND ANALYSIS OF NERVE IMPLANTATION AND EPITHELIAL CELL AXON COMPLEX

Observation of Skin Sensation

Finger skin defect is often accompanied by finger nerve injury. Nerve injury belongs to the category of peripheral nerve injury. Peripheral nerve injury refers to a clinical disease caused by ischemia, axon interruption or malnutrition and nerve conduction function damage. Nerve channel rupture leads to sensory, motor and sympathetic dysfunction of trunk or limbs. At present, there is no ideal method for the treatment of peripheral nerve injury. Nerve continuity reconstruction is the only traditional nerve anastomosis method (epineurium suture, transverse membrane suture, nerve fiber bundle suture, etc.) which has been used in peripheral nerve injury for a long time. There is no obvious nerve defect at the broken end. Under the appropriate environment, axons can germinate and expand to the bundle nucleus. Many scholars have proposed a bridging method to repair the

Figure 3.
Nerve conduction velocity was measured



biomaterial cannula of peripheral nerve injury, which has been verified by experiment or clinical application, as shown in Table 3:

Table 3.
Evaluation index and evaluation standard

Evaluation index	excellent	good	poor
Skin color	similar	slightly purple	purplish red
Appearance	2	3	5
Sweating	normal	reduced	no sweating
Pain	normal	dull	disappear

According to table 3, we should take anti infection, anticoagulant, anti-vasospasm and neurotrophic drugs regularly after the operation, closely observe the color, temperature, tension and capillary filling reaction of the flap, find out the vascular crisis in time and treat it in time. In the appropriate environment, axons can germinate and extend into the nucleus tractus. Many researchers have proposed a method of repairing peripheral nerve injury with biomaterial. In the experiment or clinical application of concentrated adhesive, the sealing water is first poured into the liquid, and then the filter paper completely sucks out the sealing water. After the preparation of concentrated adhesive, it continues to flow along the glass plate until the adhesive preparation tank is full and the adhesive is small Insert the comb carefully, pay attention not to operate after. When the glue is completely set, hold both ends of the comb vertically and gently take it out. The experimental verification is achieved, as shown in Figure 4:

Figure 4.
The number of various components corresponding to different gel volumes

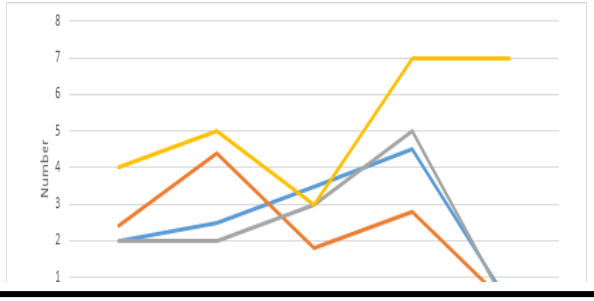


Figure 4 shows that skin biopsy for quantitative analysis of intraepidermal nerve fibers is considered to provide diagnostic information for patients with symptomatic small nerve fiber lesions and neuropathic pain. Because small nerve fiber degeneration cannot be detected by routine electrophysiological examination, it is very difficult to make a clear diagnosis in clinical practice. Although skin biopsy cannot be used to reveal the cause of small neurofibropathy, it can sometimes be used in patients with diabetes or impaired glucose tolerance. In some patients, it may be cutaneous vasculitis. The non-length dependence of nerve fiber density may also indicate the occurrence of sensory gangliopathy. Symptoms of small nerve fibers usually occur when medullary nerve fibers are involved. In these patients, routine electrophysiological examination is usually used, and skin biopsy is often not considered to be of routine value.

Ultrastructure of Synapse Was Observed under Electron Microscope

The cell body and axon of a neuron are a whole, and they often need transport and exchange. The bidirectional axoplasmic transport of axon is not only the premise of material transport and exchange between cell body and axon, but also plays an important role. On the one hand, anterograde transport transports neurotransmitters and neurotrophic factors from nerve cell body to axon end, stimulates nerve end and effector, maintains the activity and function of dominant effector; on the other hand, retrograde transport transports neurotrophic factors and neurotrophic factors from nerve end to cell body, maintains the physiological function of nerve cell body. In addition, after peripheral nerve injury, retrograde degeneration of axons in the proximal part of the injury site will occur, and the degree of retrograde degeneration is related to the injury site and severity. If the injury is serious, the closer the lesion is to the cell body, the more likely it will lead to neuronal death. Neuronal soma is the premise of axonal regeneration. If neurons die, they cannot regenerate. In this experiment, the sciatic nerve transection was close to the cell body of neurons. After the transection, only the continuous treatment of repairing nerve was carried out, so the death of neurons could not be avoided. The degeneration and atrophy of the operative side might be caused by the death of some neurons. The thickness of synaptic PSD became thinner, the curvature of synaptic interface decreased, and the width of synaptic gap increased ADAM10

deletion results in abnormal synaptic structure and reduced synaptic plasticity in monkey neurons as shown in Table 4:

Table 4.
The synaptic ultrastructural parameters of CA1 region in monkeys

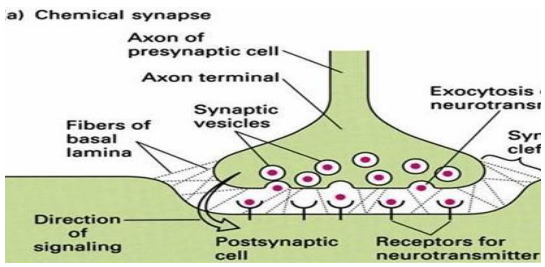
Group	control	cKO
number of synapses	37	34
thickness of PSD	32	21
width of synaptic gap	15	16
curvature of synaptic	1	1.5

It can be seen from table 4 that the synaptic ultrastructure of monkey CA1 region was observed by transmission electron microscope combined with stereology. The thickness of PSD, the width of synaptic gap and the curvature of synaptic interface were selected among many synaptic ultrastructural parameters. Mitochondria and a large number of round synaptic vesicles were found in the presynaptic area. The presynaptic membrane, postsynaptic membrane and synaptic gap can be clearly identified. The postsynaptic membrane of some synapses is obviously thicker than the presynaptic membrane.

Synaptic Plasticity

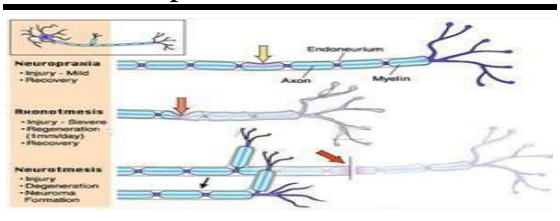
It refers to the characteristics of synaptic efficacy that can be changed for a long time, generally including structural plasticity and functional plasticity, which are interrelated and interact with each other. The plasticity of synaptic function shows the enhancement or weakening of synaptic information transmission ability, and the plasticity of synaptic structure shows the change of synaptic structure and synaptic function. The general parameters of synaptic ultrastructure include synaptic interface, thickness of synaptic dense area, width of synaptic gap, synaptic number density, synaptic area density, etc. ADAM10 CKO monkeys had abnormal spinal morphology and impaired synaptic function. Compared with the same month old wild-type monkeys, the curvature of synaptic interface increased in the multiple neurofibroma type 1 model monkeys, indicating the importance of synaptic interface curvature in synaptic plasticity and learning and memory function. Compared with normal monkeys, the curvature of synaptic interface and the thickness of PSD in the CA1 area decreased, the width of synaptic gap increased, and the spatial learning and memory were impaired. Finally, the results of transmission electron microscopy showed that the curvature of synaptic interface decreased, the thickness of postsynaptic dense zone decreased, and the width of synaptic gap widened in CKO monkeys as shown in Figure 5:

Figure 5.
Synaptic connection
(http://alturl.com/fz8tv)



From Figure 5 we can see that ADAM10 and synapse associated protein 97 (SAP97) anchor the function and occurrence of synapses, and ADAM10 deficiency leads to synaptic dysfunction. The expression of synaptophysin and PSD-95 decreases and the ultrastructure of synapses are abnormal. The aggregation of a β and the tight binding of β - amyloid protein with PIRB receptor on nerve cells activate the process of intercellular movement and erode the synapse of nerve cells, resulting in the disorder or even loss of synaptic contact, as shown in Figure 6:

Figure 6.
Axon of nerve cell
(http://alturl.com/iuedt)



Quantitative analysis of intraepidermal nerve fibers in skin biopsy is considered to provide diagnostic information for patients with symptomatic small nerve fiber lesions and neuropathic pain. Because small nerve fiber degeneration cannot be detected by routine electrophysiological examination, it is very

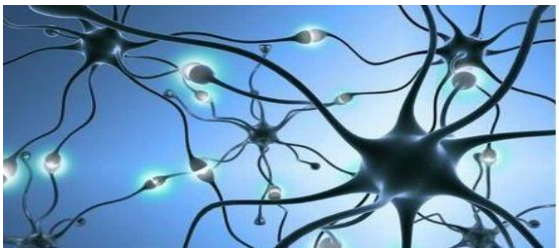
difficult to make a clear diagnosis in clinical practice. Although skin biopsycasnnot be used to reveal the cause of small nerve fiber lesions, the expression values of different genes in different samples are shown in Table 5 :

Table 5.
Differential gene expression in different samples

Groups	Up-regulation	Down-regulation
1d	300	123
3d	521	456
1w	1023	1170
3w	590	145

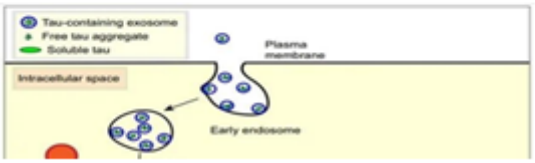
Synapse is the basis of nerve pulse transmission (between neurons or between neurons and cells), and it is the connection between neurons and the key parts of nerve transmission in function. Synapses are composed of presynaptic membrane, synaptic gap and postsynaptic membrane. At present, there are three known proteins related to synaptophysin, vesicle associated membrane protein and synaptophysin, as shown in Figure 7:

Figure 7.
Neural network axons
(http://alturl.com/tmhy8)



A synaptic protein closely related to synaptic plasticity was studied. Postsynaptic density protein (PDP) is one of the proteins that regulate postsynaptic and axonal pathways to promote axonal elongation and density in PC12 cells. It affects the remodeling of synaptic structure and function and plays a very important role in the development and regeneration of neurons, as shown in Figure 8:

Figure 8.
Brain hemodynamic response pattern (
http://alturl.com/mnzi2)



In the peripheral nervous system, the morphological changes of the epidermal nerve and intradermal nerve, small swelling and varicose veins were observed by observing the skin biopsy of the distal leg of healthy people. Accompanied by large axon swelling, it is considered to affect the differentiation of normal nerve fiber structure cells, plays an important role in animal growth and development and body damage repair, participates in the differentiation of many cells and plays an important role. It can promote the differentiation of hematopoietic stem cells, combines with hematopoietic stem cell genes and negatively regulates the expression of Ge, which is the target gene of miR-181c. It can catalyze histone methylation and miR-181c overexpression, and promote the differentiation of esch cells.

CONCLUSION

In this paper, we studied the method of nerve implantation. We used the model of nerve interface and the algorithm of nerve electrode to compare the experiment between the implanted nerve and the non-implanted monkey. We observed the synaptic ultrastructure under the electron microscope. It showed that the nerve implantation stimulated the skin sensory organs, and the regenerated axons grew and extended along the appropriate physical channels to replace the degenerated and missing axons. The second tibia toe free flap can be used to repair the skin and nerve defects of fingers. The Schwann cells secreted neurotrophic proteins and cell adhesion molecules, and the regenerated axons were

induced to enter the bugner band through the gap between the nerve ends. Promote regeneration and repair tension. After peripheral nerve injury, whether it can regenerate successfully depends on maintaining the activity of nerve body, preventing irreversible degeneration and maintaining growth state. The key is to provide a good environment for the damaged peripheral nerve and promote nerve regeneration and functional recovery. But in clinical work, often accompanied by nerve defects, it must be through nerve repair in order to achieve the recovery of nerve function[21].

REFERENCES

1. Huang C, Zhang Y, Liu M, Huang J, Zhang W. Effect of persistence and protophase motor nerve baby-sitting on nerve function recovery in nerve root re-implantation for brachial plexus avulsion injury. Chinese Journal of Trauma. 2016;32(8):759-762.
2. Yumoto E, Sanuki T, Toya Y, Kodama N, Kumai Y. Nerve-muscle pedicle flap implantation combined with arytenoid adduction. Archives of Otolaryngology–Head & Neck Surgery. 2010;136(10):965-969.
3. Sobotka S, Chen J, Nyirenda T, Mu L. Outcomes of muscle reinnervation with direct nerve implantation into the native motor zone of the target muscle. Journal of reconstructive microsurgery. 2017;33(02):077-086.
4. Kodama N, Kumai Y, Sanuki T, Yumoto E. Arytenoid adduction combined with nerve-muscle pedicle flap implantation or type I thyroplasty. The Laryngoscope. 2017;127(1):159-166.
5. Raskin JS, Hansen D, Mohan A, Pan I-W, Curry DJ, Lam S. Perioperative antibiotic use in vagus nerve stimulator implantation: a clinical series. Child's Nervous System. 2017;33(5):801-804.
6. Weeks B, Bao G, Gilbert TM, Emdur L. Hypoglossal Nerve Stimulator Implantation in a Non-Academic Setting: Two-Year Result. Laryngoscope investigative otolaryngology. 2018;3(4):315-318.
7. Sobajima M, Ueno H, Onoda H, et al. Transcatheter aortic valve implantation improves cardiac sympathetic nerve activity on 123I-metaiodobenzylguanidine myocardial scintigraphy in severe aortic valve stenosis. Circulation Journal. 2018;82(2):579-585.
8. Spindler P, Vajkoczy P, Schneider UC. Surgical revision after Vagus Nerve Stimulation. A case series. Epilepsy & Behavior Reports. 2021;15:100437.
9. Ansó J, Dür C, Gavaghan K, et al. A neuromonitoring approach to facial nerve preservation during image-guided robotic cochlear implantation. Otology & neurotology. 2016;37(1):89-98.
10. Sefien I, Hamada S. Facial nerve stimulation as a complication of cochlear implantation. Indian Journal of Otolaryngology and Head & Neck Surgery. 2019;71(4):474-479.
11. Gong Y, Wei X, Li Y. Preoperative diagnosis and evaluation of cochlear implantation in patients with cochlear nerve deficiency. Lin chuang er bi yan hou tou jing wai ke za zhi= Journal of clinical otorhinolaryngology, head, and neck surgery. 2018;32(10):794-798.
12. Amjad A, Shaheer M, Rafique A. Retinal Nerve Fiber Layer Thickness Changes after Phacoemulsification with Intraocular Lens Implantation. Journal of the College of Physicians and Surgeons Pakistan. 2018;28(12):919-922.
13. Shang C. Emerging paradigms in mind–body medicine. The Journal of Alternative & Complementary Medicine. 2001;7(1):83-91.
14. Zhang R, Cao L, Wang Y, et al. A unique methylation pattern co-segregates with neural tube defect statuses in Han Chinese pedigrees. Neurological Sciences. 2017;38(12):2153-2164.
15. Wada F, Nakata A, Tatsu Y, et al. Myosin Va and endoplasmic reticulum calcium channel complex regulates membrane export during axon guidance. Cell reports. 2016;15(6):1329-1344.
16. Oh G, Ebrahimi S, Wang S-C, et al. Epigenetic assimilation in the aging human brain. Genome biology. 2016;17(1):1-11.
17. Zhou J, Jiang J, Wang S, Xia X. Epithelial cell adhesion molecule-1 (ECAM1) is required in the maintenance of corneal epithelial barrier integrity. Cell biology international. 2016;40(1):49-54.
18. Shen J, Overland M, Sinclair A, et al. Complex epithelial remodeling underlie the fusion event in early fetal development of the human penile urethra. Differentiation. 2016;92(4):169-182.
19. Tsai S, Chang W-C, Chavanich S, Viyakarn V, Lin C. Ultrastructural observation of oocytes in six types of stony corals. Tissue and Cell. 2016;48(4):349-355.
20. Wang J, Shi Y, Yang S. Ultrastructural observation of morphologically abnormal sperm: Advances in studies and application. Zhonghua nan ke xue= National Journal of Andrology. 2016;22(1):67-71.
21. Farahaninia M, Hoseinabadi TS, Raznahan R, Haghani S. The teach-back effect on self-efficacy in patients with type 2 diabetes. Rev Diabet Stud. 2020;16(1):46-50. doi:10.1900/RDS.2020.16.46