Analysis on Recent Artificial Retina in Electrochemical and Mechanical Approaches

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Abstract: Outer retinal degeneration diseases, such as retinitis pigmentosa and age-related macular degeneration, are the main eye diseases that cause blindness. Although the molecular genetics of retinitis pigmentosa has made great progress in recent years, no obvious breakthrough has been made in the treatment. The use of retinal pigment epithelial cell transplantation, or the transplantation of retinal slices including photoreceptors, has major problems in case selection, immune rejection, efficacy and safety. If a certain method is adopted to generate the perception of light and the corresponding electric current or release neurotransmitters, the inner retina, i.e., the inner nuclear layer and ganglion cells are activated, and nerve impulses are generated and transmitted to the visual cortex. Vision, this device that can activate the inner retina is called an artificial retina (retinal prosthesis). Activation of the inner retina by means of retinal prosthesis (artificial retina) will be a promising approach for treatment of outer retina degenerative diseases. Great efforts have been paid to evolve special new devices in recent years.

1 INTRODUCTION

The design principle of the retinal implanted electrode system is to replace the damaged photoreceptor function, that is, to effectively capture the visual image of the surrounding environment, convert the visual signal into a neuroelectric signal, and activate the inner retina to form vision (Humayun et al. 1994). The production of vision depends on three major tissues and organs: the eyeball (mainly the retina), the optic nerve, and the visual cortex. So, it is necessary for developing prostheses that can replace these three tissues, namely retinal prostheses, optic nerve prostheses, and visual cortex prostheses in order to restore vision. The current approaches are mainly facing obstacles in the artificial retina implant location, materials selection and how to efficiently encode and decode chemical and electrical signals, Therefore, this article will review recent studies and try to promote the development of artificial retina in achieving the capacities of wide field of view, high resolution and low aberration sensitivity.

The three types of visual prostheses have different stimulation sites. The visual cortex prosthesis uses microelectrodes to directly stimulate the primary visual cortex, which can produce light perception, but cannot form an image. Optic nerve prosthesis stimulates nerve bundles and does not require a complete retinal structure. However, it has low resolution, difficult surgery, and high risks. It is still in the basic research stage. The retinal prosthesis is to implant microelectrodes or photoelectric arrays at specific locations on the retina, convert additional video and image information into electrical impulses, stimulate specific nerve cells, then transmit them to the visual cortex and brain center through neural pathways (Rizzo et al. 2014).

The main function of the retinal implanted electrode system is to replace the damaged photoreceptor layer, accept and convert the light signal of the environment. The key to its successful vision depends on the biological activity of the inner retinal neurons. Electrode pulses can affect many inner and outer layers of the retina. At present, it is generally believed that the ganglion cell body, axon and proximal segment are the first targets of extracellular stimulation (Weiland et al. 1999). Based on the principle that the inner retinal nerve conduction is only limited to the electrical stimulation area, only the axons of the retinal ganglion cells in the electrode stimulation area are activated. This lays the theoretical foundation for retinal positioning electrical stimulation and makes it possible to form

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geometric images with simultaneous multi-point electrical stimulation.

Researchers used bullfrog, rabbit, and mouse animal models to study the number, size, and current threshold of electrodes needed to produce effective vision. It is found that the current value of the 200μm diameter distribution with an interval of 200μm is within the safe current value range of long-term retinal stimulation (Weiland et al. 1999). Electric pulses below the lower limit of nerve stimulation cannot produce light perception. Higher than the upper limit of nerve stimulation may cause tissue damage. The electrical stimulation threshold will be manually adjusted after retinal chip implantation until the patient has light perception. After the patient is familiar with the device, the electrical stimulation threshold will change. The adaptation program needs to be re-adjusted (Humayun et al. 1999). The adaptation program converts the grayscale value of the image to a specific value. Then it can be projected onto the retinal electrode chip through the visual processing unit to generate the corresponding electrical stimulation.

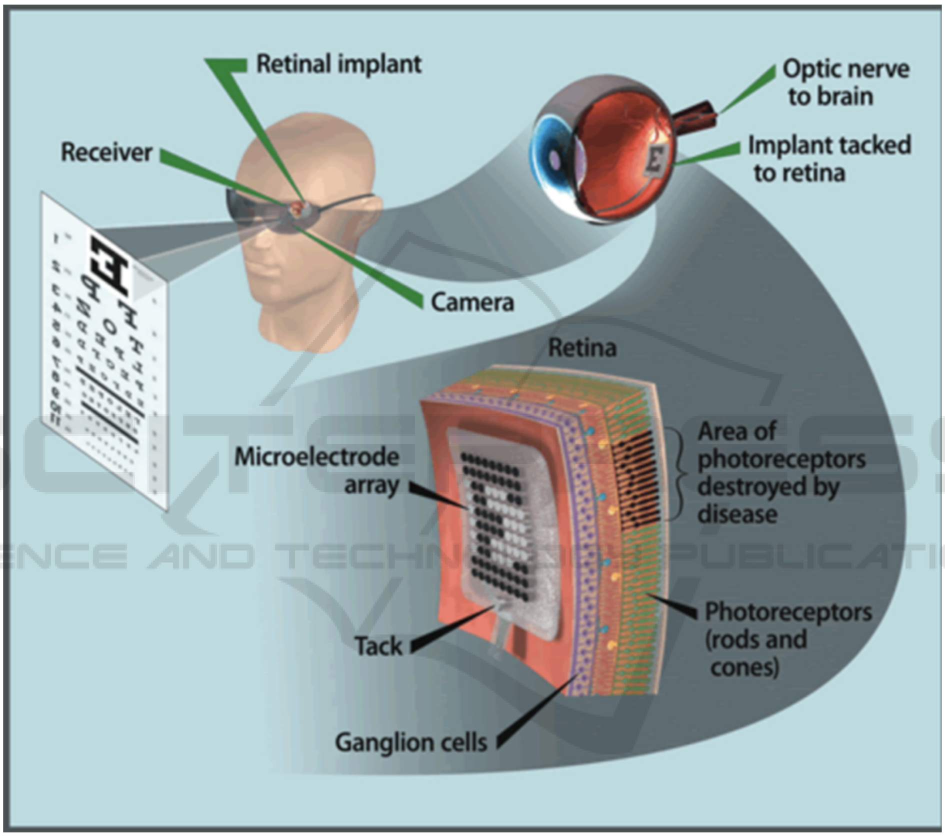

Figure 1: The working principle of artificial retina

2 TYPES OF ARTIFICIAL RETINA

There are three kinds of artificial retina devices which are placed on the inner surface of the retina, placed on the under the retina and chemical prosthesis. The recent progress in three approaches to artificial retina implementation: epiretinal prosthesis, subretinal prosthesis and chemical prosthesis is reviewed.

2.1 Epiretinal Prosthesis

Epiretinal prosthesis is to arrange the electrodes for electrical stimulation close to the inner limiting membrane of the retina, without damaging the structure of the eyeball other than the fixed point of the electrode arrangement. The non-photosensitive area on the device directly receives electrical signals containing image information, and the electrodes directly stimulate the axons of ganglion cells. If the electronic device needs to be placed outside the eyeball, a wire needs to be led out through the flat part of the ciliary body. The current surface artificial retina requires an external system for image acquisition, image processing, data and power conversion to the implant, so this information conversion is more easily controlled by the outside world. The composition of this device is a very small field sensor like a camera, which is fixed outside the eyeball or inside a plastic lens implanted in cataract surgery. Moreover, a platinum-wrapped metal wire connects it to the electrode arrangement on the top of the inner retina. stand up. The implant on the retina is first a readout chip, which receives the image information from the sensor and the electrical signal from the processing unit to generate electrical impulses, which stimulate the axons of the ganglion cells and pass into the brain through the axons.

A clinical trial of a retinal surface stimulator approved by the FDA has recently begun. An exclusive clinical trial is also underway at the Doheny Retina Institute at the University of Southern California, and 2 patients have received implants. Studies have confirmed that microelectronic devices have enough energy to directly stimulate retinal neurons, so that patients who are completely blind can feel the light consistent with the stimulation pulse. Each electrode is controllable. Under the control of a microelectronic device, when each electrode is activated, it can cause light perception. In Germany, the researchers temporarily placed a stimulating device on the retina of a test subject (before eye surgery, with normal photoreceptors, not blind). The results showed that there was light under a very low stimulation current. These results supports the results of previous preclinical trials of multiple research groups. What is more, in the case of outer retinal degeneration, the retina requires higher current stimulation, which is more difficult to stimulate than the healthy retina without loss of photoreceptors (Zhou et al. 2007).

2.2 Subretinal Prosthesis

Subretinal prosthesis is implanted between the retinal pigment epithelium and the sensory layer of the retina. The advantage is that the implanted electrodes are close to the retinal bipolar cells, the stimulation current required is small. Some devices are designed to directly generate stimulus current from light without an external power source; while others are designed with an external power source to amplify the electrical signal generated by the light. This device is composed of thousands of microelectrodes, containing photosensitive micro photodiodes, integrated on a very thin board (thickness 50-100μm, diameter 2-3mm). The photodiode is irradiated by light and converted into a tiny current on each microelectrode. The current is "injected" into the remaining neurons of the retina, and the middle and inner layers of the retina serve as the processing part of visual information. In addition, coating glycoproteins (such as laminin) on the surface of the micro-photodiode can increase biocompatibility. Besides, optobionics has been approved by the FDA for clinical trials using artificial silicon retinas in recent years (Hauer et al. 2007). This device is an array of micro-photodiodes, implanted in the subretinal space, and powered by light only. In June 2000 and July 2001, 3 people received implants on 2 occasions. It was reported at the ARVO meeting in 2002 that the implant still had electrical function and remained in place, which could indirectly improve visual function, but under normal light conditions, the device itself could not directly activate the retina. Researchers such as the University of Tubingen in Germany have also developed a device. They confirmed that in the long-term loss of photoreceptors in the retina, passive light reception cannot generate enough current to induce a direct response of retinal neurons. In order to solve this problem, they used external infrared energy to provide greater energy to the implant to generate electrical stimulation pulses. In addition to the energy supply device, the micro photodiode located under the retina can receive light and transmit stimulation pulses to the stimulation electrodes under the retina. Recently, a research group at the University of Houston used ceramic optoelectronic materials to make implants. Japan's Nidek Co., Ltd. produced a subretinal electrode array with a wire connected to the electronic device in the vitreous cavity through the retina (shown in Figure 2) (Gu et al. 2020). Chemical prosthesis method can release neurotransmitters in the target area of the retina has been proposed, but its feasibility is still at the stage of demonstration. The Kresge Institute of Ophthalmology at Wayne State University has proposed a microfluidic device that can be used to stimulate the cortex and retina which can stimulate neurons.

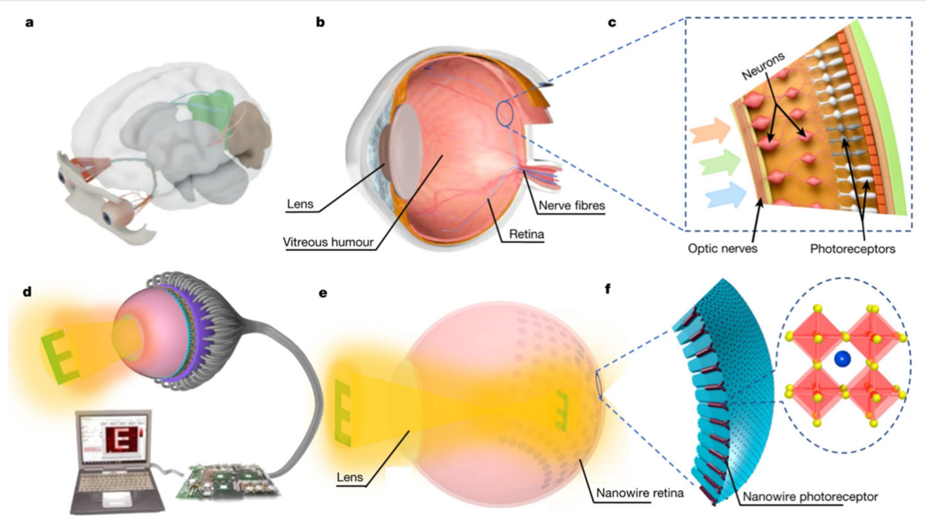

Figure 2: Electrochemical eye with a hemispherical retina.

2.3 Chemical Prosthesis

Retinal implanted electrodes are the most successful artificial vision implant system so far. The reasons are as follows: (1) The complicated fatality rate of intracranial optic cortex and optic nerve implanted electrodes is high. With the continuous improvement of vitreoretinal surgery technology, retinal implanted electrode surgery. The risk of continuous reduction in the incidence of surgical complications has gradually been accepted by authoritative institutions. (2) Retinal implanted electrodes avoid the complex processing and transmission of visual signals in the subretinal, midbrain and visual cortex. Stimulate at the beginning of the visual pathway It is easier to produce effective vision. (3) Due to the fusion of multiple photoreceptor cells in the peripheral area of the retina during the signal processing of the visual pathway, and a bipolar cell, it is further fused and connected to the retinal ganglion cells to transmit visual signals. The ratio of photoreceptor cells, bipolar cells and retinal ganglion cells is 1:1:1. Therefore, placing a multi-electrode stimulation chip in the macula area is more likely to produce Holmes retinal topological vision.

3 LATEST RESEARCH AND DISCUSSION

At present, the research of artificial retina has reached an important stage, that is, implanting a device in the blind to replace the lost function (Wang et al. 2020). There are often robots with artificial eyes in science fiction novels, and bionic eyes that are connected to the human brain to restore the vision of the blind. Scientists have spent a lot of energy to develop such devices. However, making spherical human eyes-especially hemispherical retinas-is a huge challenge, severely limiting the functions of artificial and bionic eyes. The team of Fan Zhiyong, the member of which are from the Hong Kong University of Science and Technology, the University of California at Berkeley and Lawrence Berkeley National Laboratory reported an innovative, concave hemispherical retina, which consists of a series of nano-level light sensors (photoreceptors) that mimic the human retina Photoreceptor cells in Researchers apply this kind of retina to electrochemical eyes, which have multiple functions equivalent to human eyes and can complete the basic functions of acquiring image patterns. The retina of the human eye is hemispherical. In addition, its optical layout is more sophisticated than the flat image sensor in the camera: the dome shape of the retina naturally reduces the light transmission through the lens, thereby making the focus sharper. The core component of the bionic electrochemical eye is an array of high-density photosensitive elements as the retina. Besides, the photosensitive element is formed directly in the pores of the alumina hemispherical film. Thin flexible wires made of liquid metal are sealed in a soft rubber tube to transmit the signal from the nanowire light sensor to an external circuit for signal processing. These wires simulate the nerve fibers that connect the human eye and brain. The most impressive is the high-resolution imaging of this artificial retina, which is due to the high density of the nanowire array. In previous artificial retinas, photoreceptors were first fabricated on a flat and rigid substrate; later, they were either transferred to a curved support surface or folded into a curved substrate. This limits the density of imager units because there must be space between them for transport or folding. In contrast, the nanowires in this new device are formed directly on the curved surface, allowing them to be more closely bound together. In fact, the density of nanowires is much higher than the photoreceptors on the human retina. The signal from each nanowire can be obtained separately, but the pixels in current devices are composed of three or four nanowires. The overall performance of artificial eyeballs represents a leap forward for such devices. Nevertherless, there is still a lot of work to be done. Firstly, the photoelectric sensor array is only 10×10 pixels size large, and the gap between the pixels is about 200-μm, which means the light detection area is only 2 mm wide. In addition, the manufacturing process involves some expensive and low-throughput steps. For example, researchers used an expensive process called focused ion beam etching to prepare holes for the formation of each nanowire. In the future, high-throughput manufacturing methods must be developed to significantly reduce costs to produce larger arrays of photosensitive elements. Nonetheless, this work adds a strong touch to the breakthroughs made in the past few decades. This breakthrough was achieved by imitating camera-like eyes and imitating insects-like eyes. Realized by compound eyes. In view of these developments. It seems possible for us to witness the widespread application of artificial and bionic eyes in daily life in the next decade (Stiles et al. 2010).

What is more, Chinese researcher Feng Miao's team proposed that a brain-like visual sensor based on the vertical heterojunction of two-dimensional materials can be built through the "atomic Lego" method. These vertical structures can not only naturally imitate the vertical layered structure of the retina, but also contain the differences in the heterojunction. Two-dimensional materials can be used to simulate the functions of different cells in the retina. And the number of electrodes in the artificial retina system is an urgent hardware system difficulty that needs to be overcome at present. Realize the activation of independent electrodes corresponding to independent retinal ganglion cells and improve the visual resolution.

At the same time, researchers the United States designed and constructed a spherical anterior retinal chip that conforms to the macular curvature to expand the retinal stimulation area and reduce the electrode-retinal distance. Research on other hardware systems, such as the development of intraocular cameras, is used to replace external Glasses and cameras can be set to improve the patient's perception of spatial positioning, and it also has huge development potential. Studies have shown that it is a feasible new method to elicit visual cortex action potentials through retinal implants, but it is not certain whether this device can achieve a certain degree of independence for the blind. There are still many problems to be solved. For example, it is necessary to know whether the sense of orientation, motor perception, and feature positioning are in the visual cortex, how to achieve the long-term stability of the implant, whether the retinal neurons can withstand long-term stimulation without changes in their own shape and function, and blind people receive implants. The type of image that can be felt after entering.

4 CONCLUSIONS

As the first way for humans to obtain and process information, the human visual system has a physiological mechanism that is significantly better than that of optical systems. For the research of the human visual system, people can achieve a wide range of applications in biomedicine, machine intelligence, and visual simulation. It is a research topic with far-reaching prospects. The final goal of artificial retina research is to use microelectrode arrays to directly stimulate internal nerve cells to replace the diseased retina, thereby restoring the patient's vision. People need to study the biological structure of the retina and the information processing mechanism. Furthermore, people also need to make microelectrodes that can be integrated with biological nerves in terms of electronics. Although artificial retina chips have been successfully developed, they have been transplanted into human eyes for experiments and have achieved certain results. There is still a certain distance from practicality and economy. And there is no unified model in the basic theory.

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