Retinal Ganglion Cell Responses to Programmed Electrical Stimulation with Implantable Microcontacts

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Resumo -. Apresentamos aqui os resultados da estimulação elétrica em retina de embriões de pintinhos (E16 a E20). A estimulação é feita através de arrays planares de microeletrodos posicionados sobre a membrana limitante interna. O objetivo é avaliar propriedades funcionais dos implante e investigar padrões de disparo de células ganglionares em função da amplitude do estímulo e configuração dos eletrodos no implante.

Abstract -. We present here the results of electrical stimulation of the retina of chicken embryos (E16 to E20). The stimulation is performed by means of planar microelectrode arrays positioned on the inner limiting membrane. The objective is to evaluate the funcional properties of the implants and investigate firing patterns of ganglion cells as a function of the stimulus amplitude and electrode configuration.

(Keywords: retina implant, chick, electrical stimulation, multielectrode array)

Introduction

This work has been developed as part of a Retina Implant project, funded by the German Federal Ministry of Research and Education. The project aims at helping blind people who suffer from retinal degenerative diseases as retinitis pigmentosa or macular degeneration[1]. The implant encompasses the development of a retina encoder, which translates light patterns into impulse sequences, and a stimulator, implanted in the eye. The stimulator contains a microelectrode array to electrical stimulation of the retina and the electronics necessary to decode the pulse sequences.

The purpose of the present work is to evaluate the functional properties of implantable non-penetrating microcontact arrays and to define optimal ranges for retinal electrical stimulation parameters. With this objective, ganglion cells of eye cup preparation from chicken embryos are electrically stimulated and their response patterns evaluated.

Methodology

Experiments are carried out on E16 to E20 chicken embryos. Immediately after the chick is decapitated, the eye is cut at the equatorial plane and the vitreous humor removed[2]. The posterior chamber is immersed in a petri dish perfused at a rate of 2ml/min with Ringer solution containing 0.1M NaCl, 6mM KCl, 1mM $MgCl_2$, 1mM NaH_2PO_4, 1mM $CaCl_2$, 30 mM $NaHCO_3$ and 20mM glucose; pH is adjusted to 7.4 with either Tris (2.5mM) or carbogen (95% O_2 and 5% CO_2). Temperature is maintained constant at 31°C (±1°C).

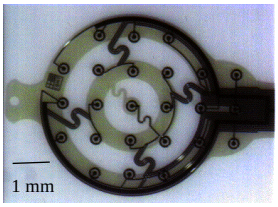


Figure 1.- Planar electrode array (FhG IBMT[3]) for retinal stimulation. Horizontal bar stands for 1mm.

Stimulation arrays are developed by our partners in St. Ingbert and Duisburg (IBMT and IMS, Fraunhofer Gesellschaft, Germany) in several geometries[3]. An example of a planar structure containing 24 electrodes is shown in figure 1. It is placed on the retinal surface by means of a precision micromanipulator. The recording electrode (tungsten, 1MΩ tip impedance) is then posititoned near the array, and brought to a ganglion cell. Ganzfeld light stimuli are applied and spike forms recorded (for subsequent sorting), as shown in the first part of figure 3. Light is turned off, and then electrical stimulation is

initiated using a computerized programmable stimulus pattern generator (PSPG)[4].

The used single biphasic stimulation pulses are always charge balanced, with current amplitudes from 50 to 300µA and duration from 100µs to 1 ms per phase. Up to 3 stimulating electrodes are selected simultaneously. Recorded signals are amplified (WP-I ISO-DAM), band-pass filtered (from 100Hz to 2kHz), and digitally recorded. Standard statistical analysis is done off-line.

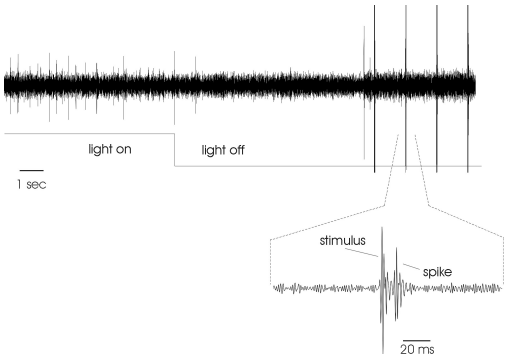
Results

Electrode arrays are composed of 4 to 24 contacts, disposed in either rectangular or round geometries. A schematic example of an array with rectangular arrangement of electrodes is shown in figure 2. The simultaneous monopolar stimulation pattern is indicated next to the selected electrodes. The initial (anodic) phase is concomitant in both active electrodes, and they are stimulated against ground.

Figure 2.- Example of simultaneous monopolar stimulation. Schema of a planar 8-electrode stimulation array, with active electrodes in black.

Figure 3 shows an example of a ganglion cell response to light and electrical stimulation of 100µA amplitude. Standard spike sorting is applied analysing amplitude and width. Responses to stimulation above threshold were found to be either single spikes or bursts of activity (not shown). Distance from the array to the retinal surface is in the range of 1mm and it is estimated according to the shadow projected from the array on the retinal surface when the preparation is illuminated with microscope light.

Figure 3.- Ganglion cell recording from E20 chick during light and electrical stimuli. Stimulation



(current) pulses: 100µA, biphasic, monopolar mode, total duration of 300µs.

Various electrode configurations (from the same array) are selected in the same experiment and the firing patterns to each arrangement compared. Preliminary results show that the threshold varies a lot depending on the electrode configuration. We found thresholds from 50 to 150µA.

Discussion and Conclusions

The targets of the electrical stimulation in the scope of the retina implant project are the ganglion cells, as they are the output of the retina, and as a significant percentage of them are presumably still healthy even in advanced stages of retinal degenerative diseases. Because of that it is of interest to determine whether one can appropriately stimulate this retinal layer with planar electrode arrays.

As we detected variations on the threshold values inside each experiment depending on the electrode configuration, we conclude that the electrical field generated by the different selected electrodes may easily access ganglion cells with different threshold values.

We showed here that stimulation threshold values can be achieved in the order of 100µA with a separation of the non-penetrating arrays from the retinal surface in the range of 1mm. Currently we are testing the direct contact of the array to the inner limiting membrane, in order to determine minimal stimulation thresholds.

References

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