TOWARDS A CORTICAL VISUAL NEUROPROSTHESIS FOR THE BLIND

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Abstract: **Our main objective is to demonstrate the feasibility of a cortical neuroprosthesis, interfaced with the visual cortex, as a means through which a limited but useful visual sense may be restored to profoundly blind people. Although there are still a number of important unanswered questions and many problems have to be solved before a Cortical Visual Neuroprosthesis can be considered a viable clinical therapy, our results show that stimulation of occipital cortex is able to elicit visual perceptions at least in ca. 50 % of blind subjects, and suggest that multiple intracortical microelectrodes could be used for a long-term stable and safe clinical neuroprosthesis.**

Keywords: **Neuroprosthesis, Intracortical microstimulation, Artificial Vision, Visual cortex, Transcranial magnetic stimulation.**

Introduction

Loss of vision poses extraordinary challenges in our society which relies heavily on sight. Currently there is no effective treatment for some patients who are profoundly visually handicapped due to degeneration or damage to: 1) the retina; 2) the optic nerve, or 3) the brain. New hope has been generated recently by showing that electrical stimulation of almost any location along the visual path can evoke the perception of visual perceptions called “phosphenes” [1,2,3,4,5].

Several laboratories worldwide are developing microelectronics prosthesis intended to interact with the remaining health retina or optic nerve [4,5]. However there are potential drawbacks to use the retina or optic nerve as the point of entry to the nervous system. First, the technological problems of producing suitable electrode arrays are significant. Second there is surgical difficulty of placing an array of electrodes against the retina or optic nerve in such a way that it will remain in place permanently. The current level of research activity may solve these and other related problems, so that these prosthesis could become useful for diseases such as retinitis pigmentosa and age related macular degeneration. However the output neurons of the eye, which in turn give rise to the optic nerve axons, often degenerate in many retinal blindnesses and therefore a retinal or optic nerve approach would not be always helpful.

We have decided to work on stimulation of the primary visual cortex because the neurons in higher visual regions of the brain (visual cortex) often escape from this degeneration. If these higher visual centers can be stimulated with visual information in a format somewhat similar to the way they were stimulated prior to the development of total blindness, a blind individual may be able to use this stimulation to extract information about the physical world around him/her. Such an artificial vision system should be able to provide simple but useful visual perceptions in individuals with profound loss of vision due to disease or injury. This concept is supported by several studies, which demonstrate that localized electrical stimulation of the human visual cortex can excite topographically mapped phosphenes [1,2,3,6].

Materials and Methods

The present research has been designed to study the more effective means of stimulating cortical tissue through multiple intracortical microelectrodes and to develop a non-invasive methodology to establish the degree of remaining functional visual cortex in blind subjects.

We used arrays of 100 or 25 penetrating silicon electrodes (Utah Electrode Array, UEA), specifically designed to focally stimulate or record cortical neurons located in a single layer up to 1.5 mm beneath the surface of the cerebral cortex. The arrays were inserted on the visual cortex of Halothane anaesthetized animals (cats, rabbits and rats) in a sterile surgical environment with the help of a pneumatically actuated impulse inserter (Bionic Technologies, LLC).

A programmable, battery powered miniaturized stimulator (Biomedical Technologies SL) was used to inject different currents into single electrodes. Microelectrode impedances were measured and stored by the stimulators. After several time intervals (ranging from 12 hours to 6 months) the animals were sacrificed. The microelectrode arrays were then explanted and the implant site and surrounding tissue removed and processed histopathologically.

A requirement for clinical application of a cortical prosthesis, aside from safety considerations, is proper, non-invasive patient selection criteria. The primary visual cortex of potential candidates for this neuroprosthetic devices has to be capable of processing visual information, i.e. not have been plastically transformed to process tactile or auditory information. We used Transcranial Magnetic Stimulation (TMS) as a non-invasive and painless methodology to establish the degree of remaining functional visual cortex in blind subjects. TMS was delivered with a figure-of-eight coil (Cadwell Labs, Kennewick, WA, USA) to 28 positions arranged in a 2x2 cm grid over the occipital area. A frameless image-guided neuro-navigational device (Brainsight 1.4?, Rogue Research, Montreal, Canada) was used to describe the position of the actual sites of the stimulation coils relative to the cortical surface. A digitizing tablet connected to a PC computer running customized software, and audio and video recording were used for detailed and accurate data collection and analysis of evoked visual perceptions. The protocol was applied on a group of 13 legally blind volunteers. All gave their written informed consent prior to entering the study, which had been approved by the institutional review board.

Results

Our results show that intracortical microelectrodes are well tolerated by the cortex, although sometimes there is a chronic inflammatory response characterized by astrocytes and macrophages which proliferate in the vicinity of the electrode tracks (Figure 1). Most of the electrode tracks exhibited a thin fibrous encapsulation around them, but neurons near the electrode tips appeared normal.

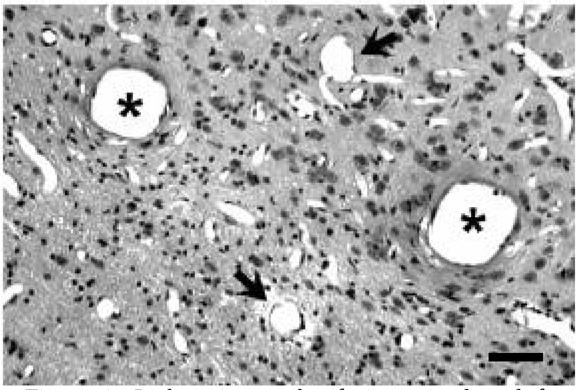

Figure 1: Light micrograph of tissue implanted for 3 months with the UEA. Neurons in close proximity to the tracks (asterisks) appear normal. Notice that it is difficult to distinguish the tracks from the normal blood vessels (arrows). Bar= 50 ?m

TMS was able to reliably evoke phosphenes in 54% of blind subjects by using short trains of 4 consecutive 15-Hz TMS pulses (particularly those severely visually impaired but with some residual vision and late blind subjects) although not in all sampled positions, hence the relevance of a systematic mapping. Evoked perceptions were topographically organized. Despite minor inter-individual variations, the mapping results were reproducible and showed good congruence among different subjects.

Discussion

Our main objective is to demonstrate the feasibility of a cortical neuroprosthesis, interfaced with the visual cortex, as a means through which a limited but useful visual sense may be restored to profoundly blind people. This visual perception, although limited, could provide a substantial improvement in the standard of living of blind and visually impaired persons.

Penetrating electrodes have been used extensively in acute and chronic recording experiments [7], however implantation of penetrating electrodes is intrinsically more invasive than application of surface elecrodes. Our results show that intracortical microelectrodes could be used safely in long-term applications, although more studies regarding safety and preservation of neuronal tissues as well as optimizations of stimulating parameters are needed preceding any clinical trial. In this context, we propose that TMS could be used as a standard methodology for the pre-surgical evaluation of blind patients prior to neuroprosthestic implantations.

Conclusions

If we can understand more about the fundamental mechanism of neuronal coding, and about how to safely stimulate the nervous system, there will real potential to apply this knowledge clinically. Although there are still a number of important unanswered questions and many problems have to be solved before a Cortical Visual Neuroprosthesis can be considered a viable clinical therapy, our results suggest that multiple intracortical microelectrodes could be used for a long-term stable and safe clinical neuroprosthesis.

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