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Laser driven optical prosthesis (LASDOP) - Pluridisciplinary project for the development of a retina stimulation.

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Abstract. This paper presents a pluridisciplinary project, aiming to develop a retinal stimulation, which results of the meeting of researchers from various backgrounds (ophthalmologists, biologists, physicists, re-educators ...). The keynote of the project is the conception of a model known as artificial vision, which we prefer to refer as retina nerve stimulator to give patients a new vision capability. We decided to develop a epi-retinal stimulation, since this choice could benefit to patients suffering from photoreceptor diseases such as Age Related Macular Degeneration (ARMD) or retinitis pigmentosa (RP). In France, it is estimated that 60000 blind people are concerned. The recovery of a deficient visual function would consist at first glance to restore preferentially the central visual acuity. In fact, clinical blindness studies show that the first need of such patients is the recovery of the peripheral visual field in order to recover some mobility autonomy. The effort of all the pluridisciplinary research teams involved in the project would allow to fully validate the stimulation technique and would allow to start a second step dealing with the encoding of pertinent information from image sequences and the study of related phosphene mechanisms.

Keywords: Retina, Stimulation, Prosthesis,

1. Introduction.

This project is the result of a meeting of professionals coming from very different horizons (physicists, electricians, surgeons, ophthalmologists, physiologists, rééducateurs, orthoptistes, instructors in locomotion, occupational therapist, psychomotor therapist and biologists.). The project originated from an idea to create an incoming model into the framework usually recognized under the term of "artificial vision".

2. Project concept

The conception of such a project comes back to answer three major questions:

- a). In what part of the organism must we stimulate the visual chain?
- b). To what types of patient and pathologies must we address our research?
- c). What types of visual results is it necessary to search for and to privilege?

a) Where to stimulate the visual chain?

The psychosensory visual acquisition chain spreads from the eyeball and passes by way of the optical canals, optic nerve, chiasma and retrochiasmatic optical canals to the primary visual cortex.

Different solutions were considered by several teams:

- a) Direct stimulation by implanted electrodes of the occipital cortex [1].

- b) Stimulation of the optic nerve.[7]
- c) Stimulation of another sensory zone of substitution (language or dorsal epidermis).
- d) Stimulation of the retina [2-6].

It is this last solution that we kept. The goal is to use, if possible, the nervous conduction of the neuronal chains protect from the second and third neurons, the electric stimulation being at the origin of a phosphene type luminous sensation.

b) From the strategic choice, what types of patients are susceptible to benefit from this solution?

Some illnesses (e.g. pigmentary retinitis or macular degeneration due to age) only destroy the photosensitive cells of the retina and in particular the first neurons responsible for photonic signal transduction in electric neuronal signals.

It has been estimated in France that as many as 60 000 blind people possess axons of the third neuron (ganglion cells) and consequently have optic nerve fibers which are still functional.

c) From this report, what "primary" visual sensations should be favoured amongst these patients?

The initial idea of restoring a deficient visual function often consists in wanting to restore a central visual discrimination acuteness of the foveolar vision type. In fact, when one is interested in the world of clinical blindness, one perceives that the primary need of a completely blind patient is the restoration of peripheral visual field with visions of low-frequency type in order to be able to analyze shapes and obstacles in an environmental space, particularly in "view" of recovering a certain autonomy of movement. A patient therefore who has retained good central visual acuteness and a tubular visual field, is certainly a lot more handicapped than a patient afflicted by DMLA who has lost their central vision but kept a peripheral visual field intact. This fact is particularly well known by the teams responsible for the readaptation of visual deficiencies.

3. Outlines of the LASDOP project

- e) Coding camera data.
- f) Retinal stimulation.
- g) Creation of a vision by phosphenes.
- h) Image analysis.
- i) Construction of the psychovisual diagram.
- j) Conception of a stimulator with the criteria of surgical compatibility.

The choice of the system of electric retinal stimulation is essential. A number of teams have already tried direct electric stimulation using epiretinal or sub-retinal implants. These technic however, are limited by the size and number of electrodes. Results have shown bad spatial resolution as well as a reduction in the efficiency of contact due to the build up of gliosis around the electrodes. We chose one fashion of stimulation even confidential original.

Numerous steps however still remain to be completed. Having taught physicists and biologists the necessity of communicating and working together on all the different concepts, the following steps have been agreed upon:

- k) The choice of stimulus.
- l) In vitro testing on different experimental benches (slices of retina, measuring position of the whole retina).
- m) A study of interaction stimulus - tissues (definition of mechanisms of stimulation of the neurons and a study of the chosen stimulus).
- n) An electrophysiological study.
- o) Modeling.
- p) Implantation on volunteers.
- q) Functional and cognitive rehabilitation.

To date, the first results have been encouraging and in particular those concerning stimulation tests of in vitro retina slices. The results have given rise to the hope of pursuing the studies of this project that we prefer to qualify as retinal stimulation rather than artificial vision.

4. Other experiences:

Numerous teams on the international scene (USA, Germany, Belgium, Japan, Australia etc.) have already developed some projects on the theme of artificial vision. Clinical tests have been carried out since 1998, but with only short term success. These experiments have concerned about twenty sub-retinal implants, about twenty epiretinal implants and two optic nerve implants. The results of these clinical tests are again very imprecise. Encouraging points arising from these studies however concern the detection of the movement of a luminous target, the capacity to detect contrasting objects and the reduction in the time to perceive these with practice. However bad retention over a period of time for some, little or no reproduction, bad resolution and slowness in character recognition with an equal loss of retinopathy have also been noted. It should also be noted that electrical stimulus of the retina has shown certain limits in particular concerning the size of the electrodes. Electrodes of a few hundred micrometers are at the origin of bad spatial resolution while several dozen micrometers are at the origin of an elevated load density have given rise to a deterioration of the electrode and a sensitivity to the distance between the electrode and the neuron.

Finally, certain long-term effects have been noted with in particular the reactions of gliosis around the electrode and a subsequent reduction in the efficiency of contact.

5. State of advancement of the project

1. The stimulator Electric stimulation is at the origin of certain modifications in the polarization of the membrane responsible for the creation of nervous impulses and phosphene sensation. However, the difficulty of tolerance by the retinal tissue to these electrodes has brought about a reflection upon the interface between photons and neurons in an effort to stimulate the membranes while decreasing the ominous effects of the electrodes on retinal tissue.
2. Stimulated tissue: It was necessary to understand the mechanisms of stimulation and in particular the place of this stimulation: in this case it concerns the 2nd neuron, the 3rd neuron or directly the axonax extensions of the 3rd neuron and/or the optic nerve. To study this, some experiments have been done. The first stimulation experiment concerned an in vitro study of a retinal slice. This was achieved under labview permitting a control of the current source and of the low-frequency generator with the acquisition of the modulated signal measured by the station patch-clamp. The test was done on a slice of retina containing a "patched" ganglion cell. The treatment of the data should permit an understanding of the interactive mechanisms entering into consideration in the behavior of the target cell. Other in vitro tests are in preparation, in particular to observe in real time the propagation of the potentials of action along the axon and the other inter neuronal connections and also to refine the work of modeling of the phenomenon. Experimental measurements on a retina as a whole are also being considered. The objective here is to electrically or optically stimulate precise zones of a complete isolated retina in order to achieve the acquisition of the potentials of action of every point of the retina and to compare the optic and electrical stimulations.
3. Vision by phosphenes: This one will have for goal the analysis of the chain visual psychosensorielle and notably the interrelationship between the stimulus and the sensations with for goal the extraction of the applicable stimulus.

6. Partners of the project

1. Équipe STINIM

2. INSERM
3. CNRS
4. University of Montpellier UM1
5. University of Montpellier UM2
6. EMA (Civil engineering school of Alès)
7. ARAMAV
8. CHU of Montpellier
9. CHU of Nîmes
10. University United
11. Institute of the neurosciences of Montpellier

The financial involvement of the foundation of EADS has permitted the completion of two theses, a post doctorate study and the purchase of various facilities.

7. Conclusions

In conclusion, this project like so many other so-called projects on artificial retinas is still from achieving a true bionic eye.

In fact, it is a lot more about the achievement of a new mental approach to a totally blind patient and as such allows him to have the spatial reference marks as those found in a partially-sighted person.

To do this, it is more precisely about having access to the anatomical site of this mental approach than to occipital brain, while using those paths which are still intact such as the optical canals of the 2^{èmes} and 3^{èmes} neurons of the visual chain.

In practice the anticipated results of these projects are for the meantime a lot nearer of those obtained using electronic canes that all those that one could hope to get later with real bionic eyes.

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