

## SELECTIVE STIMULATION OF THE HUMAN OPTIC NERVE

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### ABSTRACT

A blind volunteer affected with retinitis pigmentosa was intracranially implanted with a self-sizing cuff electrode around her right optic nerve. The nerve cuff electrode included 4 monopolar contacts. Its leads were brought through the skin where they ended in an external connector<sup>12</sup>. After recovery from surgery, electrical activation of the implanted optic nerve was undertaken. A specially dedicated Computer Based Stimulator was used. Stimulation consisted in charge balanced biphasic rectangular pulses. The stimulation resulted consistently and exclusively in visual sensations. The thresholds have remained stable for 14 months, so far. Phosphenes were broadly distributed throughout the visual field. They were either solid surface, or organized in rows, arrays, or clusters of dots. A topological organization was observed between phosphene location and the stimulating contact. Increasing the stimulation frequency decreased the current threshold for perception. The results of this experiment are consistent with the hypothesis that a visual prosthesis, based on electrical stimulation of the optic nerve, can be developed for human subjects with retinitis pigmentosa.

### INTRODUCTION

Various attempts to artificially elicit a visual sensation in blind individuals have been undertaken<sup>4,9</sup>, among which Brindley's investigation on occipital cortex stimulation<sup>1</sup> is noteworthy. Recently, artificial stimulation of the peripheral visual system has also been attempted, in cases of retinitis pigmentosa. In this disease indeed, while photoreceptor cells progressively disappear, cells in other retinal layers among which the ganglion cells, can remain alive<sup>7,10</sup>. Accordingly, acute electrical activation of these cells within a blind patient's eye using retinal implants is now investigated<sup>5,8</sup>. In the present study, another approach for the artificial stimulation of the peripheral visual system was considered. A 59 years old volunteer with retinitis pigmentosa<sup>2</sup> has been chronically implanted with a self sizing cuff electrode<sup>6,11</sup> around her right optic nerve. This work consists therefore in an alternative to retinal implant for vision rehabilitation in totally blind retinitis pigmentosa patients. The experiments reported here comply with the Declaration of Helsinki, and were approved by the Ethics committee of the School of Medicine of the University of Louvain.

### METHODS

The 4-contact cuff electrode was intracranially implanted. Its leads were brought outside the skull, and through the skin where they ended in an external connector. Stimulation was either monopolar, using a surface indifferent anode, or bipolar between two contacts within the cuff. Charge density was always kept below 150  $\mu\text{C}/(\text{cm}^2 \cdot \text{phase})$  up to 50 Hz [below 50  $\mu\text{C}/(\text{cm}^2 \cdot \text{phase})$  up to 333 Hz], corresponding to a charge per phase of 300 nC/phase (respectively 100 nC/phase) with a contact area of 0.2 mm<sup>2</sup>. Determination of current

intensity thresholds for generation of a phosphene was always done using the 2-staircase limit method<sup>3</sup>.

To assess phosphene location, a pointing hemisphere with a radius of 0.45 m was used. The volunteer's head was maintained in front of the hemispheric surface using a contention frame supporting her forehead, chin and parietal skull, and her right eye was positioned at hemisphere center. The right EOG was recorded, and eye movements were monitored with a TV camera. When ready for a stimulus, the volunteer places her head in fixed position, constrained by the frame, and reaches into the hemisphere to place her left index finger on the fixation point (a polymer disk at the intersection of the visual axis with the hemisphere). She was then instructed to "look at" the fixation point with a steady gaze throughout the stimulation test run. The test run was delimited by two beep sounds. With the left forefinger still in contact with the fixation point, as a proprioceptive reference, the evoked phosphene was then indicated, with the right hand fingers, as a shape on the hemisphere. Phosphene characteristics were recorded, which included position, dimensions and organization; subjective brightness; dots diameter; foreground and background colors; motion; etc.

## RESULTS

After recovery from surgery, electrical activation of the optic nerve was progressively undertaken up to a level of two 3-hours-stimulation sessions a week, using single pulses, and trains. The perception thresholds we measured were consistent with the strength duration relation. For 100  $\mu$ s single pulses, their mean value was around 800  $\mu$ A shortly after the implantation. We have not observed a threshold increase over the time since implantation. Some 16 months after surgery, the mean threshold obtained in the same conditions was around 450  $\mu$ A. Transverse thresholds reached generally twice or more the corresponding monopolar thresholds. This did indirectly confirm the proper electrode position. Electrical stimuli applied to the contacts in the self-sizing spiral cuff electrode have never evoked sensations other than visual.

Most phosphenes were reported to consist of a set of dots either in a cluster of 2 to 5, or arranged in rows, arrays, or lumps of 6 to 30. Dot diameter ranged from 8 to 42 minutes of arc. Solid lines, bars, or triangles devoid of dot structure were also reported, usually near perception threshold. Phosphene area (or envelope area for dot phosphenes) generally ranged from about 1 to 50 square degrees. Brightness was graded on a subjective scale of 1 to 9. Phosphenes were often reported as colored. Blue, white, or yellow colors were described. Phosphenes were reported to have been perceived over a large portion of the visual field, up to 35° upwards and 50° downwards on the vertical meridian and 30° leftwards and 30° rightwards on the horizontal meridian. Near threshold, we found a good retinotopic correspondence between the contact position used for a given stimulation within the cuff electrode, and the quadrant of the visual field in which the volunteer drew the related phosphene.

As expected, phosphene location depended on gaze direction. A steady gaze oriented sideways with respect to the fixation point during the stimulus, or a saccade ending just before the stimulus, resulted in a phosphene location consistently referring to gaze orientation at the time of the electrical stimulation. Similarly, any gaze displacement, either after a while, or immediately after the stimulus, resulted in a phosphene location steadily referring again to gaze orientation at the time of the stimulation, in this case, before the movement. Stimulation thus resulted in phosphenes coded in spatial co-ordinates i.e.: the algebraic subtraction of gaze co-ordinates from retinal co-ordinates frozen at stimulation time. Therefore, in order to secure an accurate measurement of phosphene attributes, care was taken to explain to our subject the importance of maintaining a fixed gaze during the presentation of each test stimulation.

## DISCUSSION

The axons of retinal ganglion cells in this retinitis pigmentosa blind volunteer have thus been successfully activated by electrical stimuli applied to the optic nerve to evoke many distinct phosphenes over a large portion of the visual field. Slight changes in the attributes of the phosphenes seem to occur over time, which suggest that some form of learning or remodeling may occur. The overall picture that emerges from these preliminary studies is that of a dormant sensory system that can be reactivated and potentially used for functional purposes. The results of these experiments are therefore consistent with the hypothesis that a visual prosthesis, based on electrical stimulation of the optic nerve, can be developed for human subjects who have intact optic nerve fibers.

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## REFERENCES

1. Brindley, G.S. & Levin, W.S. The sensations produced by electrical stimulation of the visual cortex. *J. Physiol. (London)* **196**, 479-493 (1968).
2. Delbeke, J. *et al.* Use of surface electrodes to assess the electrical excitability of pre-chiasmatic visual pathways. *Pflügers Archiv Eur. J. Physiol.* **435**, R244 (1998).
3. Guilford, J.P. *Psychometric methods* (McGraw-Hill, New York, 1954).
4. Hambrecht F.T. in *Neuroprostheses* (Eds Brindley G.S. & Rushton D.N.) 147-165 (Baillière Tindall, London, 1995).
5. Humayun, M.S. *et al.* Visual perception elicited by electrical stimulation of retina in blind humans. *Arch. Ophthalmol.* **114**, 40-46 (1996).
6. Naples, G.G., Mortimer, J.T., Scheiner, A. & Sweeney, J.D. A spiral nerve cuff electrode for peripheral nerve stimulation. *IEEE Trans. Biomed. Eng.* **35**, 905-916 (1988).
7. Prince, M.R. *et al.* A morphometric analysis of the midperiphery in post-mortem retinitis pigmentosa (RP) eyes. *Invest. Ophthalmol. Vis. Sci.* **39**, S969 (1998).
8. Rizzo, J.F., Socha, M., Edell, D., Antkowiak, B. & Brock, D. Development of a silicon retinal implant: surgical methods and mechanical design. *Invest. Ophthalmol. Vis. Sci.* **34**, 1535 (1994).
9. Schmidt, E.M. *et al.* Feasibility of a visual prosthesis for the blind based on intracortical microstimulation of the visual cortex. *Brain* **119**, 507-522 (1996).
10. Stone, J.L., Barlow, W.E., Humayun, M.S., de Juan, Jr, E. & Milam, A.H. Morphometric analysis of macular photoreceptors and ganglion cells in retinas with retinitis pigmentosa. *Arch. Ophthalmol.* **110**, 1634-1639 (1992).
11. Veraart, C., Grill, W.M. & Mortimer, J.T. Selective control of muscle activation with a multipolar nerve cuff electrode. *IEEE Trans. Biomed. Eng.* **40**, 640-653 (1993).
12. Veraart C., Raftopoulos C., Mortimer J.T., Delbeke J., Pins D., Michaux G., Vanlierde A., Parrini S., and Wanet-Defalque M.C. Visual sensations produced by optic nerve stimulation using an implanted self-sizing spiral cuff electrode, *Brain Research* **813**: 181-186 (1998).