Artificial vision

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ARTICLE

Abstract

Outer retinal degenerations such as retinitis pigmentosa (RP) and age-related macular degeneration (AMD) lead to blindness because of photoreceptor degeneration. To test whether controlled electrical stimulation of the remaining retinal neurons could provide form vision, we electrically stimulated the inner retinal surface with micro-electrodes inserted through the sclera/eye wall of 14 of these patients (12 RP and 2 AMD). This procedure was performed in the operating room under local anaesthesia and all responses were recorded via a video camera mounted on the surgical microscope. Electrical stimulation of the inner retinal surface elicited visual perception of a spot of light (phosphene) in all subjects. This perception was retinotopically correct in 13 of 14 patients. In a resolution test in a subject with no light perception, the patient could resolve phosphenes at 1.75° centre-to-centre distance (i.e. visual acuity compatible with mobility; Snellen visual acuity of 4/200).

Key words Age-related macular degeneration, Artificial vision, Blind, Implant, Retina, Retinitis pigmentosa, Visual prosthesis

Age-related macular degeneration (AMD) and retinitis pigmentosa (RP) are the leading causes of irreversible vision loss in the elderly. In these retinal dystrophies, the photoreceptors (rods and cones) are damaged. At present, in these patients visual rehabilitation involves the use of magnifiers, telescopes and other low vision devices. However, these modalities only function when there are some photoreceptors remaining. For those with near total loss of photoreceptor function, attempts at conveying visual information via electrotactile and vibrotactile devices have been made.[1] Other efforts have focused on transplanting photoreceptors[2] or electrically bypassing the damaged retinal neurons by stimulating at a more proximal site such as the visual cortex.[3] Electrical stimulation at more distal neuronal levels, closer to the photoreceptors, has received little attention but may provide an alternative in blinding photoreceptor disorders in which at least some of the retinal neurons remain intact. Electrical stimulation through a contact lens electrode has elicited large ill-defined phosphenes in patients with advanced photoreceptor degeneration. What remained unanswered was whether electrical stimulation of the eye/retina could produce localised visual percepts that might allow the generation of a two-dimensional array of phosphenes to provide 'pixelised visual input'. For example, a 1024 pixel image (32 × 32 array) subtending a visual angle of 1.7° would allow reading vision at the level of 20/26 and a coarser array of 25 × 25 would enable mobility in environments not requiring a high degree of pattern recognition.[4]

Patients and methods

Fourteen subjects were tested after institutional review board approval at Duke University Eye Center, and at the Wilmer Ophthalmological Institute at Johns Hopkins Hospital. All patients had bare to no light perception vision due to photoreceptor loss, except for the second AMD patient who was legally blind (visual acuity <20/400). All experiments were performed in the patient's worse seeing eye. The subjects and their families signed informed consents prior to the testing. All 12 RP subjects had typical end-stage RP, except subject 2 who had a retinal dysfunction of unknown cause from birth and had never had any form vision. The first AMD subject had lost his vision as a result of a large subretinal haemorrhage due to choroidal neovascularisation, and despite surgical evacuation of this haemorrhage did not regain his vision. The second AMD patient had end-stage geographic atrophy involving the entire macular region.

Before the intraocular surgical procedure, electrical pulses generated by the same current source to be used for retinal stimulation were delivered via a contact lens electrode to the eye. This was done as a screening test to confirm that the subject could perceive light when the eye was stimulated globally, ruling out complete loss of all retinal neurons.

Three types of intraocular stimulating micro-electrodes were used. The first probe consisted of two Teflon-coated platinum wires. The exposed tips of these wires were moulded into hemispheres each of 200 μm diameter, with a centre-to-centre separation of 500 μm. The Teflon-coated wires were then embedded in silicone and housed in a retractable stainless

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steel sleeve. This protective sleeve was insulated from the wires and during stimulation was retracted approximately 7 mm away from the stimulation site. The second micro-electrode was designed to test resolution. This device consists of three electrodes of varying sizes formed by transversely cutting coaxial conductors. The conducting material was gold-plated copper wires. The centre conductor diameters were 50, 100 and 100 μm; centre-to-shield dielectric thickness 60, 90 and110 μm; shield thickness 50, 50 and 80 μm. This multi-electrode was encased in a stainless steel cannula that was insulated from the conductors. Probe 3 was developed to test whether the perception of shapes similar to the geometry of the stimulating electrode could be conveyed by electrically stimulating the retina underlying the electrode. This probe consisted of two platinum (90%) and iridium (10%) wires embedded in silicone and then housed in a stainless steel cannula. At the stimulating tip the wires were bent to run in parallel across a homopolymeracetal surface. Each wire was exposed for a length of 850 μm and had diameter of 125 μm. Lastly, the fourth micro-electrode was either a 5 × 5 or a 3 × 7 array of electrodes. These array electrodes were made of platinum metal in a soft silicone matrix and the electrode sites were either 400 or 700 μm diameter discs for the 5 × 5 and 3 × 7 arrays respectively. Different patterns of electrodes were activated to determine whether the patient could correctly identify this pattern.

All four types of electrodes were hardwired to a computer. Specifically, stimulus delivery was controlled by computer hardware and software and outputted to optically isolated constant current generators that subsequently injected this controlled pulse to the electrodes stimulating the retina. The stimulus used was a charge-balanced cathodic first bi-phasic square-wave pulse with and without an interphase delay. After a local anaesthetic injection at the planned site of micro-electrode insertion, the stimulating electrode was introduced through the eye wall and after traversing the intraocular cavity positioned either touching or just above the retinal surface. This setup allowed us not to block optic nerve conduction and thus permitted an electrically elicited retinal response to reach the visual cortex. During the test the patients were asked to do the following: (a) to describe the visual sensation elicited by retinal electrical stimulation, (b) to count each time they experienced a visual percept so it could be correlated with the stimulus frequency and to let us know if and when the visual percept reached 'flicker-fusion', and lastly, (c) when more than one percept was elicited to approximate the shape and spatial separation between them.

Results

Table 1 shows the pre-test vision status, and the diagnosis for each patient. Table 2 gives the threshold charges to elicit the patients' perceptions and the shape and colour of the visual perceptions as described by each patient.

Table 1. *Subjects' diagnosis and preoperative vision*

Subject	Diagnosis	Pre-operative visual acuity
1	RP	NLP
2	Retinal degeneration	LP
3	RP	NLP
4	RP	LP
5	AMD	NLP
6	RP	LP
7	RP	LP
8	RP	LP
9	RP	NLP
10	AMD	20/400
11	RP	LP
12	RP	LP
13	RP	LP
14	RP	LP

RP, retinitis pigmentosa; AMD, age-related macular degeneration; LP, light perception; NLP, bare light perception.

Phosphenes were elicited in all 14 subjects. The phosphene was described as brief and correlated exactly with the timing of electrical stimulation. The initial charge levels to elicit the response were higher by a factor of 2–3 than those needed later in the same test period. In all but subject 2, visual percepts were correctly localised to the retinal area being stimulated. Subjects 1 and 3, both RP patients, further described seeing movement when the probe was displaced across the retinal surface while delivering stimulus pulses.

In the second experiment with patient 1, a resolution test was performed using the second probe type. During this test, the centre conductor of two adjacent electrode sites was used in a monopolar fashion. Stimulating with a centre-to-centre separation of 435 μm, the smallest available, the patient described two spots of light each ¼ inch (6 mm) in diameter separated by ¼ inch (6 mm), and described these objects to be at 1 ft (30 cm) from him. In two tests to date, both in RP patients, we increased the stimulus frequency to see whether the visual percept could be seen as being continuously on. Electrical 'flicker-fusion' occurred in both patients, at approximately 50 Hz. The stimulus was described as becoming 'brighter' at higher frequencies.

Table 2. *The shape and colour of subjects' electrically elicited visual percepts, and the charge needed to elicit the response*

Subject	Percept shape	Percept colour	Charge (mC)
1	Letter 'H'	Yellow–green	0.4
2	?	?	0.95
3	Match-head	Yellow	0.16
4	Pin	Yellow	3.2
5	Pencil	White	6.0
6	Pea	Yellow	2.8
7	Pin	Yellow	1.6
8	Pin	Yellow	1.8
9	Pin	White	1.1
10	Pin	White	0.3
11	Pin	Blue	2.4
12	Pin	Yellow	1.0
13	Pin	White	1.2
14	Box	White	1.4

mC, millicoulombs.

Probe 3 was used to evaluate the effect of probe geometry on the elicited image configuration in the AMD patient with the history of a large subretinal haemorrhage. The patient described his percept as a 'pencil' held at arm's length. The patient added that it was approximately 4 times as long as wide.

Discussion

Focal electrical stimulation of the retinal surface of 14 patients blind from photoreceptor loss elicited localised visual percepts. Eleven subjects with the characteristics of typical RP and two subjects with long-standing AMD described spatial and temporal aspects of the percept, including localisation. The 13 subjects' ability to detect electrical stimulation at the inner retinal surface despite bare or no light perception vision and the ability of the patient with geographic atrophy to see the electrical stimulation in the area of a complete scotoma in the macular region indicates that at least some of the inner retinal neurons are functional despite decades of severe photoreceptor loss. The ability to resolve closely spaced electrodes further lends support to the idea that electrical stimulation of the remaining retinal neurons may actually afford some resolution. The ability to convey shapes via electrically stimulating with electrodes at the retinal surface is also evidence that the end goal of providing form vision to these blind patients may be possible by this approach. The threshold charge densities at the stimulating electrodes were within safe limits for chronic neural stimulation in the majority of our tests. These charge requirements may further be decreased as the stimulating electrode is brought closer to the retinal surface and possibly by altering the stimulus waveform parameters and electrode geometries.

As for subject 2 and his failure to distinguish anything beyond flashing lights, we feel that this may either be due to the fact that the insult to his visual system occurred at such an early stage that it resulted in significant transneuronal degeneration or because the subject had never had form vision he could not convey to us what he saw.

Other technological and physiological hurdles remain, ranging from powering and hermetic sealing of such a device to the many retinal functions such as colour coding and logarithmic gain control that have yet to be addressed. Fortunately, a number of these issues have begun to be addressed to some extent in other prostheses and the work from image sensing arrays.[5]

Our findings demonstrate, for the first time to our knowledge, that local electrical stimulation of the retina can elicit discrete visual percepts in blind patients. If a visual prosthesis such as proposed here is feasible, it would restore or enhance vision in many people for whom no other treatment is expected to be available in the foreseeable future. Thus, we feel that further research is warranted into controlled prolonged electrical stimulation and strategies to improve the resolution, so that ultimately an intraocular visual prosthesis can be built.

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