

Visual sensations produced by intracortical microstimulation of the human occipital cortex

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1 Introduction

WHEN THE visual cortex in the occipital lobe is electrically stimulated, human subjects see circumscribed and often punctate sensations of light, called phosphenes. Several groups have investigated the possibility of using stimulation with electrodes placed on the surface of the cortex to develop a prosthesis for the blind that might be of value in reading and mobility (BRINDLEY and LEWIN, 1968; BRINDLEY, 1973; 1982; DOBELLE and MLADJEVSKY, 1974; DOBELLE *et al.*, 1976). Problems with surface stimulation include high currents for eliciting phosphenes, interactions between phosphenes generated by simultaneously stimulated electrodes, and occasional persistence of phosphenes following cessation of stimulation. Because non-human primates have been able to detect significantly lower currents with intracortical stimulation of the visual cortex (BARTLETT and DOTY, 1980), we wanted to validate these findings in awake humans and to determine whether the percepts so evoked are suitable for a functional prosthesis. We found that electrical current thresholds for producing phosphenes by intracortical microstimulation are 10–100 times lower than those produced by stimulation with non-penetrating cortical surface electrodes, that phosphenes can be resolved with simultaneously stimulated electrodes as close as 700 μm , and that the phosphenes have simple forms that are stable and predictable. These results are encouraging for the possibility of a visual prosthesis based on intracortical microstimulation.

2 Methods

Three normally sighted patients who were undergoing occipital craniotomies under local anaesthesia for excision of epileptic foci were studied for approximately one hour

each. The nature and possible consequences of these experimental studies were fully explained to them before informed consent was obtained. The patients had been on various anticonvulsive medications which were tapered 48–72 h before surgery and were withheld on the morning of surgery. Preoperative medications included diazepam, droperidol and fentanyl. The only medication given during surgery was the local anaesthesia, bupivacaine hydrochloride sometimes mixed with lidocaine. During the one hour study time 80–150 stimulus presentations were tested, of which 30–50 per cent were above threshold for producing phosphenes. Prior to testing with intracortical micro-electrodes, a hand-held probe with a 0.75 mm diameter platinum ball stimulating electrode was placed on the pial surface of the visual cortex to identify regions capable of producing phosphenes near the central or foveal region of the subject's visual field. All stimulation locations were within 2 cm of the posterior pole of the occipital cortex. During stimulation trials, the subjects fixed their gaze on a point in the centre of a white screen and reported the details of the phosphenes including the position and size by reference to calibrated markings on the screen.

Following the initial mapping with the surface electrode, we inserted microstimulating electrodes into the cortical regions that were topographically associated with phosphenes in the most central portions of the subject's visual field. Single microstimulation electrodes were fabricated from 37.5 μm diameter iridium wire that was microwelded on one end to a 25 μm diameter gold lead prior to electrolytically sharpening the free end in a taper to approximately 2 μm diameter (SALCMAN and BAK, 1976). The entire assembly was then insulated with Parylene-C (LOEB *et al.*, 1977). The geometric areas of the electrode tips were controlled by using a high voltage arc discharge to remove the Parylene-C and covered the range from 40 μm^2 to 800 μm^2 . The exposed iridium tip was then electrochemically activated to increase its charge-carrying capacity (ROBBLEE *et al.*, 1983). Two- and three-electrode arrays

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were made by attaching single electrodes together in the region of their weld joints with epoxy prior to the Parylene coating step. Electrode tip spacings were varied from 250 μm to 1000 μm . The electrodes were sterilised in ethyl-

The lowest thresholds of 20 μA were obtained in the first subject (SE) when microelectrode tips were located about 2–3 mm deep. Fig. 2 compares the thresholds at various depths with the threshold for the ball electrode on the pial

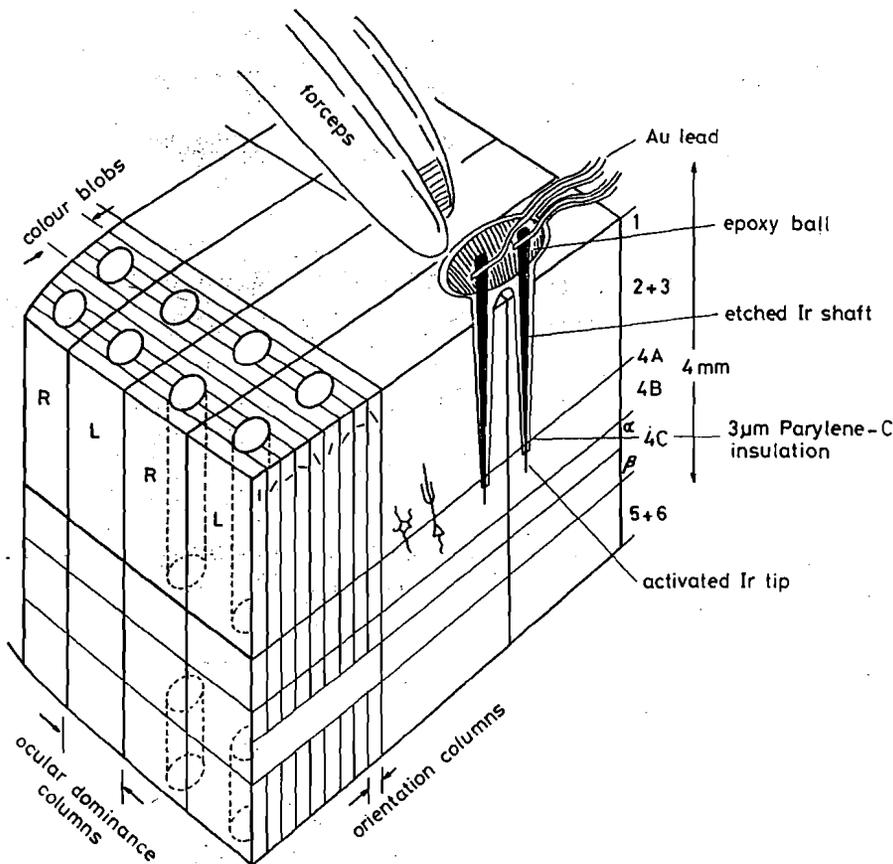


Fig. 1 Typical dual microelectrode shown in relationship to the layers and columns of the primary visual cortex (LIVINGSTON and HUBEL, 1984)

ene oxide and outgassed for 48 h prior to use. Constant-current, capacitor-coupled biphasic pulses (0.2 ms per phase, 100 pulses s^{-1} , 0.1–1 s train length) were delivered by photically isolated stimulators. The maximum charge density per phase was limited for electrochemical safety to 5 mC cm^{-2} for cathodic-first pulses and 40 mC cm^{-2} for anodic-first pulses (ROBBLEE *et al.*, 1983).

Fig. 1 shows the approximate relative dimensions of a typical microelectrode array with respect to the anatomical layers and functional columns in the primary visual cortex. Arrays of 1–3 microstimulating electrodes were inserted, using hand-held forceps, to predetermined depths.

3 Results

Electrical stimulation above perceptual threshold levels elicited an immediate and unambiguous response from subjects, who initially seemed startled by the appearance of a phosphene. In all patients surface stimulation reproduced the previously described (BRINDLEY and LEWIN, 1968; BRINDLEY, 1973; 1982; DOBELLE and MLADJEVSKY, 1974; DOBELLE *et al.*, 1976) phenomenon of punctate phosphenes during brief trains of biphasic pulses with thresholds of 1–2 mA. For both surface and intracortical stimulation, the phosphenes were readily described and consistently and precisely mapped in the contralateral visual field. The only consistent difference in their appearance was that surface-evoked phosphenes tended to flicker, regardless of stimulus parameters. The intracortically evoked phosphenes were described as steady, with crisp onset and offset that corresponded to the stimulus train as judged by the subject when given a simultaneous auditory cue.

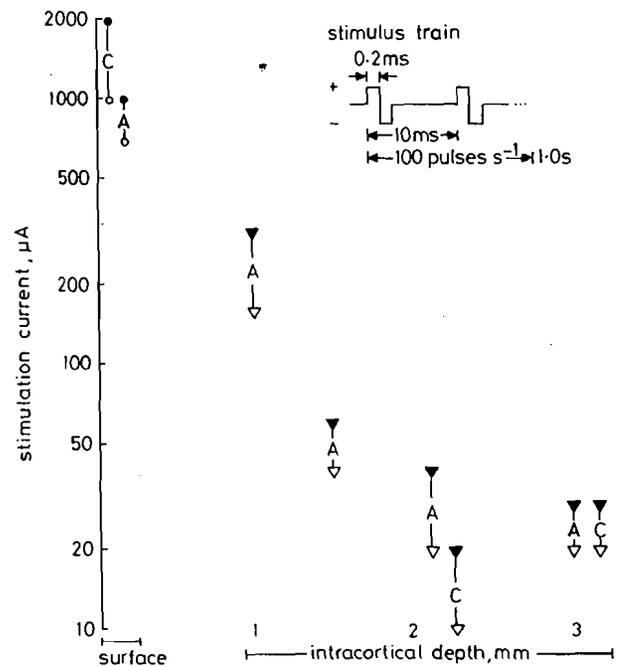


Fig. 2 Minimum stimulus currents (log scale) that evoked phosphenes (filled symbols) and the next lower level tested that did not (open symbols) with a cortical surface electrode and with a microelectrode having an exposed surface area of 200 μm^2 at different intracortical depths during a single cortical penetration. C denotes a biphasic stimulus with the first phase cathodal; A denotes inverted or anodic-first waveforms. The insert shows a typical test train (1 s long, 100 pulses s^{-1}), in this case with anodic-first biphasic

surface at the location of microelectrode insertion. In this patient, biphasic pulses with a leading anodal phase had lower thresholds at the surface, whereas cathodal leading pulses were more effective intracortically.

The second and third patients had minimum intracortical thresholds of $80\ \mu\text{A}$ at a depth of 4 mm (subject DS) and $200\ \mu\text{A}$ at a depth of 4.5 mm (subject DC). Although higher than we obtained in the first patient, they were still much lower than these subjects' surface thresholds, both of which were 2 mA.

Most of the phosphenes elicited at the lowest thresholds of intracortical stimulation in subject SE had a circular shape and subtended approximately $1\text{--}2^\circ$ of visual arc (at about $7\text{--}10^\circ$ from the fixation point), although one was described as 'an oblique line, narrow, blue'. They were almost all strongly coloured, usually blue or yellow (although one was consistently described as red). Increasing the stimulus intensity generally made the phosphenes brighter but often somewhat smaller. Trains of interleaved stimuli presented simultaneously on two adjacent electrodes spaced $0.7\text{--}1.0$ mm apart tended to produce fused percepts, described as 'two blobs fusing' or 'like a teddy bear'. With tips only 0.3 mm apart, the percept elicited by interleaved stimulation of both sites was described as a singular, round shape.

Following surface stimulation of the left occipital pole at levels as high as 5 mA, patient SE reported spontaneous aura-like visual sensations which were different from the small flashing lights associated with his epileptic seizures. We were able to elicit phosphenes by intracortical stimulations within the subject's central 2° of visual field against both this epileptiform background 'light' and the normal visual input from the retina which appeared to have remained unaffected. No epileptiform activity was experienced by the other two subjects during our experiments.

The second and third patients reported phosphenes that were punctate (probably less than 0.2° of visual arc) and essentially colourless ('white' or 'yellowish'). In both, most of the one hour study time was consumed attempting to find lower threshold sites, and so few psychophysical details were obtained. However, in one case, interleaved stimulation of two sites 0.9 mm apart, each of which produced a 'tiny, white dot' when stimulated alone, resulted in an 'elongated line', radially orientated, which did not have enlargements like a dumb-bell.

4 Discussion

The most important findings relative to the design of a visual prosthesis are that intracortical microstimulation in humans produces phosphenes at much lower thresholds than surface stimulation and that these phosphenes are small and usually simple sensations of light rather than complex shapes. The most striking qualitative difference from the surface stimulation studies reported by BRINDLEY and LEWIN (1968) in blind subjects is that intracortical phosphenes in sighted patients do not flicker. However, DOBELLE *et al.* (1974) reported that some of their blind patients did not experience flickering during surface stimulation. It is our feeling that persistence of phosphenes following cessation of the stimulus train and flicker as has been reported by others with surface stimulation (BRINDLEY and LEWIN, 1968; BRINDLEY, 1973; 1982;

DOBELLE and MLADEJOVSKY, 1974; DOBELLE *et al.*, 1976) signifies neuronal activity patterns such as those seen with epileptiform afterdischarges (POLLEN, 1977). The lowest thresholds seemed to be associated with somewhat larger, coloured phosphenes, suggesting that we may be starting to see the percepts encoded by single ocular dominance columns or colour blobs in the absence or reduction of surround inhibition. However, such an interpretation remains highly speculative.

The next stage of research into the feasibility of a visual prosthesis will require a chronically implanted microelectrode array in a blind volunteer. This will allow detailed psychophysical descriptions of phosphenes produced by a wide range of temporo-spatial patterns of electrical stimulation. The studies described here provide general guidelines for the typical specifications of intracortical electrode arrays, including penetration depth and tip spacing. It seems likely that thresholds in a fully alert, experienced subject with a chronic implant will be lower than we found in this study and may even approach the $1\text{--}5\ \mu\text{A}$ levels that have been reported in monkeys using chronically implanted microstimulation electrodes and behavioural detection methods (BARTLETT and DOTY, 1980). If so, it may be possible to make much stronger inferences about the percepts encoded by electrical activity in small populations of cortical neurons.

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