A hearing prosthesis for severe perceptive deafness—Experimental studies

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Introduction

In the last few decades advances in science and surgery have permitted man to repair or replace almost every organ in his body. This is not the case, however, with the brain and spinal cord as these structures will not regenerate. Nevertheless, with recent developments in neurophysiology and technology it is becoming possible to correct brain and spinal cord dysfunction. For example, a multiple electrode array has been implanted over the visual cortex of a blind patient to help overcome this sensory disability (Brindley and Lewin, 1968). Attempts have also been made to cure severe nerve deafness by implanting electrodes in the cochlea, auditory nerve and central auditory pathways, and stimulating the auditory system electrically (Djourno and Eyries, 1957; Doyle et al., 1964; Simmons et al., 1964; Simmons et al., 1965; Michelson, 1971).

One of the first recorded attempts to stimulate the auditory nerve was by Lundberg in 1950 (cited by Gisselsson, 1950), who did so with a sinusoidal current during a neurosurgical operation. The patient, however, could only hear noise.

A more detailed study was performed by Djourno and Eyries (1957), and the stimulus parameters appear to have been well controlled. In their patient, the electrodes were placed on the auditory nerve, which was exposed during an operation for cholesteatoma. The patient was able to appreciate differences in increments of 100 pulses/sec, up to a frequency of 1000 pulses/sec. He was also able to distinguish certain words such as 'papa', 'maman' and 'allo'.

Another investigation was carried out by Simmons et al. (1964) who were able to stimulate the auditory nerve and inferior colliculus in a patient undergoing a craniectomy for a cerebellar ependymoma. The patient was able to differentiate different frequencies from 20–3500 pulses/sec., and at 850 pulses/sec. had a difference limen of 5 pulses/sec. Stimulation of the inferior colliculus, however, produced no hearing sensation. In this study, the patient had satisfactory cochlear function, and thus his ability to detect a frequency of 3500 pulses/sec. was probably due to the fact that hearing was electrophonic in origin.

From the work of Djourno and Eyries (1957) it appeared that electrical stimulation of the auditory nerve could not reproduce frequencies
above 1 kHz. This failure to respond to higher frequencies was probably due to the fact that the auditory nerve, because of its refractory period, is like other nerves in the body and cannot be stimulated more rapidly than 1000 pulses/sec.

Although a nerve fibre will not fire more rapidly than a rate of 1000/sec., it can fire in phase to acoustic stimuli up to 5 kHz (Rose et al., 1967). This means that, in response to a 5 kHz tone, an auditory nerve fibre could fire every fifth cycle of the stimulus at a constant phase of the sine wave. If we consider a large population of nerve fibres responding to a 5 kHz tone, then some will fire every cycle.

This ability of nerve fibres and cells to fire in phase with a sound wave could explain how frequency is coded, and is the basis of the volley theory of hearing. This is illustrated in Figure 1 which shows auditory nerve cell action potentials firing in phase with a 300 Hz sine wave.

![Auditory nerve cell action potentials firing in phase with a 300 Hz acoustic signal.](image)

**300 Hz**

Consequently, if the auditory nerve is to be stimulated in accord with the volley theory, an electrical stimulus should be found which will cause the nerve cells to fire in phase, but not necessarily with each cycle, so that a response to high rates of stimulation can be obtained.

Information about the frequency of a sound may also be conveyed to the brain on the basis of the place theory. In this case it does not matter whether the nerve cells fire in phase with the sine wave, but the important thing is to stimulate the correct nerve cells. The hearing receptors in the inner ear, and the cells and fibres in the central nervous system are arranged in an orderly anatomical way so that they will respond to a
A hearing prosthesis for severe perceptive deafness limited range of frequencies along a scale from low to high. This is illustrated in Figure 2. This means that if we want to reproduce a 5 kHz tone artificially by electrical stimulation, those auditory nerve fibres should be stimulated which normally convey this information. This may be done surgically by placing electrodes close to the auditory nerve fibres where they fan out to supply the organ of Corti.

This was performed by Doyle et al. (1964) who reported inserting an array of electrodes into the cochlea of a patient with total perceptive deafness. The electrodes were designed to limit the spread of the electrical field, and they were stimulated in sequence with threshold square waves which had speech signals superimposed upon them. Although the four electrodes were not especially implanted to take advantage of the spatial distribution of auditory nerve fibres responding to different frequencies, this could have been the reason for the satisfactory result obtained.

A more extensive study was reported by Simmons et al. (1965), and Simmons (1966), who described the results of implanting six electrodes into the modiolus of the cochlea in a patient with very severe perceptive deafness. The electrodes were implanted along the modiolus so that nerve fibres representing different frequencies could be stimulated. The patient was then tested to determine the effect of alterations in the frequency and intensity of the signal. Monopolar and bipolar stimulations were compared, speech and pulse-encoded speech were given, and the waveform of the stimulus was also varied.
The results indicated that the patient could detect a change in pitch up to a frequency of 300 pulses/sec. Single stimuli produced a pitch sensation, and there was also correlation between the position of the electrode and the pitch elicited with stimulation, so that a rough frequency scale was apparent. This is evidence in support of the place theory of hearing. When speech signals were used as electrical stimuli, the patient could not understand their meaning, but could recognize them as speech, possibly from their rhythm.

More recently Michelson (1971) implanted electrodes in the basal turn of the cochlea by inserting them through the round window membrane. Two of the four patients operated on were able to distinguish changes in the rate of stimulation up to 10,000 pulses/sec; however, speech comprehension was unsatisfactory. Although electrical stimulation of the inner ear by this method is an interesting development, and warrants further investigation, it is likely that some of the results obtained from these patients were due to the electrophonic effect, and not direct stimulation of the auditory nerve fibres. Perception of changes in rates of electrical stimulation in excess of 1000–2000 pulses/sec suggests an electrophonic effect and furthermore, as each unoperated ear still had residual hearing, stimulation could have occurred by bone conduction as described by Flottorp (1953).

In the case reports described above, experience with direct electrical stimulation of the auditory nerve and its terminal fibres indicates that the surgical treatment of perceptive deafness is possible. A number of problems will have to be solved, however, before satisfactory speech intelligibility can be achieved.

Electrical stimulation of the auditory nerve could not be expected to produce hearing in patients with damage to the higher auditory centres. Many children and some adults with perceptive deafness, however, have a lesion involving the cochlea and not the higher centres (Ormerod, 1960), and could be helped when their deafness is severe.

It would also be desirable to have clinical tests which enable patients to be selected into those most likely to benefit from the operation. Tests of speech intelligibility and the presence of recruitment are satisfactory when some residual hearing remains, but in patients where severe or total deafness is present these methods would not be adequate. It is possible that an objective test of hearing using preliminary electrical stimulation of the cochlea could be devised.

The type of electrodes used, and their method of implantation will also have to receive careful consideration. Simmons (1967) has shown that when electrodes are chronically implanted their resistance increases, and this could lead to unreliable stimulation. He has also demonstrated that when electrodes are chronically implanted in the cochlea of cats through an incision in the round window, the surgical trauma need not cause
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permanent damage. The factors responsible for degeneration of the organ of Corti and auditory nerve fibres were unpredictable, however, infection was found to consistently produce widespread destruction of tissue.

Consequently, the site and method of implantation are important as the neural pathways can be damaged, and this would prevent electrical signals being transmitted to the higher centres. Destruction of the cochlea can lead to transneuronal degeneration in the cochlear and superior olivary nuclei up to a year after the production of lesions (Powell and Erulker, 1962). This need not occur, as Schuknecht (1953) has shown that experimental damage of hair cells does not cause secondary nerve degeneration. This only occurs when the changes in the organ of Corti become so severe that they involve the supporting cells.

Not only do these technical problems require solution, but a greater understanding of the encoding of sound is desirable. As emphasized by Lawrence (1964), the terminal auditory nerve fibres are connected to the hair cells in a complex manner, which could make it difficult for electrical stimulation to simulate sound.

As the results of electrically stimulating the auditory nerves of patients have not been entirely satisfactory in helping them communicate, further understanding of the problems involved is desirable. Fortunately, a great deal of the research necessary can be undertaken on animals, and it is hoped the findings may be applied directly to patients.

In the experimental studies to be described we have examined the properties of electrodes; the histological changes in the brain and cochlea following the long term implantation of electrodes; and, finally, the parameters of the electrical stimulus that are relevant to the perception of hearing.

**Electrodes**

When stimulating the inner ear electrically the immediate and long term properties of the electrodes are important as their impedance will vary with time, rate and strength of stimulation. This will result in variations in the current used to stimulate the terminal auditory nerve fibres; and apart from causing variations in results, it may produce thermal and chemical damage of the fibres.

These variations in impedance are due to a number of factors. At the low rates of current flow that are desirable in stimulating the auditory nerve fibres, changes in impedance largely depend on the reversibility of the electrode system. A reversible electrode is one in which current can pass from either the electrode into the solution or out through the other electrode without producing a net voltage drop at the interfaces (Dewhurst, 1966). This is illustrated in Figure 3 which shows that with a reversible electrode a small change in voltage produces a linear increase in current. On the other hand, with an irreversible electrode a larger
change in voltage is required to produce an initial current flow. Reversible electrodes may consist of a metal or a non-metal in contact with a solution of its own ions, for example, Zn and Zn$^{++}$ Cl$^{-}$; a metal and a sparingly soluble salt of the metal in contact with a solution of a soluble salt of the same anion, for example, Ag-AgCl and Cl$^{-}$; and an unattackable metal, for example, gold or platinum immersed in a solution containing oxidized and reduced states of an oxidation-reduction system.

The impedances of silver-silver chloride, stainless steel and platinum electrodes implanted in the cochleas of three cats were measured for different currents, and rates of stimulation. The results can be seen in
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Figure 4, and show that for silver-silver chloride electrodes there was little difference in impedance measurements for small and large currents. On the other hand, the greatest differences were observed for the platinum electrodes. These results therefore indicate that silver-silver chloride electrodes were the most, and platinum the least reversible.

When high current densities are produced in the electrodes, the variations in impedance are largely due to the fact that the rate of electrolysis exceeds the rate ions can diffuse to the electrode. This impedance

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**Fig. 4.**

Impedance measurements of silver-silver chloride, stainless steel and platinum electrodes implanted in the auditory nerves of cats. Impedance measurements were made for different currents and rates of stimulation.
increases with the duration of the period of electrical stimulation, and explains why in Figure 5 the immediate poststimulus impedance recorded from one stainless steel electrode pair was higher than the prestimulus impedance. High current densities may also cause thermal damage of the auditory nerve fibres.

![ELECTRODE IMPEDANCE PRE AND POST STIMULATION OF A STAINLESS STEEL COCHLEAR ELECTRODE](image)

Fig. 5. Pre- and post-stimulation impedance measurements from a stainless steel electrode implanted in the cochlea of a cat.

Finally, when a metal electrode is introduced into the scala tympani or vestibuli a double layer of ions develops at the solid-liquid interface. This acts like a capacitor, and consequently for low rates of stimulation the impedance is greatly increased as shown in Figures 4 and 5.

In selecting the type of electrode to be used they should be chemically inert as they need to be chronically implanted. Chemical irritation of tissues may be produced by three factors: firstly, toxic ions may be present in the electrode, particularly heavy metal ions; secondly, the electrode may be attacked by biological fluids which could give rise to toxic products; thirdly, electrical stimulation may involve an interchange of metal between the electrode and tissue fluid. If silver-silver chloride electrodes are chronically implanted toxic silver ions may be released over a period of time. When current is passed through stainless steel electrodes iron is deposited in the tissue, and for this reason they are also not entirely satisfactory. Consequently, gold or platinum electrodes are to be preferred for electrical stimulation of the inner ear.
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The insulation of cochlear electrodes is of great importance as they need to be bent, and may impinge against sharp bony spurs. They should be completely insulated except at the tip where stimulation is to occur. The insulating material should have good biological tolerance, low electrical conductivity, resistance to mechanical trauma, flexibility to allow bending without breaking, resistance to fluids and enzymes, imperviousness to moisture, resistance to heat to allow autoclaving, easy application to the metal and be commercially available.

The electrodes should produce no mechanical disturbance or destruction of tissues and also cause no heating of the tissues. A good anchorage is essential for a lasting implant.

Materials used to fix the electrodes in place should act in the presence of moisture and the solvent should be non-toxic to nerve fibres. In our studies we have found that the solvents for certain dental cements are toxic to the inner ear and produce a reduction in the cochlear microphonics when applied to the round window. These are also likely to be toxic to nerve fibres and for this reason are best not used in close proximity to the cochlea.

Histological changes in the cochlea and central auditory pathways

It is important as a pre-requisite to any method of implanting electrodes in the cochlea in humans to know what histological changes occur, and how the technique of implantation affects the terminal auditory nerve fibres, and the higher central auditory pathways. Consequently, all the temporal bones and brains of the cats in a series of experiments have been sectioned, stained and studied.

The temporal bones and brains were stained with haematoxylin and eosin to show the presence of fibrosis in the cochlea, the state of the spiral ganglion cells and terminal auditory nerve fibres, as well as the presence of fibrosis around the electrode tracks in the brain. The brains were also stained by the method of Nauta and Gygax (1951), and the cochlear nuclei and superior olives studied in particular for evidence of terminal axon degeneration, as a study by Powell and Erulkar (1962) has shown that destruction of the cochlea could lead to nerve degeneration in these higher centres.

The results of this study showed that when infection involved the cochlea there was marked atrophy of the organ of Corti and in one case the infection involved the surrounding temporal bone. The degeneration of the spiral ganglion cells and auditory nerve fibres was not as marked as the degeneration of the organ of Corti would suggest, and this is supported by the work of Schuknecht (1953), who showed that this was more likely to occur when the changes were so severe that they involved the supporting cells. This would also explain the fact that in the serial
sections of the brains stained by the Nauta and Gygax method (1951), there was no evidence of axon degeneration.

The results of this study therefore indicate that when electrodes are inserted into the cochlea every precaution must be taken to prevent infection. Unless severe, however, auditory nerve degeneration is not so likely to occur.

Auditory brain cell responses to electrical stimulation of the cochlea and auditory nerve

In this series of experiments the auditory nerves and cochleas of seven cats were stimulated electrically in a number of different ways to see whether the firing patterns of auditory nerve cells produced in response to sound could be reproduced by an electrical stimulus (Clark, 1969). The experiments were also carried out to help determine whether stimulation in accordance with the volley theory or place theory of pitch perception is more likely to be of value in reproducing hearing artificially. According to the volley theory of pitch perception the brain cells fire in phase, but not necessarily in response to each sine wave of the acoustic signal. According to the place theory the location of the cell stimulated is of importance in the perception of pitch and not the rate of stimulation.

Stimulating electrodes were placed in the auditory nerve, and recording electrodes inserted into the superior olive, a second order cellular station in the central auditory pathway.

The responses of the cells to sound were first recorded by photographing the action potentials on the cathode-ray oscilloscope (Figure 6a). When the auditory nerve was stimulated electrically with sine and square waves, cells could not be made to fire more rapidly than 200/sec. Figure 6 shows the action potentials that occurred in response to a sound of 700 Hz which was close to the unit's characteristic frequency. Electrical stimulation of the auditory nerve with sine and square waves at the same rate, could not reproduce this firing pattern (Figures 6b and 6c).

The responses from the auditory cells were from a randomly selected sample in the superior olive, but did not indicate the responses of the total population of cells. For this reason macro-electrodes were also inserted into the superior olive, and they recorded the field potentials or electrical activity from a large number of cells. When the auditory nerve was stimulated with electrical square waves at rates from 1 to 500/sec. it was found that the field potentials were reduced at rates greater than 300/sec. (Fig. 7). From this combined evidence it would therefore appear that it is not possible to reproduce pitches greater than 300 Hz by electrical stimulation of the auditory nerve if the volley theory is important in coding frequency.

In this study not only were stimulating electrodes implanted in the auditory nerve, but they were also applied to the round window and basal
A hearing prosthesis for severe perceptive deafness turn of the cochlea. In this latter case high rates of electrical stimulation could induce cells with high characteristic frequencies to fire, but not of course at similar high rates of electrical stimulation. An example of a cell firing consistently amidst the electrical artefact of a 7000/sec. electrical stimulus can be seen in Figure 8. When using stimulating electrodes applied to the round window it was not possible, however, to excite cells with low characteristic frequencies, and this was probably due to the distance of the apical turn from the round window and the electrical resistance properties of the cochlea.

The results of this experimental study on brain cell responses to electrical stimulation of the auditory nerve and cochlea indicate that the
components of speech with frequencies less than 300 Hz may be conveyed by global electrical stimulation of the auditory nerve. It also seems desirable to selectively stimulate different auditory nerve endings in accordance with the place principle so that sufficient information can be conveyed to the patient to make speech comprehension possible.

**Behavioural responses in the cat to electrical stimulation of the cochlea and auditory nerve**

There are limitations to the assessment of electrical stimulation of the auditory nerve as an effective means of restoring hearing, when brain
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...cell responses are used as the criterion of success. The relation between the perception of sound, and the pattern of brain cell firing is still not clearly understood.

![Diagram](image)

**FIG. 8.**

The responses of a cell in the trapezoid body of the cat to a tone of 7000 Hz and electrical stimulation of the cochlea at a rate of 7000/sec (Clark, 1969).

For this reason a further series of studies have been undertaken using alert cats which were conditioned and trained to respond to sound of different frequencies, and rates of change of frequency. Their behavioural responses were then compared with those obtained by electrical stimulation of the terminal auditory nerve fibres in the cochlea.

In some experiments the electrodes were implanted directly into the cochlea by drilling the overlying bone of the basal and apical turns (Fig. 9), and in others they were introduced through the round window. To make sure that when the auditory nerve fibres were stimulated electrically the cat was not hearing by the electrophonic effect, only those cats were included in the series where cochlear microphonic potentials could not be recorded. In one animal a further study was also carried out after the cochlea had been irradiated with 2000 rads to destroy the organ of Corti.
In one series of experiments a pair of electrodes was inserted into that portion of the cochlea excited maximally by a frequency of about 8000 Hz, and a second pair into that part excited by a frequency of about 500 Hz (Fig. 9). The response thresholds for different rates of electrical stimulation of both electrodes were then determined. It was assumed that if the volley theory is important in the coding of sound the response threshold would be lower for low rates of stimulation of the apical electrode, as this was inserted into an area of the cochlea most responsive to low frequency sound.

The results were rather unexpected (Fig. 10), and showed that the cat was more sensitive to low rates of stimulation of the basal or high frequency end of the cochlea. These findings were also confirmed by a further series of experiments, and suggest that the cat could in fact perceive low frequency sound when the basal turn of the cochlea was excited, or alternatively, was responding to a more non-specific aspect of the electrical stimulus. The results are of interest as psychoacoustic experiments have shown that missing fundamentals which have a low pitch are perceived by exciting the basal turn of the cochlea. Michelson (1971) also reports that low frequency pitch was perceived by his patients when a round window electrode was inserted into the basal turn of the cochlea.
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As these studies indicated that the basal turn or high frequency end of the cochlea was sensitive to low rates of electrical stimulation we performed a further study. In this series of experiments cats were conditioned to respond to a sound with a changing frequency. Electrodes were then introduced into the basal turn of the cochlea through the round window, and the responses to changes in the rate of an electrical stimulus were then compared with those obtained for a frequency modulated sound.

The results showed that the cat could respond to low rates of stimulation of the basal turn, and in this series the difference limens for electrical stimulation were similar to those for sound of the same frequency. Precautions were also taken to ensure that the results were not due to the electrophonic effect, and this is supported by the fact that the difference limens for electrical stimulation at rates in excess of 1000 pulses/sec. were much longer than for sound.

It is of practical importance that the basal turn of the cochlea will respond to low rates of electrical stimulation, as this region is accessible.
to surgical approaches. The results of these conditioning studies also showed that it may be possible to reproduce pitches up to 1000 Hz using an electrode introduced into the basal turn of the cochlea through the round window. For this reason it seems hopeful that it should be possible to reproduce sufficient speech information to make communication feasible for the totally deaf person.

Summary

These basic studies on experimental animals have made it possible to determine more precisely the perceptual limits that can be obtained by electrical stimulation of the auditory nerve. They show the type of electrodes that should be used, and the most appropriate methods of implantation. They also suggest that if methods of electrical stimulation take advantage of both the place and volley theories of pitch perception it should be possible to convey sufficient information to make the perception of speech possible.

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