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SINGLE NEURON RECORDING FROM MOTOR CORTEX AS A POSSIBLE SOURCE OF SIGNALS FOR CONTROL OF EXTERNAL DEVICES

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For the severely handicapped patient, such as a quadriplegic, a large number of independent signals would be desirable to control neuromuscular stimulators that could impart movement to the paralyzed limbs. We have investigated the possibility of making long-term connections to the central nervous system with microelectrodes. Monkeys have been implanted with arrays of intracortical electrodes for periods of up to 37 months, indicating that long-term connections to the nervous system are possible. A second question investigated was whether the implanted monkeys could learn to modify the firing patterns of recorded neurons to control a device outside of their bodies. Through the use of an 8 target tracking task a monkey was able to produce an information transfer rate of 2.45 bits/sec when cortical cell signals were the monkey's output. The same task was performed having the monkey move a handle by wrist flexion and extension (i.e., using the intact motor system as the output). The information transfer rate increased to 4.48 bits/sec, or less than a twofold improvement. Thus, the direct output of cortical cells can provide information transfer only moderately less precise than the intact motor system. Our preliminary studies have been encouraging on obtaining connections to the nervous system to control external devices. However, numerous improvements are required in electrode design, fabrication, implantation, and signal processing techniques before this method of obtaining control signals would be feasible for human applications.

INTRODUCTION

For the severely handicapped patient, such as a quadraplegic, a large number of independent signals would be desirable to control neuromuscular stimulators that could impart movement to the paralyzed limbs. Some of the choices for control signals are speech, movement or EMG activity of still-

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functional muscles, and direct connections to the nervous system. All of these control sources have been investigated to some degree for controlling external assist devices. In principle, a promising source of control signals when a large number of independent signals is required, with direct connections to the nervous system. Connections can either be made to functional nerves or the central nervous system.

For a number of years we have been concerned with the techniques necessary to make long-term connections to the central nervous system and with an evaluation of whether an animal can use the firing patterns of single cells to control external devices. The electrodes (4) we have used were developed in the Laboratory of Neural Control at NIH and consist of 25 μm iridium wires electropolished to a 1 μm tip. The electrodes are 1.5 mm long, so that when they are implanted in the motor cortex the tips are usually in the pyramidal cell layer, where cells with direct outputs to the spinal cord exist. A 25 μm gold wire is microwelded to the upper end of the microelectrode to provide a very flexible electrical connection to a head mounted connector which allows the electrode to "float" with movements of the cortex. The microelectrode and gold wire are insulated with a vapor-deposited polymer (2), Parylene-C, that in animal studies provide long-term integrity and minimal tissue reaction (3). The electrode tips are exposed with a high-voltage arc. Arrays of up to 12 electrodes are fabricated in conjunction with a multipin connector.

In our animal studies, the electrodes were implanted in the motor cortex of monkeys under sterile operating conditions. The skin overlying the area of implantation was removed and a 20 mm diameter trephine hole was made over the area of the motor cortex. The dura was removed to expose the cortical surface. The connector of the electrode array was cemented to the skull and then each electrode was inserted with a fine forceps. In some implants the electrodes were attached to the pia with cyanoacrylate glue, which was essential for stabilization in cat experiments but of questionable benefit with monkeys. The trephine hole was closed with a Plexiglas chamber that formed a water tight seal to the cranium. The chamber was then filled with Ringer's solution to reestablish cerebral spinal fluid pressure and stabilize cortical movements. A sketch of the implanted electrode array is shown in Fig. 1.

After recovery from surgery the majority of electrodes recorded single unit activity. With our initial attempts at long-term recording (5), single unit activity was lost after six months. The impedance of one of the electrodes, measured at 1 kHz, along with neural activity at selected times during the implant is shown in Fig. 2. Neural activity was recorded from at least 8 different neurons with this electrode during the course of the implant, indicating that the electrode was slowly migrating through the cortical tissue. The average recording time from the "same" neuron was 8 days while the longest recording time was 23 days (see Ref. 5 for criteria of "same").

With a later implant two of the eleven electrodes were still recording unit

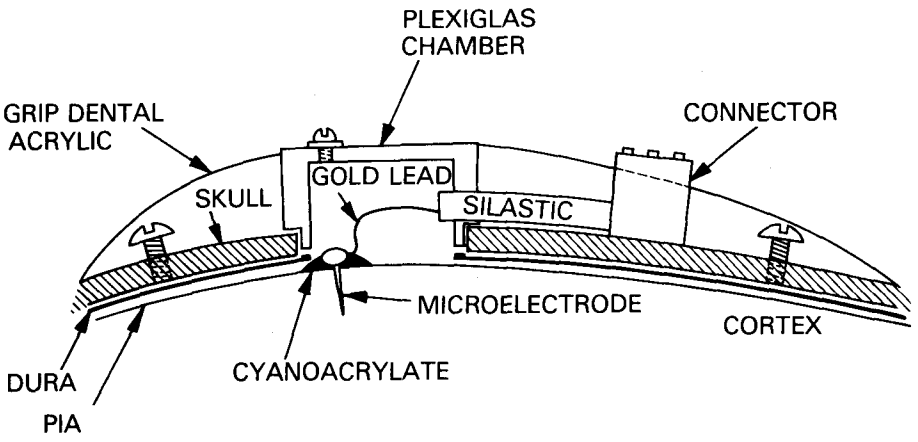

FIGURE 1. Implant arrangement for intracortical chronic recording microelectrodes (with permission of Academic Press, from Ref.5).

activity at the time the monkey was sacrificed more than 37 months after implantation (3). Figure 3 shows a scanning electron micrograph (SEM) of one of the electrodes that was still recording neural activity at the end of the experiment. With this implant the maximum time that activity was recorded from the same neuron was 108 days.

The impedance remained relatively constant for two of the electrodes over the 37 month implant. However, there was a sudden drop in impedance during the implant for the other 9 electrodes, suggesting a failure of the insulation. SEM's of the failed electrodes showed cracks in the Parylene-C along grain boundaries of the etched iridium shafts. Thus, it appears that long-term connections can be made successfully to the nervous system in the sense that a small number of channels carrying single unit signals can be maintained for periods of several years, although the available technology is still only marginally reliable.

A second area of concern with obtaining signals from the nervous system is to determine whether an animal can learn to use the activity of single cortical neurons to control an external device. Our experience involves operant conditioning of cortical cell firing patterns (6). The basic arrangement is shown in Fig. 4. The monkey is seated in a primate chair facing a row of eight target lamps, denoting required firing rates, each of which is surrounded by an annular cursor lamp that indicates the actual firing rate of the neuron being conditioned. The target and cursor lamps are numbered 1 to 8 from left to right. Target 1 corresponds to the lowest firing rate while target 8 is the highest rate. When a limiter circuit is acting all rates above position 8 are included in zone 8. Two alternating targets are presented to the monkey. A trial is initiated when the first target light appears. This target remains on until the monkey produces a neural firing rate that causes the cursor light to match the target light continuously for 450 msec. When this occurs the second target light is illuminated and a 4 sec period is allowed

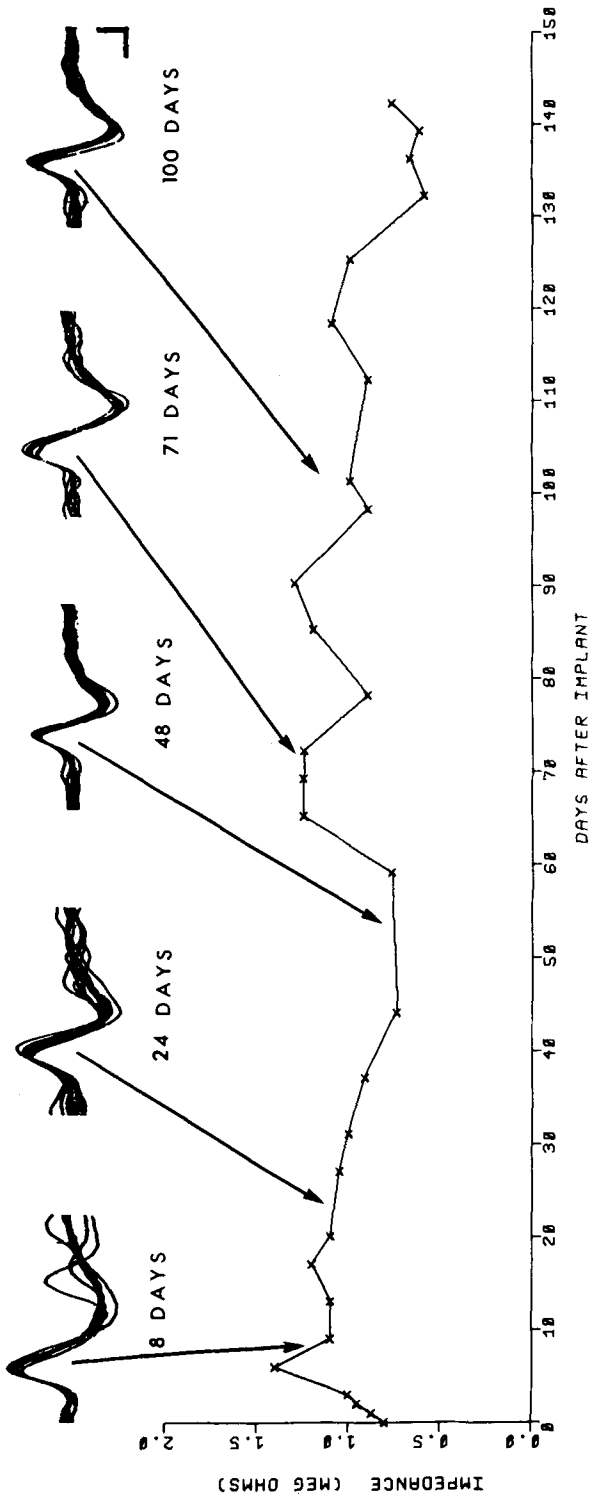

FIGURE 2. Impedance of one of the chronically implanted electrodes, measured at 1 kHz, over a period of 5 months. Superimposed action potentials are shown for 5 different recording days. Calibration 50 μV, 0.2 msec (with permission of Academic Press, from Ref. 5).

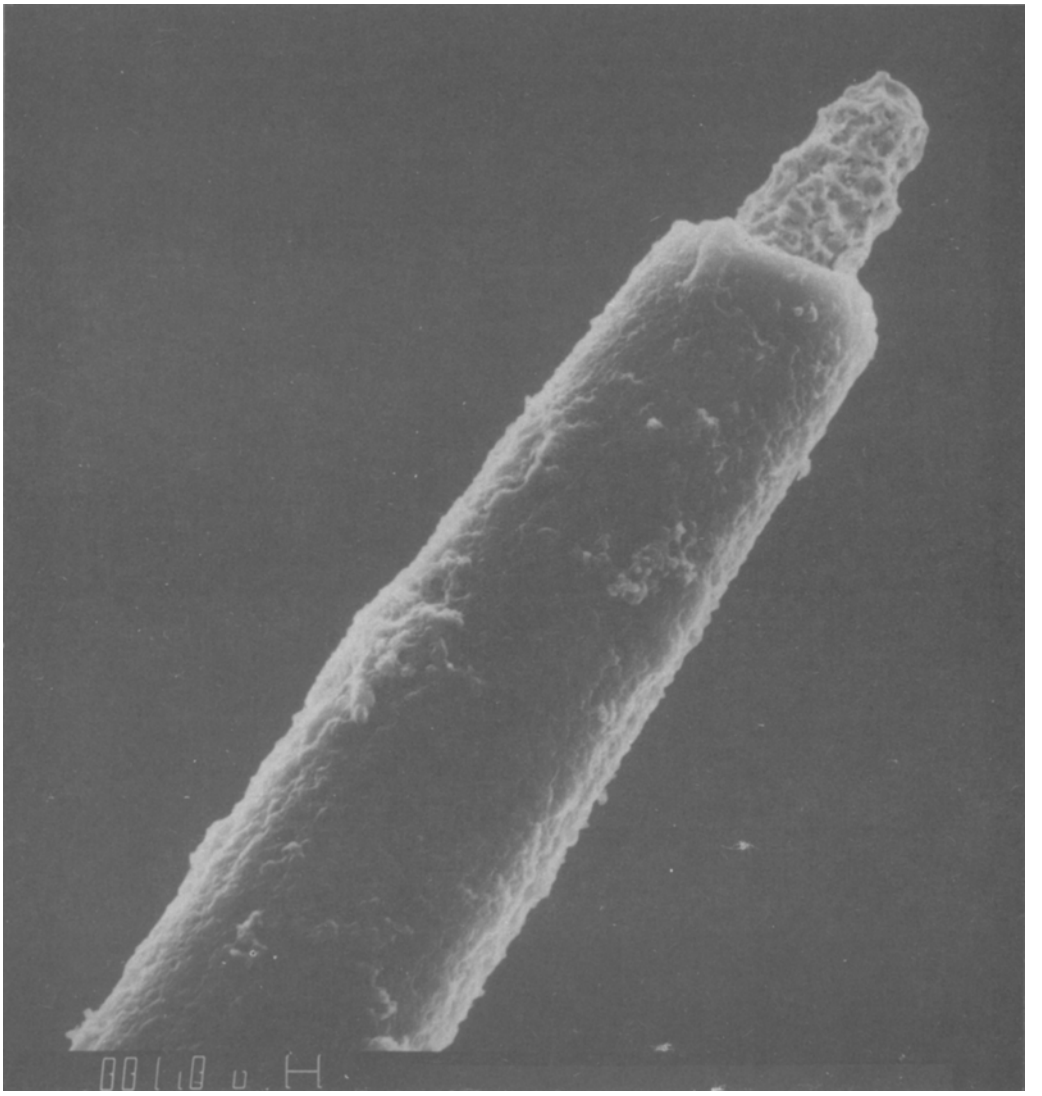

FIGURE 3. Microelectrode that had been implanted for more than 37 months. The roughening of the tip was produced by the high voltage arc removal of the Parylene-C; calibration 1 μm.

for the matching and hold phase of 450 msec. A successful match of the second target within 4 sec produces a liquid reward. Five seconds after the start of a trial the first target is again illuminated regardless of the outcome of the previous trial. A run consists of 25 rewarded trials, and cells used for runs that had greater than 50% rewarded trials were considered "conditioned." Twenty-six of twenty-eight neurons tested were eventually "conditioned" by this criteria.

With control of neuron firing patterns established at this level of com-

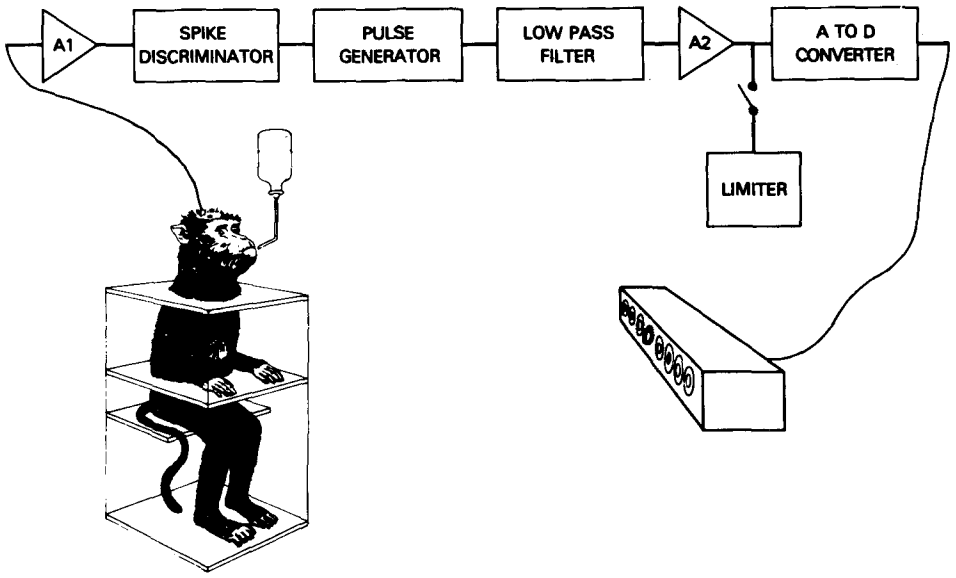

FIGURE 4. Arrangement for operantly conditioning cortical neuron firing patterns.

plexity, a more complex eight target random tracking task was then devised that allowed assessment of information transfer rates between target presentation and neural controlled responses (7). The performance of each run was measured in terms of the percentage of correct trials and the information outflow rate (IOR). Information theory defines the amount of information in a random sequence of targets as

$$I = \log_2(N_T) \text{ bits,} \tag{1}$$

where

I = information in bits,
N_T = number of different targets.

The information content of the eight target task is 3 bits. The IOR is a measure of the information input to the system and the time required to perform a correct response. It is defined as follows:

$$\text{IOR} = C \times I/(t_i - T_H), \tag{2}$$

where

C = number of correct responses,
n = number of trials per run,
t_i = time from target presentation to reward,
T_H = hold time on-target,
$t_i - T_H$ = time to target.

Each trial was limited to 8 sec, thus every missed trial required 8 sec to complete but transmitted zero information. Depending on the test paradigm used, a reward was given either for accumulating a specific time on target during the 8 sec trial, or holding continuously on target. Figure 5 illustrates

the distribution of firing frequencies of a cortical neuron, shown as the resultant cursor position, during a conditioning run when the task was to accumulate 1 sec on-target for a reward. All of the trials during a run when a specific target light was illuminated are grouped together. Although not all of the time during a trial was spent on-target, the highest percentage of time was on or very close to the desired target.

In order to see how precisely the monkey controlled the firing rate of a cortical neuron, the instantaneous firing rate was plotted in Fig. 6 for each target during the 1 sec preceding a reward. In each panel, the bands show the target zone (except for target 8 where firing rates above the horizontal line were included in zone 8 by the use of the limiter circuit). The feedback the monkey received was the instantaneous firing rate filtered by a low pass filter (cutoff frequency 1.5 Hz) and then quantized to the 8 cursor positions. The data shows fine control of the firing rate, yet more precise control could possibly be achieved by changes in the task, filtering, and feedback display.

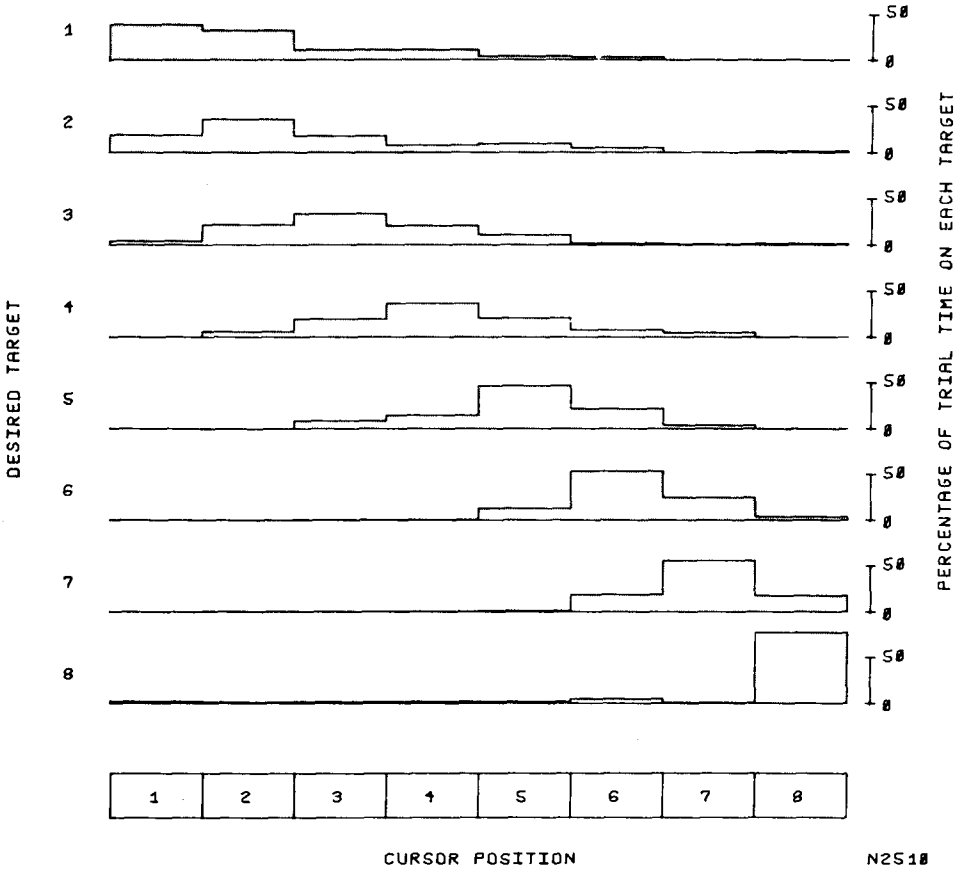

FIGURE 5. Distribution of cell firing frequencies when a specific target light was illuminated. The limiter of Fig. 4 was activated so all firing rates beyond target 8 appeared as being on level 8. (with permission of Academic Press, from Ref.7).

The best performance obtained with the 8 target task and a 1 sec accumulated time on-target, when cortical cell signals were the monkey's output, was 2.45 bits/sec. The same task was performed having the monkey move a handle by wrist flexion and extension (i.e., using the intact motor system as the output). The information transfer rate increased to 4.48 bits/sec, or less than a twofold improvement. Thus, under some restricted conditions, the direct out-

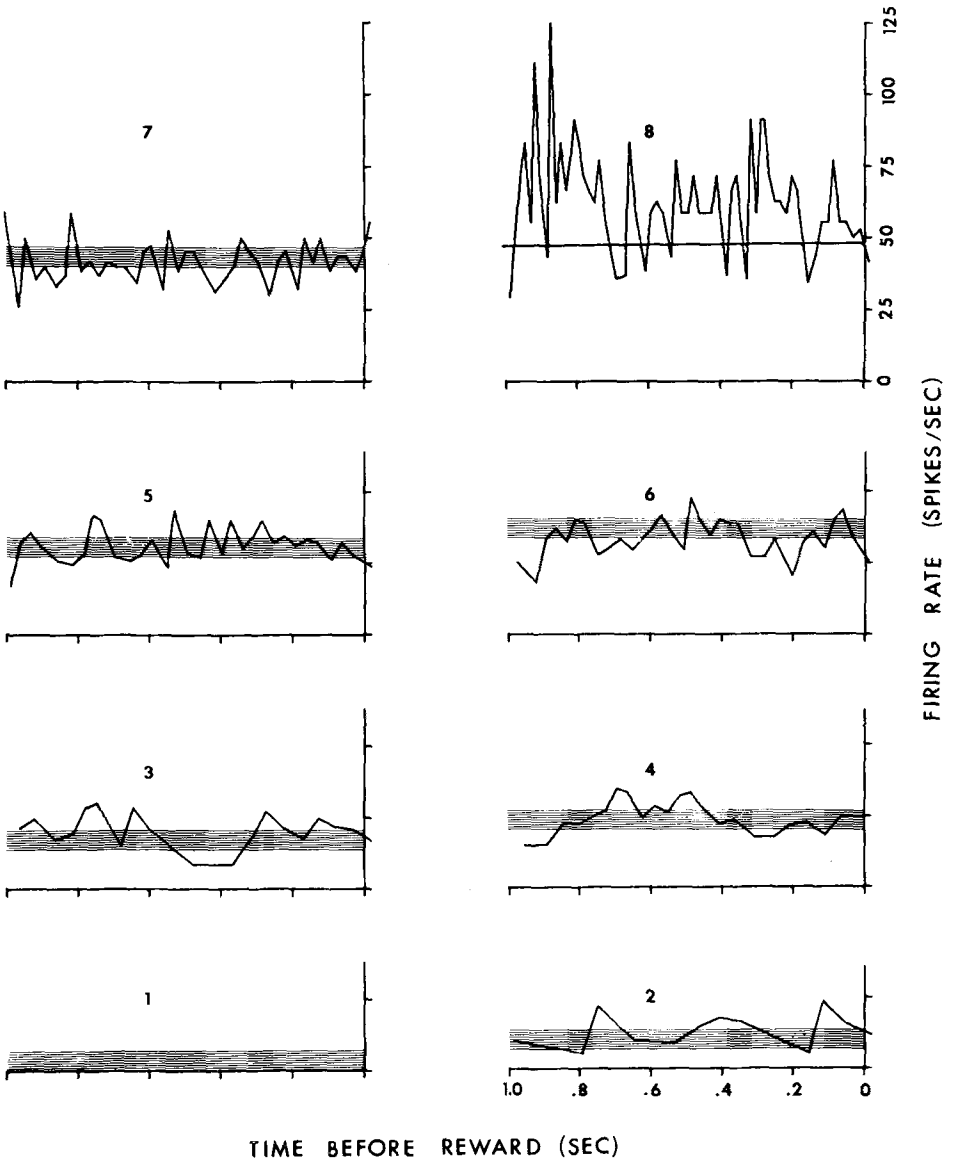

FIGURE 6. Instantaneous firing rate of a cortical neuron for the 1 sec period prior to a reward. The bands show the range of firing rates that correspond to each target light. For target light 8 the limiter was activated accepting all firing rates above the line as level 8. The numbers above each graph indicate the illuminated target (with permission of Academic Press, from Ref. 7).

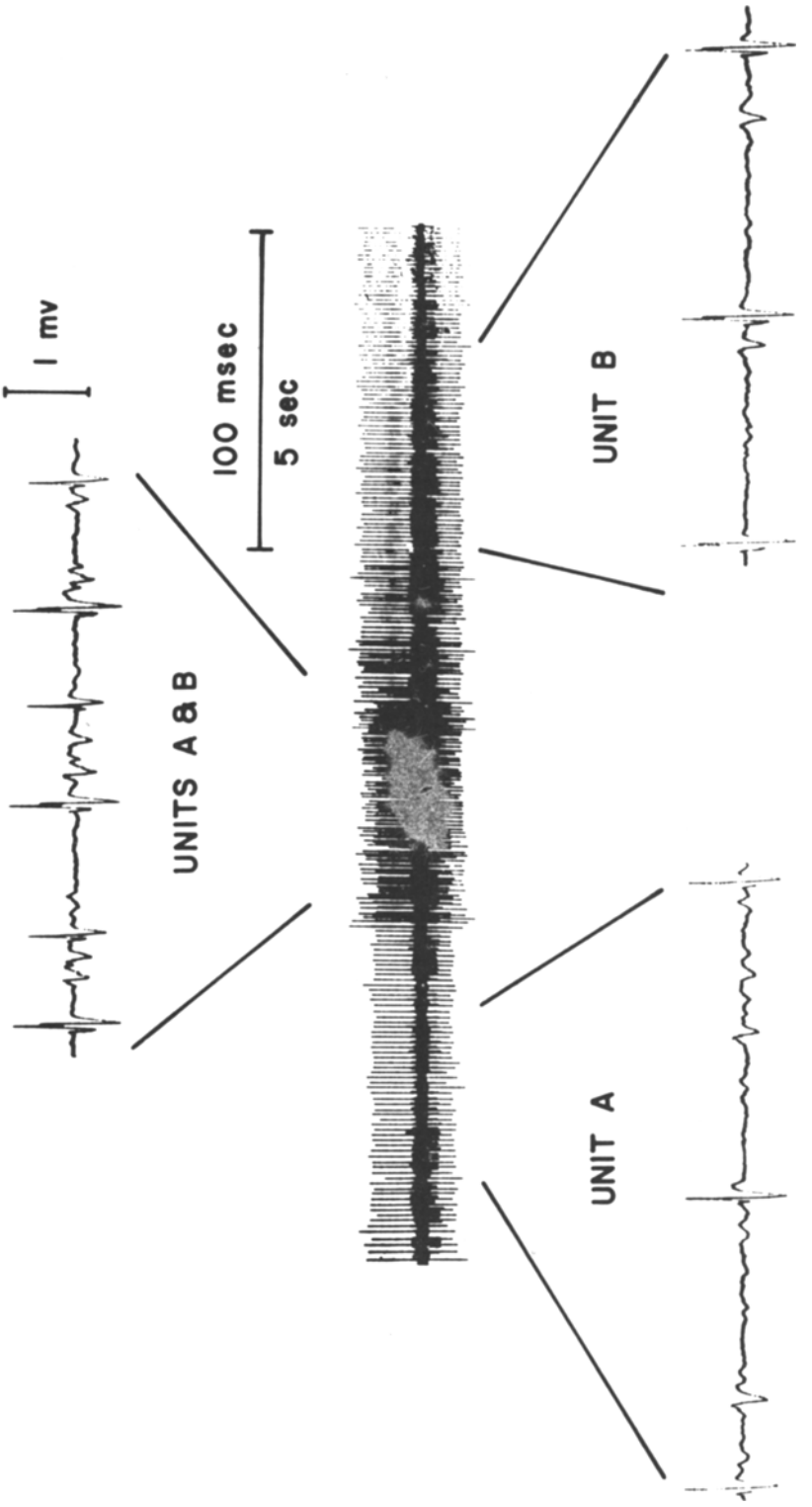

FIGURE 7. Selective control over the recruitment of two motor units in abductor pollicis brevis. The task was to activate unit A, then unit A and B, and finally unit B (with permission of Academic Press, from Ref. 8).

put of cortical cells can provide information output rates only moderately less precise than the intact motor system.

For the less severely handicapped patient, the possibility of using single unit EMG recordings might provide a number of independent channels of information. The work of Basmajian (1) suggested that multiple channels of independently controlled single unit EMG activity could be obtained from a single muscle. In order to evaluate this possibility with humans Thomas *et al.* (8) inserted fine EMG electrodes into a muscle and asked the subject to activate several motor units by a mild contraction of the muscle. Two discriminable motor units were selected and distinct auditory feedback was provided when each unit fired, along with the oscilloscope display of the waveform of each unit. The task was to demonstrate independent control over the two motor units by firing each independently and also simultaneously on command. Figure 7 illustrates successful control over two motor units. This result was an exception to the general finding that, in most muscles studied, independent control of two motor units was not possible. Only in anatomically defined muscles that had different physiological actions was independent control possible. Thus, only one channel of information appears to be obtainable from a single physiologically defined muscle.

As a further test of control of human motor unit firing patterns the same 8 target random tracking that was used with monkeys was employed. The best performance obtained was 2.73 bits/sec, which was comparable to the performance of the monkey in controlling a cortical neuron. Because only one channel of information appears feasible from a given muscle, the simplest approach to obtain this signal is with gross EMG electrodes that record the activity of the majority of motor units in the muscle. The 8 target tracking task used with the monkey was also evaluated under this condition and the best IOR obtained was 2.99 bits/sec. From our studies, two sites appear promising for obtaining signals to control external devices. Single unit EMG recording can be ruled out in favor of the simpler technique of gross EMG recording. For the severely handicapped patient, cortical recordings might with further development be feasible as a source of independent control signals. Recording from nerves, as discussed by Hoffer in his article might also be a possible site of control signals. Our preliminary studies have been encouraging in obtaining connections to the nervous system to control external devices. However, it is clear that numerous improvements are required in electrode design, fabrication, implantation, and signal processing techniques before the use of cortical signals are feasible for human applications.

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