at 40 000 samples/s. Online spike discrimination is controlled interactively by the user and applies standard techniques of waveform template matching to isolate the neural activity from the lower background noise. The system saves spike waveforms and timestamps to the computer hard drive for all of the channels simultaneously, and can be accessed in real-time using client programs. This architecture has been extended to include online analysis of the cortical signal and will eventually be used to drive the robotic arm. Based on previous work [1]–[6], the system has been designed to derive velocity every 20 ms.

Using the system described above, client programs can be written which can make the necessary calculations to relate the neural activity to a control signal at 50 Hz. To run a robotic arm, an on-off signal, direction, and speed must be derived at every instant in time, and can be related back to the original arm movement for comparison. Over a two-month time period (83 640 time windows of activity analyzed), the system correctly predicted when the hand was in motion 81% of the time—with the most consistent errors occurring at the beginning and end of the movements. Overall, the median angle formed between the true and the derived movements was 22.3° for targets that were separated by a minimum of 60°. Individual whole movements (formed from the integration of the individual velocity vectors) ended closest to the correct target 68.5% of the time (1398 of 2040 trials), allowing the determination of the correct movement solely based on the endpoint. From the day with the most accurate results, 99 out of 200 neural trajectories landed within 3.0 cm of the true endpoint of the hand (located 10 cm from the center of the cube), and 87.5% of the trajectories were closest to the correct target, displaying the potential consistency that can be achieved with simultaneous neural recording. When both the hand was in motion and the system correctly determined a velocity for comparison, the median vector correlation between the true and the derived velocity was 0.82.

Research is being directed at the formation of a real-time control signal to drive a cortical motor prosthesis. Although the accuracy of the current system is limited, it does provide 3-D motion control, deriving direction, speed, and movement initiation and termination, from the firing activity of motor neurons. Using the system described above, the conversion from neuronal activity to movement on a millisecond time-scale is attainable. Sensory feedback allows for learning and cortical remodeling, which should improve the accuracy of the device through visual biofeedback. Once the animal is allowed to interact with the robotic arm as the task is being performed, we expect that the ability to control this device should improve. Therefore, further refinements in technology coupled with the addition of interaction with our device should aid us in accomplishing our goal of an implantable, intracortical BCI.

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Direct Control of a Computer from the Human Central Nervous System

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***Abstract*—We describe an invasive alternative to externally applied brain–computer interface (BCI) devices. This system requires implantation of a special electrode into the outer layers of the human neocortex. The recorded signals are transmitted to a nearby receiver and processed to drive a cursor on a computer monitor in front of the patient. Our present patient has learned to control the cursor for the production of synthetic speech and typing.**

***Index Terms*—Brain–computer interface (BCI), cortex, locked-in patients, Luman brain implantation, neurotrophic electrode.**

I. Introduction

Patients with locked-in syndrome are alert and cognitively intact, but cannot move or speak. They face a life-long challenge to communicate. They may use eye movements, blinks or remnants of muscle movements to indicate binary yes or no signals. To enhance communication for these patients several devices have been developed including EEG control of a computer. These systems can provide these patients with the ability to spell words as shown by Birbaumer *et al.* [6], and control of hand opening and closing as shown by Peckham and his colleagues [7]. In theory, however, none of these systems can produce the speed and precision that ought to be provided by directly recording neural activity from the human cortex.

Our approach is to implant the human neocortex using the Neurotrophic Electrode that uses trophic factors to encourage growth of neural tissue into the hollow electrode tip that contains two wires [1].

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The neural tissue is held firmly within the tip because it grows through both ends and joins with neighboring neuropil. This has provided stable long-term recordings in the rat and monkey for up to 16 months [1], [2], [4] and in the patient described later who continues at 16 months. The histological analysis in rats and monkeys shows normal neuropil without neurons but with an abundance of myelinated axons [3]. The same action potentials are recorded over long time periods and behavioral correlates are described [2], [4]. Recently, this same type of electrode has been implanted into three patients. The first patient was an ALS patient who died 76 days after implantation from her underlying disease. She showed that stable signals could be recorded and she could turn them on and off [5]. The results in the second patient demonstrate the ability of this electrode to provide long-term stable signals that can be separated from the multi-unit activity. The patient can control these signals to some extent and is able to use them to drive a cursor across a computer screen. The rate of movement of the cursor is proportional to the firing rate. He has provided learning curves whereby his performance improves with repeated execution of the same task. The focus of this paper is the performance of the patient using neural activity to drive the cursor. The third patient has been implanted too recently for any results.

II. Methods

Electrode fabrication and implantation are described [1], [2], [5] along with recording and data analysis techniques.

A. Cursor Control

The spikes associated with each recorded waveshape are converted into a pulse train. When EMG signals are substituted for neural signals (see later) these also are converted into TTL pulses. Three pulse outputs are routed to a second computer as a substitute for the "mouse" input. During normal "mouse" operation, the position of the cursor on the screen is a function of the X and Y voltage input. The signals from one pulse train determine the movement of the cursor in the X direction, the other in the Y direction. The rate of increase of firing determines the velocity at which the cursor moves over the screen. The third pulse is used to trigger the "enter" or "select" command or "mouse click." To simplify operation for the patient, we have differentiated the firing rate and removed the hysteresis. In other words, only increases in firing rate move the cursor from left to right. With decreases in firing rate or with any sustained tonic firing rate the cursor does not move. Furthermore, when the "enter" command is activated, the cursor immediately returns to the top left position on the screen. The patient receives visual feedback by observing the rate of cursor movement. Auditory feedback is provided by a brief tone that has a distinct frequency for each pulse.

B. Patient Training

The monitor is attached to a computer containing *TalkAssist* software [8] that displays either a row of icons representing common phrases as shown in Fig. 1, or a standard "qwerty" or alphabetical keyboard [9] as shown in Fig. 2.

When using the keyboard, the selected letter appears on a Microsoft Wordpad window. When the phrase or sentence is complete, it is outputted as speech [9] or printed text. There are two paradigms using the Talk Assist program and a third one using the visual keyboard. *In the first paradigm*, the cursor moves across the screen using one group of neural signals and down the screen using another group of larger amplitude signals. Starting in the top left corner, the patient enters the nearest (or leftmost) icon which is the target. He remains over the icon for 2 s so that the speech synthesizer is activated and phrases are outputted such as "See you later. Nice talking with you." *In the second paradigm*, the patient is expected to move the cursor across the screen from one icon to the other. The patient is encouraged to be as accurate as possible, and then to speed up the cursor movement while attempting to remain accurate. *In the third paradigm*, a visual keyboard is presented on the monitor and the patient is encouraged to spell his name as accurately and quickly as possible and then spell anything else he wishes.

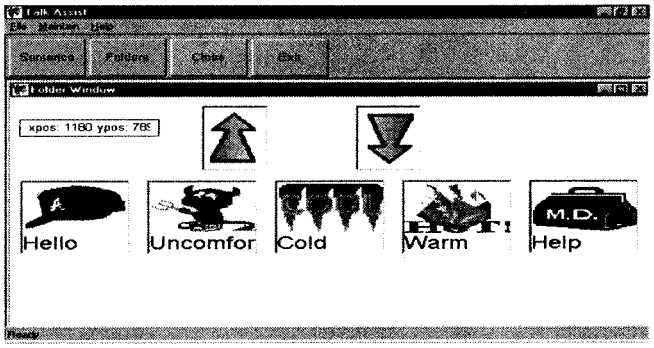

Fig. 1. A row of five icons is shown that produce phrases such as "Hello, my name is JR," "I feel uncomfortable," "I feel too cold," I feel too warm," "Please help me. I am in pain." The large up and down arrows bring up another row of icons when clicked. The left side of the screen shows a read out of the X and Y pixel position of the cursor. When the cursor reaches the right side of the screen, it wraps around to the left. The icons are activated by an enter command or a dwell time control.

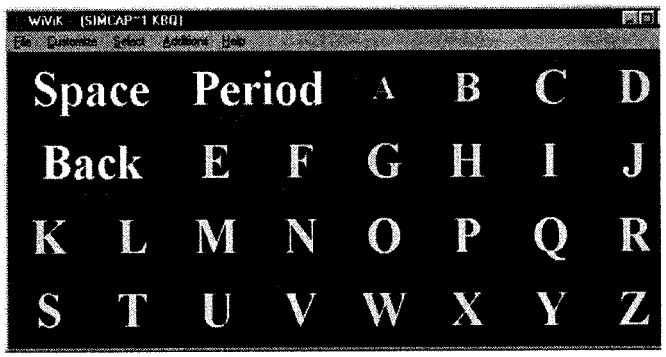

Fig. 2. The cursor is driven from left to right across the X and Y dimensions of the screen. The letters or punctuations are activated by an enter command or by a dwell time control. When a letter is activated, the cursor jumps back to the "Space" key, saving wrap-around time. Activating the "Space" or "Period" key produces synthetic speech consisting of the preceding sentence. Activating the "Back" key deletes the last letter or punctuation (space or period).

III. Results

Our first implanted patient, MH, was able to control multiunit firing using visual and auditory feedback [5] until her death 76 days post implantation. Recorded signals implied that growth of neural tissue into the electrode was possible in humans. She could turn the signals on and off on request, thus demonstrating binary output. Our second patient, JR, continues to control a computer cursor 17 months after implantation. He suffered a brainstem stroke in December 1997. He has residual facial movements only, cannot speak around his tracheotomy, has disconjugate eye movements with nystagmus, but is cognitively intact and alert. Neural signals appeared as expected (from the first patient and in all animal studies) near day 20, and stabilized at about three months. Robust signals continue at day 426 at the time of writing. Multiple signals of different amplitudes can be recorded unless JR is tired, toxic or on analgesics. Presently, he is given Neurontin and Fentanyl for pain associated with a severe decubitus ulcer and peripheral neuropathy so

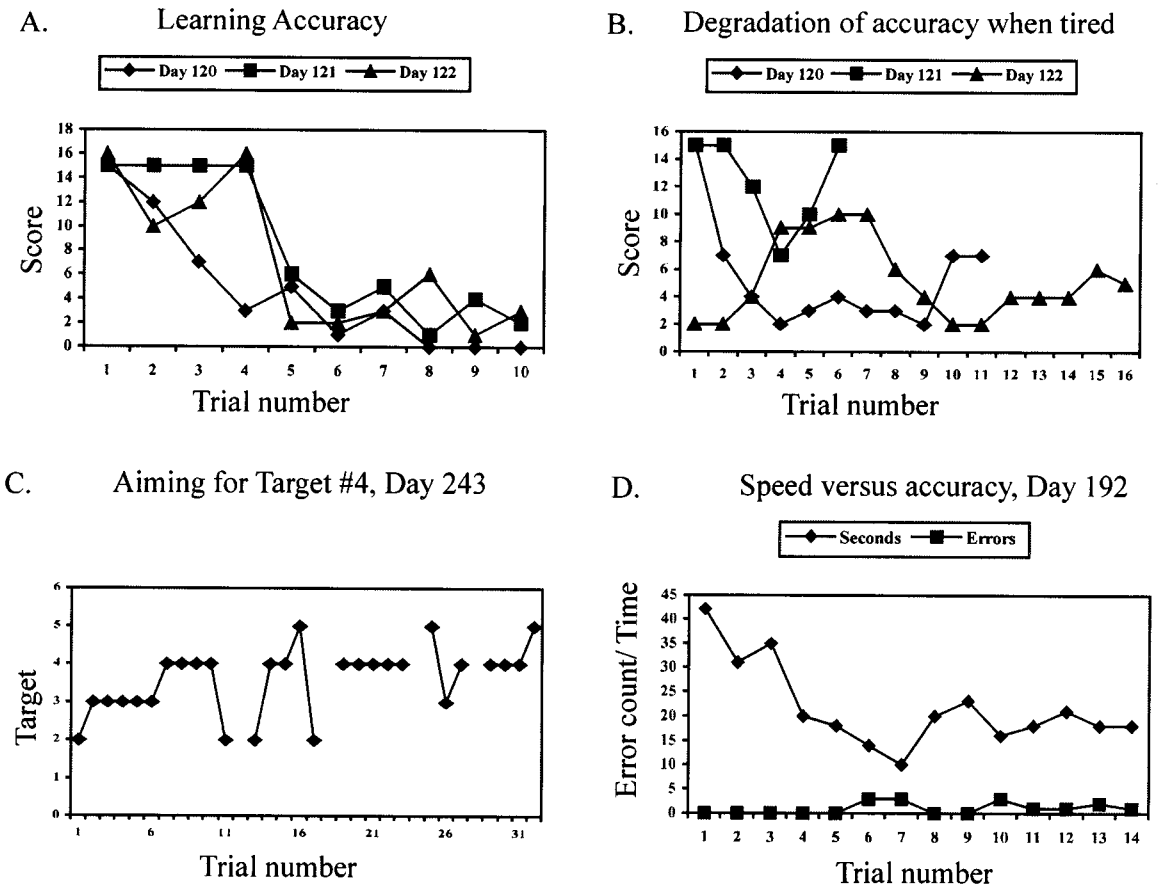

Fig. 3. As discussed in the text, panel A demonstrates three learning curves and maintenance of adequate performance. Panel B demonstrates data from the same session in which the patient lost his accuracy due to fatigue. Panel C demonstrates accuracy when aiming for target number 4 as described in the text. Panel D demonstrates the trade off between speed and accuracy.

he works with great difficulty and for short periods of time. Difficulties with the electronics include intermittent signal from one of the implanted devices. Thus one electrode in JR has not been used.

In JR, at month two after implantation, the neural signals fired in relation to mouth and tongue movements. At month four they appeared to fire with eye and eyebrow movements as determined by observing the patient during activation and by questioning him. From month five onwards, JR makes no movements during activation of the signals. He has learned to use these neural signals to control the X direction of a cursor on a computer screen. Initial attempts produced poorly controlled movements of the cursor because no tonic firing occurred at any firing rate. Only phasic bursts occurred that sometimes continued as continuous, multiunit high frequency firings uncontrolled by the subject. To negate this unwanted constant rate, we continuously average the firing rate and subtract this from the actual rate: When rates were equal, the cursor does not move. Thus, it now moves only in response to *increases* in phasic activity. We initially allowed the cursor to drift back in the opposite direction in order to provide bi-directional movement, but this was too difficult for him to control. Now the cursor does not drift to the left, nor does it move with decreases in firing rate. It wraps around the screen when it reaches the right side. With these simplifications he has produced learning curves with a positive slope in all three paradigms.

Paradigm #1: In the first paradigm, he moves the cursor across and down the screen to activate icons to produce synthetic speech. This screen is shown in Fig. 1. He attempts to move from a start position on the top left corner of the screen as shown in Fig. 1, and drives the cursor across to the right and downwards to enter one of five icons in a

[4th attempt] **JOHN**

[3rd attempt] **JOHPN**

[2nd attempt] **JWU**

[1st attempt] **JOHN**

12/17/98 JRDAY265.UFF

Fig. 4. First accurate spelling of the patient's name.

[5th] **KENEDY GQLDXWAIJTF**

[4th] **PHILXKIM NMFELODY**

[3rd] **JOIH.N**

[2nd] **HIJJROHLN**

[1st] **JOHLQQQ.GYUVWABD N**

Day 266. 12/17/98

Fig. 5. First spontaneous spelling of investigator's names.

[4th]	**NOTHING**	[What were you thinking when moving the cursor?]
[3rd]	**THE WIND**	[Neural signals substituted for vertical EMG]
[2nd]	**GONE WITH**	[What is your favorite movie?]
[1st]	**BRANDON**	[Spell the new guy's name]

JRDAY423 5/24/99

Fig. 6. Accurate answering of questions.

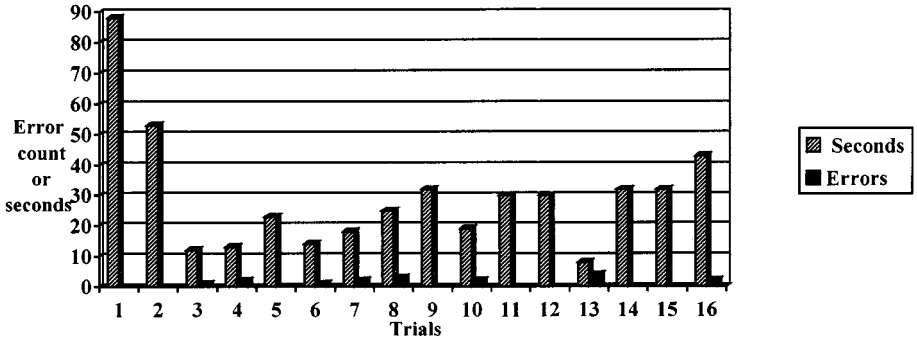

Fig. 7. Tradeoff between speed and accuracy when driving the cursor across the row of icons and suppressing the EMG activity of the eyebrows as described in the text. Time in seconds (larger bars) is shown on the abscissa along with error count (smaller bars).

row scored one (left of screen) through 16 (right side of screen). A high score indicates poor performance and a low score indicates a successful rapid movement down to the icon nearest the start position. Panel A in Fig. 3 illustrates improvement in performance during three different sessions on days 120, 121 and 122 after implantation. As illustrated, poor performance (shown in the Y-axis) on the initial trials improved on subsequent trials.

This performance did not endure, however, when JR was tired or toxic. This is shown in panel B where scores worsened (day 120), remained low (day 121) or fluctuated (day 122). On questioning he indicated his sense of effort was maximal.

In panel C, JR uses the neural signals for the X direction and the toe EMG (Adductor Hallucis muscle) for the Y direction. He moves the cursor around the screen containing five icons in a horizontal row with the fourth icon from the left being the target icon. Thus a score of four indicates accurate attainment of the target. There is no time limit. The cursor can move from left to right and top to bottom and then wrap around to the top or left side. Initially, he is inaccurate for six trials and then maintains consistent accuracy for four trials (scores 4) until he tires and becomes inaccurate. He is seen to be slowing, so he is asked whether or not he wishes to continue. He indicates "no" by one blink ("yes" by two). He rests for 3 min and on resumption he regains accuracy for two trials. A rest of 5 min produces five accurate trials in a row. A short rest results in resumption of inaccurate trials. A 5-min rest produces three more accurate trials followed by an inaccurate one and an indication that he is too tired and wishes to stop.

Paradigm #2: In the second paradigm he moves across each of five icons as accurately and quickly as possible. The start position is to the left of the row of icons. To be accurate he has to move the cursor into an icon and remain there for 2 s to produce synthetic speech. This is accurately performed in 45 s on the first trial as shown in panel D. Speed of performance increases over five trials. On the sixth and seventh trials, errors in accuracy occur. He is encouraged to slow down while maintaining accuracy. This he does. As he increases his speed, further errors occur. At the end, he indicates effort was maximal.

Paradigm #3: JR uses a pop-up keyboard on the monitor to select letters and spell phrases that are outputted either as synthetic speech or printed words. This screen is shown in Fig. 2. He has spelled his name and ours with accuracy, but is becoming increasingly unable to generate neural signals for more than a few minutes due to the effects of the analgesics already described. To facilitate his use of the keyboard, we use EMG signals that are associated with some minute recovered movements of his left neck, arm or toe, though recently even these have not been available. We use neck EMG for the select command and brow EMG for the Y direction of cursor movement. We were using left toe EMG but this has also disappeared. Occasionally we have used a constant input from a signal generator. The example in Fig. 4 demonstrates he can recognizably spell his name beginning from below. (The letters are spelled from below upwards due to the fact that the Wivik keyboard covers the lower part of the Wordpad screen allowing only one line for viewing. After each line is full, we press "return" and the "text select pointer" is returned to the top of the screen.)

In a further example, he spells his name first and then, spontaneously for the first time, several of our names. As shown in Fig. 5 (beginning from below upwards), he has many difficulties on the first two lines. Then he spells JOIH.N. To our surprise, he spontaneously spells PHIL with an X for 'and,' and then he spells KIM. This is followed by MELODY with some errors. Then he spells KENNEDY and GOLDTHWAITE with a few errors. He has not learned to use the backspace at this time.

As an internal control we have recently had an opportunity to use EMG signals (without neural signals) to determine his maximum spelling rate with EMG. In this trial shown in Fig. 6, the patient is not given a specific target word but is asked a series of conversational questions for which he determines the answer. His left eyebrow EMG drives the cursor horizontally, a signal generator provides a constant vertical displacement at a rate of 25 s per full screen, and the left neck EMG provides the "enter" command. He achieves a maximum rate of three letters in 60 s spelling "GONE WITH" shown in Fig. 6. It is his eighth session over three weeks of practice using the EMG and signal

generator. Substituting neural signals for the signal generator (vertical control) achieves an almost identical maximum rate of three letters over 72 s when spelling "THE WIND." This is his initial attempt to use neural signals in many months and it will likely improve. He uses a backspace to delete errors thus producing correctly spelled words as shown. Previous attempts months ago prior to his recent illness produced a similar rate. The answers to the various questions are shown in Fig. 6 (read upwards from first).

A. Cognitive Correlates

The fourth question in the above session concerns his thoughts while driving the cursor. As discussed at the beginning of the "results" section, in the initial months he used mouth and tongue movements, eye movements, eyebrow movements and at month five lay quietly while driving the cursor across the screen. Now, after five further months without using the neural signals due to extended illness, he appears to allow them to fire spontaneously. Thus, when asked what he was thinking about after session 423, he answers "NOTHING" as shown in Fig. 6. In the next session on day 430, he is required to fire the neural signals to drive the cursor from left to right across the five icons on the Talk Assist screen. At the same time he has to minimize eyebrow EMG to avoid driving the cursor down and out of the line of icons. Thus, he has to *dissociate* the EMG activity from the neural activity to produce the words in Fig. 4. He succeeds in moving across the full screen of icons without errors by trial five in 23 s as shown in Fig. 7 (note errors in trials 3 and 4). In subsequent trials he sometimes moves too quickly and makes errors such as driving below the line of icons, or skipping over icons. Eventually he produces accurate performance taking 19 to 32 s to cross the screen. This is similar to the prior performance shown in panel D in Fig. 1 for day 192. When asked what he is thinking, he denies thinking of moving his mouth, tongue, eyes, or eyebrows together or separately. Instead, he blinks twice (for "yes") when asked if he is thinking of moving the cursor.

IV. Discussion

These data indicate that the recorded neural signals can drive the cursor across the screen, accurately entering and resting on icons or letter squares. As shown in Fig. 3(a), improvements in performance produce positive learning curves. Accurate performance is impaired by fatigue due to repeated performances, toxicity from infections, pain or analgesics [Fig. 3(b)]. These ongoing medical problems have produced long interruptions in his training (from December 1998 to date). Despite these problems, the patient has repeatedly produced a spelling rate of three letters per minute. This is likely below the maximum rate that could be obtained by further practice, refinements in the user interface and use of at least two neural signals, one in the X direction and the other in the Y, with a third signal to provide the enter command.

JR's spelling rate of three letters per minute is approximately the same as the spelling rate attained with the use of other techniques. It compares well with Birbaumer's ALS patients who used a binary EEG control signal after many months of practice [6]. Reference [6, Table III] shows time per letter ranging from 10 to 192 s. The average time in seconds for spelling the simplest two level letter was 66 s for patient HPS and 65 s for patient MP. Three level spelling took 76 s for HPS and 54 s for MP. We expect JR and future patients to spell much more quickly.

The question of what drives the cursor is beginning to be answered. As described earlier, the patient indicates that the neural activity is no longer driven by specific face parts. Large activations of EMG activity are associated with activation of neural activity, however, as would be expected in any general activation response. Recent results are suggesting that he can dissociate EMG activity from neural activity, and that when activating neural signals he is thinking only of driving the cursor. If this is borne out by further studies of performance and the underlying neural correlates, it implies that plastic changes can be induced in the underlying cortex. In other words, the patient may develop cortex devoted to controlling the cursor. We have expectantly named this phenomenon "cursor cortex."

For the future, we will continue to work on patients with the aim of providing rapid typing and synthetic speech. In addition, we intend to provide access to some environmental controllers and access to the Internet. External BCI devices that cannot provide control of the cursor will have difficulty in allowing Internet access. An internal device providing control of the cursor such as we propose will have to provide at least an order of magnitude improvement over external BCI devices to justify invasion of the brain. Future studies will contrast communication rates of external and internal BCI devices.

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