

Information Capacity of the Corticospinal Tract Recordings as a Neural Interface

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Abstract—Recording the motor output of the central nervous system from the cervical spinal cord was investigated as a method of generating voluntary command signals, potentially to be used in quadriplegic individuals. Corticospinal volleys evoked by motor cortex stimulation were recorded from the spinal cord surface with multicontact electrodes in anesthetized cats. The multicontact recordings were analyzed for their information-carrying capacity as a neural interface. Neural signals resulting from the stimulation of various points in the motor cortex were considered as symbols of an alphabet that were sent through a discrete information channel. The information capacity of this channel at the thermal noise level of the electrode contacts was calculated. The maximum information rate was 1.57 bits in a trial for a 4-symbol alphabet. The background noise that reduces the information rate to 50% of its maximum theoretical value was defined as the half-bitrate–noise–tolerance (HBR-NoiseTol) and used as a measure of symbol distinguishability. The HBR-NoiseTol for all trials on average was $24 \pm 12\%$, $18 \pm 10\%$, and $15 \pm 9\%$ for interfaces with 2-, 3-, and 4-symbol alphabets ($n = 11$ trials). The average peak-to-peak amplitude of the neural volleys was $13.5 \pm 6.7 \mu\text{V}$ ($n = 11$). These results suggest that the corticospinal signals can be recorded with spatial selectivity from the spinal cord surface and thus warrant further investigation of their potential use for a spinal cord–computer interface.

Keywords—Voluntary command generation, Brain–computer interface, Spinal cord injury, Spinal cord recording.

INTRODUCTION

Following spinal cord injury (SCI) from trauma or disease, skeletal muscles distal to the point of damage become paralyzed because of disrupted neural conduction. In high-level SCI, there is a great need for a method that can partially substitute the voluntary control. Noninvasive approaches such as using the scalp EEG or the EMG signals from the muscles with some remaining voluntary control have provided control signals with limited information rates (see Ref. 22 for a review). Direct brain–computer interfaces with electrodes implanted in the motor cortex have gener-

ated signals with much higher signal quality that would allow reconstruction of the limb trajectories.^{3,18,21}

In this study, we are investigating an alternative approach where corticospinal tract signals extracted from the cervical spinal cord will be used as a mean of obtaining voluntary command signals. The lateral corticospinal tract (LCST) is the principal motor pathway in human, which originates in the frontal lobe of the cerebral cortex. The fibers of LCST decussate at the junction of the spinal cord and medulla and descend in the dorsolateral portion of the lateral column of the spinal cord white matter. These fibers primarily control distal limb muscles and they are the targeted group of nerve fibers for recording in this report.

Recording the motor output of the central nervous system from the spinal cord has several advantages over the cortical approaches. The cortical recordings contain complex signals from various types of cells at different levels of sensory-motor information processing. On the other hand, LCST is a bundle of axons, all oriented in the same direction, without any circuitry among them while traveling in the white matter of the spinal cord. LCST becomes close to the surface below the medulla, makes up a large portion of the spinal cord white matter at the cervical level, and carries only efferent information. These are clear advantages for extracellular recordings of neural population activity. Extraction of the voluntary control signals from the spinal cord recordings may be easier than it is from the cortical recordings and thereby allowing higher information rates.

The main objective of this study is to *investigate* the feasibility of multichannel recordings from the LCST fibers with electrodes placed over the cord surface intradurally or epidurally. Anesthetized cat preparations where the corticospinal activity was evoked by stimulation of the motor cortex with microelectrodes were used. The evoked corticospinal signals contain multiple volleys. The wave of lowest threshold and shortest latency (the ‘D wave’) is produced by direct activation of corticospinal neurons.⁷ The waves occurring with larger delays were termed the ‘I waves’ (indirect activation) and they are thought to *result* from synaptic activation of corticospinal neurons through the stimulation of cortical interneurons. In this study, the

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amplitude distribution of these signals in the recordings made with multiple contacts that are radially placed around the cord were used for spatial localization of the neural activity in the spinal cord cross section. We will refer to this as spatial selectivity in the remainder of the text. Preliminary data on these acute experiments were published in an abstract form.¹⁶

The surface recordings of the corticospinal tract need to be spatially selective in order to extract multichannel neural signals. Spatial selectivity can be obtained when recording the activity of a peripheral nerve by circumferential placement of the metal contacts around the axon bundle.^{4,10,17} A number of selectivity measures discriminating the signals on the basis of the differential distribution of the amplitudes across the recording contacts were proposed.^{4,17} However, the quantitative values provided by these measures are not very practical since they do not convey how discriminable the channels would be in the presence of noise. In a noiseless system, any level of selectivity is perfect since all the channels can be distinguished without an error. In a neural interface, however, the noise tolerance of the system will determine the actual rate of information transfer. Information transfer rate was proposed as a standard measure of performance for brain–computer interfaces based on the accuracy of the selections made by the subject.²² In this paper, we used the noise tolerance, *as an alternative measure*, to quantify the performance of the neural interface. A detailed analysis of the noise tolerance as a measure of the separation between the neural channels was published in an abstract form.¹⁵

METHODS

Electrode Fabrication

The neural recording electrodes (Fig. 1) were fabricated by placing Platinum foil contacts (thickness, 25 μm ; Goodfellow Corp., PA) between two layers of silicone sheets (thickness, 50 μm), adding some silicone elastomer (MED-4211, Nusil Technology, CA) between the layers, and curing the preparation between heated stainless steel pressure pads. Stainless steel (316 LVM) multistrand wires (1 \times 7 \times 0.008"; Fort Wayne Metals, IN) were welded to the Platinum contacts before placing them into the electrode for electrical connections. One of the silicone sheets was prestretched to give a radial curvature to the electrode such that it conforms to the shape of the dorsolateral spinal cord. Finally, square windows (250 \times 250 μm) were made in the silicone to expose the contacts on the inside. The final thickness of the electrode was about 200 μm .

Experimental Setup

Four adult cats (2.6–4.0 kg) were used in this study. Anesthesia was induced with xylazine (0.8 mg/kg, IM)

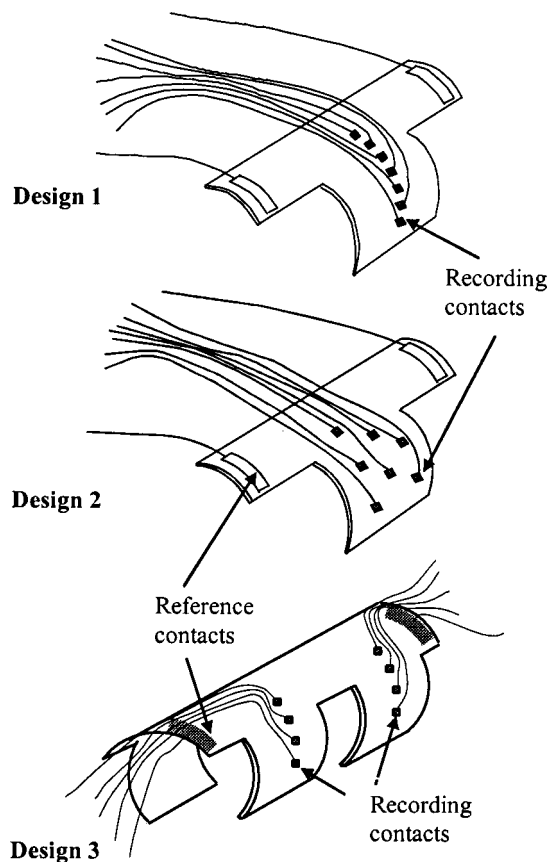


FIGURE 1. Multicontact electrode designs used for epidural and intradural recordings of the cortically evoked volleys from LCST. The separation between the reference contacts is 14 mm in designs 1 and 2, and 20 mm in design 3. The intercontact separation is 0.8 mm in design 1 and about 1.8 mm in design 3. The contacts in design 2 are placed along diagonal lines within a rectangular area of 4.5 mm (longitudinal) by 5 mm (radial). The exposed area of each contact is approximately 250 \times 250 μm . Contact impedance ranged between 7 and 20 k Ω at 1 kHz, measured in normal saline.

and ketamine hydrochloride (20 mg/kg, IM). Atropine (0.044 mg/kg, IM) and dexamethazone (2 mg/kg, IM) were administered early in the experiment to prevent secretions in the airways and CNS edema, respectively. The trachea was intubated and the cat was ventilated mechanically. The femoral vein and artery were catheterized for administration of drugs and monitoring the arterial blood pressure. Anesthesia was maintained by intravenous administration of ketamine hydrochloride using an infusion pump (10 mg/kg/h). The cat was placed in a stereotaxic frame and the body temperature was maintained between 37 and 39°C using a regulated heating pad. ECG, rectal temperature, and expiratory CO₂ (3–5%) were monitored throughout the procedure. The spinous process of the first thoracic vertebra was clamped to stabilize the cervical spinal column in a horizontal position. Dorsal laminectomy (C3–C7) and craniotomy were performed to expose the spinal cord and the left or right motor cortex around the cruciate sulcus.

Stimulation and Recording Protocol

One of the three electrode designs with multiple contacts (Fig. 1) was placed either epidurally or intradurally between the cervical spinal roots C5 and C6 (electrode designs 1 and 2) or at the C4/C5 and C5/C6 segmental borders (design 3) and the spinal cord was covered with pre-warmed mineral oil to prevent dehydration. The recording contacts were connected to the positive inputs of a multi-channel Grass amplifier (Astro-Med, Inc., West Warwick, RI). The negative inputs of the amplifiers were connected to the reference contacts on each side of the electrode. A tungsten microelectrode (0.1 M Ω) was inserted at selected points (at least 1 mm apart) into the motor cortex at a depth of 1500 μ m from the pia surface. A pulse train (PW = 0.2 ms, f = 330 Hz, duration = 45 ms) was applied to evoke muscle twitches in various parts of the contralateral front limb and occasionally in the hind limb, and thereby identify the corresponding areas of the cortex. Once a location was identified, a single pulse (PW = 0.2 ms, I = 400 or 800 μ A) was applied to evoke volleys in the descending LCST. In some experiments, the cortical stimulation train did not elicit muscle twitches later during the experiment without a marked change in the recorded amplitudes. In these cases, the spinal cord recordings were continued by allowing at least a millimeter between the cortical stimulation sites to assure that different groups of fibers were activated within LCST. A total of 256 acquisitions were averaged for each stimulus site, using the spike-triggered-averaging method. A trial consisted of many sets of multicontact traces acquired with a specific electrode design during stimulation of several points in the motor cortex.

Data Analysis and Simulations

Peak-to-peak amplitude of the largest volley (which was usually the direct wave) that occurred within 5 ms after the stimulus artifact was measured in each averaged trace at the same time instant in all the electrode contacts. A measurement vector was formed with these multicontact amplitude measurements for each stimulation point in the cortex. The number of electrode contacts determined the dimension of the vectors. Each vector was normalized such that the contact (not the whole vector) that registers the largest signal has a unit amplitude. In this analysis, the measurement vector was considered as a symbol transmitted through a noisy discrete information channel, i.e., the neural interface. The statistical distribution of the background activity in the neural recordings was tested for normality using the Kolmogorov–Smirnov (K-S) method. The K-S value, which measured the maximum deviation of the cumulative distribution function from normal, was 0.046 and hence Gaussian distribution was assumed for the background activity. Computer-generated Gaussian white noise was used to simulate various levels of the background signal. The probability of correctly classifying a newly generated (re-

ceived) symbol at the end of the information channel is unity for zero noise and it decreases with increasing noise. One can statistically find this probability using the Monte Carlo approach, i.e., with many realizations of the noise component superimposed on the original symbols. For each realization of the noisy vector, its distance from the noiseless version of the vectors in the set was calculated. The noisy vector was classified as the vector that it is closest to in distance. The percentage of the total number of realizations of the noisy vector that were classified as the original vector was taken as the probability of correct classification (p_{ii}) and otherwise as false classification (p_{ij}). Having found the probabilities of correct and false classification statistically, one can calculate the discrete information rate (bits/trial) using the classic formula given by Shannon¹⁹:

$$\text{BitRate} = - \sum_{i=1}^N P_i \log_2 P_i + P_1 (p_{11} \log_2 p_{11} + p_{12} \log_2 p_{12} + \dots + p_{1N} \log_2 p_{1N}) + P_2 (p_{21} \log_2 p_{21} + p_{22} \log_2 p_{22} + \dots + p_{2N} \log_2 p_{2N}) + \dots + P_N (p_{N1} \log_2 p_{N1} + p_{N2} \log_2 p_{N2} + \dots + p_{NN} \log_2 p_{NN})$$

where N is the number of symbols, P_i is the probability of generation for each symbol (here all are assumed to be the same and equal to $1/N$), and p_{ij} indicates probability of classifying i th symbol as j th symbol.

All possible combinations of 2-, 3-, and 4-symbol subsets were considered from the entire number of measurement vectors (symbols) available (i.e., number of stimulation sites as indicated in Table 1) in each trial. Two-, 3-, and 4-symbol subsets with maximum noise tolerance were chosen as the best combinations by an exhaustive search algorithm. The information rate versus noise and the half-bitrate–noise–tolerance (HBR-NoiseTol) were calculated for each subset. The HBR-NoiseTol was defined as the background noise value where the bit rate drops down to 50% of its maximum theoretical value. The maximum information rates are 1, 1.58, and 2 bits for an alphabet of 2, 3, and 4 symbols, respectively. Fifty percent of the maximum bit rate corresponds to the probability of correct classification (p_{ii}) of 0.89, 0.90, and 0.92 for 2-, 3-, and 4-symbol alphabets, assuming uniform distribution of the false classification probabilities (p_{ij}). Because each symbol can be used to transmit a separate channel of neural activity through this interface, the term “symbol” is used synonymously as the “neural channel” in the following.

The thermal noise due to the electrode contact impedances was assumed to be the main source of the background noise, if the activity from the spinocerebellar tract was not present. The thermal noise for the maximum contact impedance of 20 k Ω and a bandwidth of 6 kHz for the neural signals can be found as approximately 1.5 μ V_{rms}, at the body temperature, using the Boltzmann equation. The theoretical information rates were calculated at this thermal noise level.

TABLE 1. The results of data analysis from 11 trials in 4 cats.

Trial No.	Cat No.	Implant site	Elect. design	Ext/Int dural	Stim current	No. of sites	Signal (μ V)	Noise (μ V _{rms})	Noise (%)	HBR-NoiseTol (%)			Bitrate at thermal noise				Selectivity (%)			
										2 ch	3 ch	4 ch	2 ch	3 ch	4 ch	2 ch	3 ch	4 ch	2 ch	3 ch
1	1	C4-C6	3	Ext	High	10	17.3	4.8	28	26	21	17	1.00	1.55	1.57	21	18	16		
2	1	C4-C6	3	Ext	Low	8	6.6	4.6	70	36	30	25	0.83	1.13	1.10	30	28	24		
3	2	C4-C6	3	Ext	High	19	10.5	5.7	55	21	14	11	0.79	0.75	0.72	18	13	11		
4	2	C4-C6	3	Ext	Low	9	10.1	5.9	58	18	11	9	0.63	0.56	0.56	16	11	9		
5	3	C5-C7	3	Ext	High	10	6.4	2.8	44	38	31	27	0.85	1.09	1.18	31	24	23		
6	3	C5-C7	3	Ext	Low	6	6.6	2.7	41	44	35	31	0.93	1.27	1.42	36	30	28		
7	4	C5/C6	1	Ext	High	9	12.0	4.5	38	8	6	5	0.25	0.22	0.24	7	6	5		
8	4	C5/C6	2	Ext	High	7	16.5	4.4	27	14	10	8	0.80	0.94	0.91	13	11	10		
9	4	C5/C6	2	Ext	Low	7	13.5	4.1	30	13	10	7	0.60	0.57	0.58	14	10	10		
10	4	C5/C6	2	Int	High	8	27.3	4.4	16	17	10	8	1.00	1.29	1.31	13	9	8		
11	4	C5/C6	2	Ext	Low	6	21.4	4.1	19	27	16	13	1.00	1.40	1.41	23	16	14		
						<i>M</i>	13.5	4.4	39	24	18	15								
						<i>SD</i>	6.7	1.0	17	12	10	9								

Note. Some of the column labels need clarification (see the Methods section for a detailed description of these parameters): The electrode design (fourth column from left) refers to the type of the electrode used as shown in Fig. 1. The next column shows whether the electrode was implanted extradurally or intradurally. The high and low currents in column 6 refer to 800- and 400- μ A stimulation strengths with the same pulse width (0.2 ms) and train duration parameters (45 ms). The number of cortical stimulation points in column 7 indicates how many symbols are formed in a specific trial. The signal is the mean of the maximum peak-to-peak contact amplitudes of the same vectors used in calculation of the HBR-NoiseTol, information rate, and selectivity in the following columns. The noise is the rms value of the actual background noise (sensory activity) measured in the raw signals before averaging in each trial. The percent noise is the ratio of the measured background noise over the signal in percentages. The HBR-NoiseTol is calculated for 2, 3, and 4 symbols (out of the entire number of symbols in a trial) that give the highest noise tolerance as determined by an exhausting search routine. The next three columns indicate the theoretical information rates of the signals in each trial at the thermal noise level generated by a contact resistance of 20 k Ω . The last three columns show the selectivity measures based on Euclidian distance. The HBR-NoiseTol values that are higher than the actual noise and the information rates that are larger than half the maximum theoretical bit rate are shown in bold.

The Euclidian-distance-based selectivity measure defined by Chen *et al.*⁴ for peripheral nerves was adapted for the corticospinal tract recordings for comparison. The distance between the measurement vectors were calculated by taking their difference after normalizing the vector lengths to unity. The average distance of a vector from all the others in the trial, expressed as a percentage of the maximum possible distance of $\sqrt{2}$, is defined as selectivity value for that vector. The average of the selectivities for all the vectors in a trial was defined as the overall selectivity for the trial.

RESULTS

A set of averaged traces recorded with design 3 is shown in Fig. 2. The first spike to the left is the stimulus artifact. The main neural component, the “D wave,” arrives around at time equals 2 ms. The D wave is followed by smaller indirect components (“I waves”). Note that the neural volleys are recorded at different amplitudes by each one of the contacts. A single acquisition from the traces of Fig. 2 is shown in

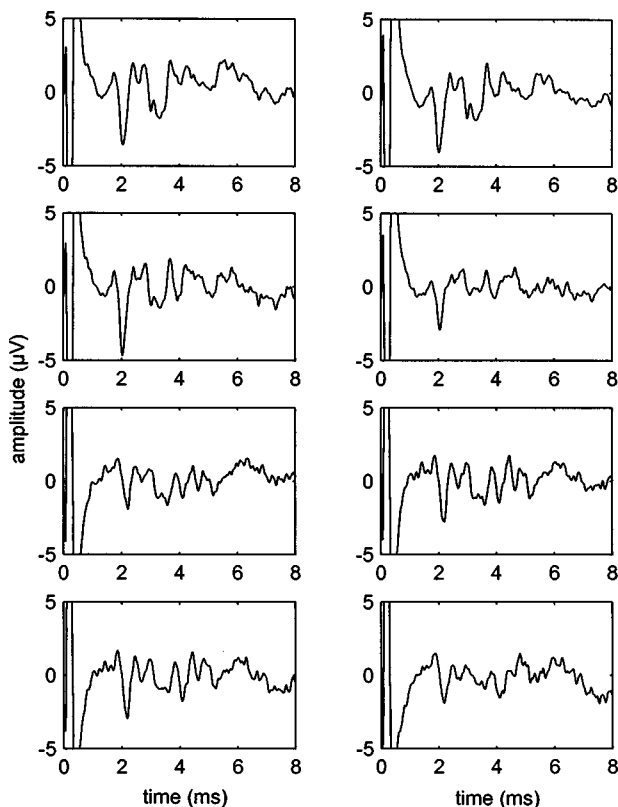


FIGURE 2. Spike-trigger averaged (256 acquisitions) multicontact signals recorded with design 3 (8 contacts) at C5/C7 level, selected from data set 5. The direct wave (D wave) appears at around 2 ms after the stimulus artifact and it is followed by indirect waves. The amplitudes of the volleys vary across the contacts. An eight-dimensional measurement vector (symbol) is formed with the peak-to-peak amplitudes of the D wave.

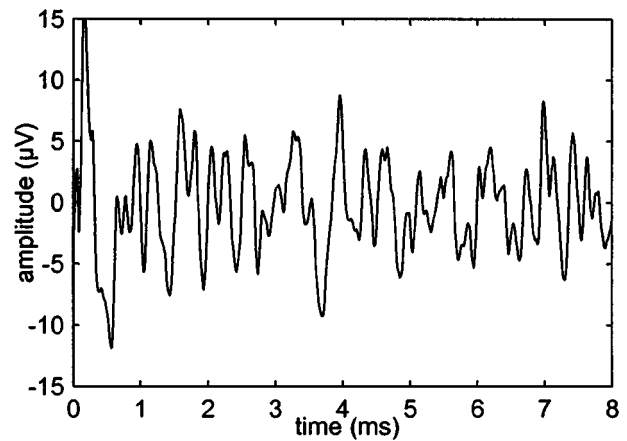


FIGURE 3. A single raw trace before averaging corresponding to the first contact in Fig. 2. The motor activity is completely obscured by the sensory activity originating in the spinocerebellar pathways.

Fig. 3 without averaging for the reader to appreciate the amount of background noise, which mostly consisted of the sensory neural activity originating from the spinocerebellar tract that is located superficially between LCST and the recording electrode.

In each trial, the mean of the peak-to-peak amplitudes of the largest contact signals from all the measurement vectors selected, the mean of the root-mean-square (rms) background noise of all the traces selected, and the percentage of the noise with respect to the mean signal amplitude are calculated (Table 1, see the explanation of columns in the footnote). Across all the 11 trials, the average signal amplitude, the background noise, and the percent noise are $13.5 \pm 6.7 \mu\text{V}$, $4.4 \pm 1.0 \mu\text{V}_{\text{rms}}$, and $39 \pm 17\%$ ($M \pm \text{SD}$), respectively (bottom rows in Table 1). Individual traces had volleys as large as $29 \mu\text{V}$ peak-to-peak in some cases.

The information rate is predicted for increasing levels of background noise for the best combinations of 2-, 3-, and 4-symbol sets in each trial using Monte Carlo simulations (50,000 realizations of the noise component). The simulated information rate is shown in Fig. 4 for the sixth trial in Table 1. The decline in the information rate begins at different background noise levels in each case. The circles indicate the point where the rate is 50% of the maximum and the corresponding noise level was marked as the HBR-NoiseTol.

The HBR-NoiseTol is shown in Table 1 for all trials. The higher the HBR-NoiseTol, the better the separation of the neural channels (or the spatial selectivity). Only in three trials (6, 10, and 11), the HBR-NoiseTol was larger than the percent noise measured in the signals for an alphabet of 2 symbols. This indicates that 0.5 bits of information rate is feasible for the actual background noise levels for 3 cases out of 11 trials. The average HBR-NoiseTol for interfaces with 2-, 3-, and 4-symbol alphabets was $24 \pm 12\%$, $18 \pm 10\%$, and $15 \pm 9\%$ ($M \pm \text{SD}$). As a reference point, the

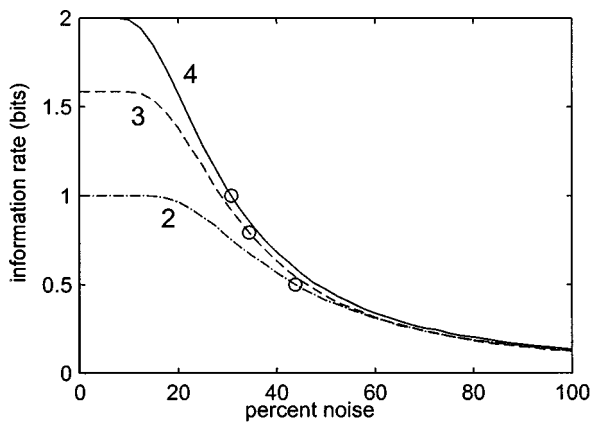


FIGURE 4. The theoretical information rate vs. the background noise level estimated using Monte Carlo simulations for data set 6 in Table 1 for 2-, 3-, and 4-symbol sets, indicated by numbers next to the traces. Fifty thousand realizations of the noise component is used for each point in the plots. The circles indicate the point of 50% maximum theoretical bit rate for the given number of symbols.

maximum theoretical HBR-NoiseTol is approximately 58, 54, and 52% for 2-, 3-, and 4-symbol alphabets, when all the vectors are orthogonal in the multidimensional space. This is the best possible scenario for channel separation that yields the maximum Euclidian-distance-based selectivity (100%).

The information rates at the thermal noise level are given in the next three columns. The information rate is as high as 1.57 bits in one case. In 6 out of 11 cases, at least half the maximum information rate was feasible at the thermal noise level for all 2-, 3-, and 4-symbol (channel) alphabets (bold numbers). In one trial, both 2 and 3 channel half bit rates (trial 8) and in three trials only 2 channel half bit rate (trials 3, 4, and 9) were achieved and exceeded. In trial 7 only, the information rate was less than half the theoretical maximum rate for any number of channels. The lowest or highest rates are not associated with the placement of the electrode (intradural vs. extradural) or with the stimulus level.

Selectivity measures based on Euclidian distance⁴ are given in the rightmost three columns in Table 1 for the same symbol sets for which the HBR-NoiseTol is calculated. These selectivity values are not necessarily the best since the symbol sets were selected from a larger pool with an exhausting search algorithm to maximize the information rates, not the selectivities. The correlation coefficient between the HBR-NoiseTol and selectivity measures was strong (larger than 0.98 for all values), however, was not directly proportional. Relative selectivity deviation from a linear line fit was 9.6% on average for all the points.

CONCLUSIONS

The results of this study suggest that multichannel ("symbols" above) recordings of the corticospinal activ-

ity is feasible with epidural electrodes on the spinal cord. This warrants further research for the use of corticospinal signals as a means of spinal cord computer interface. The information rates at the thermal noise level are useful rates for implementation of such an interface. Furthermore, we demonstrate that information capacity and HBR-NoiseTol can readily be applied to spinal cord recordings as a measure of how well the neural interface performs in the presence of noise. The HBR-NoiseTol may provide a standard measure of channel separation for comparing neural interfaces with different number of contacts and channels.

DISCUSSION

Epidural recordings of transcranially evoked corticospinal activity was introduced as a method for intraoperative assessment of the spinal cord function by Boyd² and has been investigated by a number of groups.^{1,8,11,13} However, to our knowledge, this is the first report that is making an attempt to record from the corticospinal tract with spatial selectivity. The underlying hypothesis of the proposed method is that there is a spatial organization of the fibers in the cross section of the corticospinal tract. This does not need to be a somatotopic organization similar to the one in the motor cortex, but could be any spatial organization that would result into the grouping of fibers according to, for instance, their function, target joints, target muscles, etc. Such a spatial organization can give rise to varying amplitudes in the signals recorded by the contacts placed around the dorsolateral surface of the cord and thereby allowing separation of the signals from spatially distinct fiber groups. The spatial selectivity reported here suggests the presence of such an organization. A number of groups in the past have looked for a somatotopic organization in the corticospinal tract by lesioning or injecting dyes into specific areas of the motor cortex and staining the corticospinal tract distally.^{5,6,9} The underlying hypothesis was that the somatotopic organization of the motor cortex should be retained as the fibers descend in the spinal cord. These reports in general concluded that there was no organization in the corticospinal tract below the level of medullary pyramid. However, it should be noted that the connectivity between the cerebral cortex and the spinal segments is very complex and it may not be possible to reduce it to a simple somatotopic organization. The spatial organization of the fibers in the spinal white matter can be a functional one. In this case, an attempt to study the organization in LCST with respect to the limb function rather than in relation to the anatomical organization of the cortex may reveal more information.

The electrode designs shown in Fig. 1 have contacts distributed radially around the cord to take advantage of the assumed spatial separation of the fibers described above. The principle behind selective recording is that neural signals generated at different points in the cross section of LCST induce differential signal amplitudes at the recording

contacts as a function of source-to-recording-site distance. Designs 2 and 3 consider reorganization of the fibers along the cord and make an attempt to increase the number of neural channels by longitudinal arrangement of the contacts. Other electrode designs with different contact placements and intercontact separations can be considered to maximize the number and the separation of the neural channels in the multicontact recordings. The separation between the neural channels can be further increased also by processing the signals using an unsupervised adaptive filtering technique, such as blind source separation. We reported a successful application of this method in an abstract form.²⁰

The information rates and selectivity measures given in Table 1 do not favor intradural or extradural placement of the electrodes, or one of the stimulus current amplitudes. Further tests are needed to reach a statistically meaningful difference for each one of these parameters. However, these preliminary data show that intradural placement of the electrodes may not be necessary to obtain useful levels of spatial selectivity. The best spinal segment for electrode implantation that would maximize the information rate should also be determined.

Anesthesia may account for the large cortical stimulation current required to elicit detectable corticospinal signals. Ketamine hydrochloride is a dissociative anesthetic with central sympathomimetic and parasympatholytic activity.¹⁴ If used alone, it causes hypertonus, poor muscle relaxation, and persistent pain reflex responses. These undesired effects of ketamine are offset by xylazine when used in combination. This is due to the central inhibition of intraneural transmission by xylazine,¹² which provides its analgesic and sedative effects. In this study, we tried to obtain an appropriate and stable level of anesthesia with xylazine–ketamine combination while maintaining sufficient level of neural excitability. However, it is possible that the excitability of the pyramidal tract neurons were decreased because of the inhibitory effects of xylazine. This is supported by the large interanimal variation in the recorded signal amplitudes (Table 1), which is even greater than the increase introduced by doubling the stimulation current. Signal amplitudes can be improved by increasing the separation between the two reference contacts on each side of the recording electrode. The electrode geometries shown in Fig. 1 were designed such that the electrode length is about the length of a segment in the cervical spinal cord. Longer electrodes can record larger signals, although this may increase the risk of neural trauma in case of chronic implantation.

We should point out that there are major limitations of this study in simulating the recordings of a potential human study. First, the neural signals in this work are evoked by electrical stimulation of the motor cortex whereas in conscious human subjects the activity would be generated spontaneously by the subject's volition. In humans (a total of 105 subjects), the amplitude of the low-cervical epidural recordings evoked by transcranial electrical stimulation

were similar in amplitude (15–25 μV) to those of this study.¹ However, the volitional signal amplitudes can be substantially different from their evoked counterparts. Second, the recordings from the individuals with SCI would not contain any sensory activity from the spinocerebellar tract since this pathway is severed distal to the point of recording. The spinocerebellar tract could be severed distal to the point of recording to eliminate the large sensory activity in the recordings of this study as well. However, this was not done to preserve the intactness of the spinal cord and thus the quality of the recordings. Because the sensory activity will not be present in a spinalized animal or human at a point proximal to the injury, we used the thermal noise of the electrode contacts as the main source of the background noise. The information rates were calculated at this noise level instead of the background sensory activity level measured as noise. Both of these factors discussed above would affect SNR and thereby the information capacity of the interface. It is also worth to note that the information rates calculated in this study are for unilateral placement of the spinal electrodes. We can expect twice higher rates for bilateral implantation of the electrodes. The ultimate information capacity of such an interface will depend on the speed and the strength at which the subject could generate various neural patterns. The information capacity is expected to increase also by the subject's experience over time. That is, the subject can learn how to activate the axon populations best distinguishable by the interface and switch between different patterns at increasing rates by practice.

The information rate of an interface varies by both how distant the symbols are in the multidimensional space and the noise level. The HBR-NoiseTol measure used in this study, however, varies only as a function of the distance between the symbols. The larger the noise tolerance, the larger the separation between the symbols. Thus, it is proposed as a measure of channel separation (or spatial selectivity) and not the information transfer capacity of the interface, which is determined only for a specific level of background noise. The HBR-NoiseTol measure has a number of advantages over a selectivity measure solely based on Euclidian distance between the feature vectors (symbols) formed with measurements from the neural signals.⁴ The major drawback of the Euclidian distance measure is that the selectivity decreases with the addition of new contacts in case the new contacts record the same amplitudes. This is a result of the normalization procedure of the vectors to a unit length, used in calculation of this measure. Adding a new contact, i.e., an extra dimension, brings the vectors closer after normalization if the new contact makes the same contribution to each one of the vectors. The selectivity measure should ideally not change when the information content of the contacts included in the analysis does not change. Another major drawback is that the Euclidian distance selectivity measure does not account for the background noise. Any level of selectivity would allow perfect separation of neural channels

in a noiseless environment. A realistic measure of interface capacity should be able to reflect the deterioration of the neural interface performance with increasing amounts of background noise or decreasing SNR. Moreover, the Euclidian selectivity measure for the whole electrode is not sensitive to the location of the individual vectors in multidimensional space due to averaging of the individual vector selectivities.¹⁵ This yields the same selectivity value for different placement of the vectors, although some of these vectors might be very close to each other and therefore very difficult to distinguish even in very low levels of background noise.¹⁵ The HBR-NoiseTol measure eliminates all of these disadvantages. The vectors are normalized such that the largest contact signal is unity (rather than the whole vector) and thus adding contacts do not reduce the distance between the vectors; it is sensitive to the location of the individual vectors (symbols) in the multidimensional space; and the background noise is accounted for. It is a practical measure that would allow one to have a realistic estimate of neural channel distinguishability in the presence of noise.

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REFERENCES

- ¹Burke, D., R. Hicks, J. Stephen, I. Woodforth, and M. Crawford. Assessment of corticospinal and somatosensory conduction simultaneously during scoliosis surgery. *Electroencephal. Clin. Neurophys.* 85:388–396, 1992.
- ²Boyd, S. G., J. C. Rothwell, J. M. A. Cowan, P. J. Webb, T. Morley, P. Asselman, and C. D. Marsden. A method of monitoring function in corticospinal pathways during scoliosis surgery with a note on motor conduction velocities. *J. Neurol. Neurosurg. Psychiat.* 49:251–257, 1986.
- ³Chapin, J. K., K. A. Moxon, R. S. Markowitz, and M. A. L. Nicolelis. Real-time control of a robot arm using simultaneously recorded neurons in the motor cortex. *Nat. Neurosci.* 2:664–670, 1999.
- ⁴Chen, Y., P. R. Christensen, K. D. Strange, and J. A. Hoffer. Multi-channel recordings from peripheral nerves. 2: Measurement of selectivity. In: Proceedings of the Second Annual IFESS Conference and Neural Prosthesis, BC, Canada, 1997.
- ⁵Dawnay, N. A. H., and P. Glees. Somatotopic analysis of fiber and terminal distribution in the primate corticospinal pathway. *Dev. Brain Res.* 26:115–123, 1986.
- ⁶Goode, G. E., and D. E. Haines. Origin, course, and termination of corticospinal fibers in a prosimian primate (Galago). *Brain Behav. Evol.* 12:334–361, 1975.
- ⁷Hern, J. E. C., S. Landgren, C. G. Phillips, and R. Porter. Selective excitation of corticofugal neurons by surface-anodal stimulation of the baboon's motor cortex. *J. Physiol.* 161:73–90, 1962.
- ⁸Inghilleri, M., A. Berardelli, B. Cioni, G. Cruccu, M. Meglio, and M. Manfredi. Corticospinal potentials after transcranial stimulation in humans. *J. Neurol. Neurosurg. Psychiat.* 52:970–974, 1989.
- ⁹Jeffery, N. D., and M. Fitzgerald. Lack of topographical organization of the corticospinal tract in the cervical spinal cord of the adult rat. *Brain Res.* 833:315–318, 1999.
- ¹⁰Lichtenberg, B. K., and C. J. DeLuca. Distinguishability of functionally distinct evoked neuroelectric signals on the surface of a nerve. *IEEE Tran. Biomed. Eng.* 26:228–237, 1979.
- ¹¹Loughnan, B. A., S. K. Anderson, M. A. Hetreed, P. F. Weston, S. G. Boyd, and G. M. Hall. Effects of halothane on motor evoked potentials recorded in the extradural space. *Br. J. Anaesth.* 63:561–564, 1989.
- ¹²Moye, R. J., A. Paillet, and M. W. Smith. Clinical use of xylazine in dogs and cats. *Vet. Med. Small Anim. Clin.* 68:236–241, 1973.
- ¹³Pelosi, L., G. Caruso, and P. Balbi. Characteristics of spinal potentials to transcranial motor cortex stimulation: Intraoperative recording. In: Non-Invasive Stimulation of Brain and Spinal Cord: Fundamentals and Clinical Applications, edited by P. M. Rossini and C. D. Marsden. New York: Alan R. Liss, 1988, pp. 297–304.
- ¹⁴Pratila, M. G., and S. V. Pratila. Anesthetic agents and cardiac electromechanical activity. *Anesthesiology* 49:338–355, 1978.
- ¹⁵Sahin, M. Noise tolerance as a measure of channel discrimination for multi-channel neural interfaces. In: 23rd Annual International Conference of the IEEE Engineering in Medicine and Biological Science, Istanbul, Turkey, 2001.
- ¹⁶Sahin, M. Selective recordings of motor signals from the corticospinal tract. In: Proceedings of the Sixth Annual IFESS Conference and Neural Prosthesis, Cleveland, OH, 2001.
- ¹⁷Sahin, M., and D. M. Durand. Selective recordings with a multi-contact nerve cuff electrode. In: 18th Annual International Conference of the IEEE Engineering in Medicine and Biological Science, Amsterdam, the Netherlands, 1996.
- ¹⁸Schwartz, A. B. Motor Cortical activity during drawing movements: Population representation during sinusoid tracing. *J. Neurophys.* 70:28–36, 1993.
- ¹⁹Shannon, C. E., and W. Weaver. *The Mathematical Theory of Communication.* Urbana: The University of Illinois Press, 1949, pp. 34–48.
- ²⁰Tie, Y., and M. Sahin. Separation of multi-channel spinal cord recordings using unsupervised adaptive filtering. In: Proceedings of the Second Joint EMBS/BMES Conference, Houston, TX, October 2002.
- ²¹Wessberg, J., C. R. Stambaugh, J. D. Kralik, P. D. Beck, M. Laubach, K. J. Chapin, J. Kim, J. S. Biggs, M. A. Srinivasan, A. Mandayam, Nicolelis, and A. L. Miguel. Real-time prediction of hand trajectory by ensembles of cortical neurons in primates. *Nature* 408:361–365, 2000.
- ²²Wolfaw, R. J., N. Birbaumer, W. J. Heetderks, D. J. McFarland, P. H. Peckham, G. Schalk, E. Donchin, L. A. Quotrono, C. J. Robinson, and T. M. Vaughan. Brain-computer interface technology: A review of the first international meeting. *IEEE Tran. Rehab. Eng.* 8:164–173, 2000.