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A new type of microelectrode for obtaining unitary recordings in the human spinal cord

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Object. In this paper the authors report on the conception and adjustment of a microelectrode used to obtain unitary recordings in the human spinal cord.

Methods. To overcome the difficulties related to intraoperative pulsations of the spinal cord, the authors opted to use a floating microelectrode. Because the recordings are obtained most often from spontaneous activities, it is difficult, with a single microelectrode, to separate spikes from electrical artifacts that are related to the switching of devices. Consequently, the authors designed a dual microelectrode made of two tungsten-in-glass–attached microelectrodes separated by 300 µm. Because the two electrodes cannot obtain recordings in the same neuron, it is possible to distinguish unambiguously spikes (recorded on one tip) from electrical artifacts (recorded simultaneously on the two tips). The dual microelectrode is 2 cm long, with a 20-µm tip length, and 800 to 1200–Ohms impedance. This microelectrode can be implanted "free hand," in the dorsal horn, by using a microsurgical forceps under a surgical microscope. The data analysis is performed off-line with spike sorter hardware.

In the dorsal horns in 17 patients who were selected to undergo a dorsal root entry zone (DREZ) rhizotomy to treat various pathological conditions, unitary recordings were obtained using this double microelectrode. The authors recorded 57 neurons in good conditions of stability and isolation.

Conclusions. The microelectrode described in this paper was successfully used to obtain recordings in neurons in more than 85% of the patients. This simplified, floating double microelectrode can therefore be considered for use in microsurgical DREZ rhizotomy to obtain unitary recordings in the human spinal dorsal horn.

KEY WORDS • dorsal horn • microelectrode • spinal cord

KNOWLEDGE of the neurophysiological mechanisms of pathological states can be enhanced by obtaining unitary electrophysiological recordings. This is true not only in animal models [1,2,20,27,28] but also, after this first step has been achieved, in human disease states as well.[13,14,19,24,29] Indeed, such microelectrode recordings allow better localization of the pathological activities and, in some cases, a real-time monitoring of the surgical intervention. This is particularly important for the treatment of chronic pain syndromes, as, for example, when the thalamus is a target for surgery.[8] For many years unitary recordings have been performed in the dorsal horn of the spinal cord in cats and rats,[1,15,18] thus allowing characterization of different pathological situations in terms of the spiking patterns of neurons (especially in experimental pain models).[4,15,17,18,23] However, such recordings have been very rarely obtained in humans. One case was reported by Loeser and colleagues[16] in 1968, and four cases by Jeanmonod, et al.,[10] in 1989. These studies concerned only a very small number of isolated single units. This is because patient preparation is demanding, and the stability of the electrode is poor, due to pulsations of the spinal cord. Such instability precludes the use of a micromanipulator, and in the aforementioned studies[10,16] the authors opted to use a floating microelectrode. Although Puletti and Blomquist[21,22] in 1967 developed a microdrive dedicated to spinal cord microelectrodes, we too chose to use a floating microelectrode because of its simplicity. Stability was not the only problem, and we report here the way in which we conceived and developed a new floating microelectrode for dedicated use in obtaining unitary recordings in the human spinal cord.

Many technical obstacles had to be overcome to achieve this goal. 1) Because our recordings are most often of spontaneous activities and because of the narrow band widths of the filters used, it is often difficult to separate spikes from electrical artifacts related to various electrical devices present in the operating room. Therefore, we developed a new dual type of microelectrode that has the advantage of doubling the probability of recording units and allowing spikes and artifacts to be easily sorted. 2) The duration of the surgery must not be increased by more than a few minutes. 3) A compromise must be reached, as far as tip length and impedance are concerned, between the probability of re-

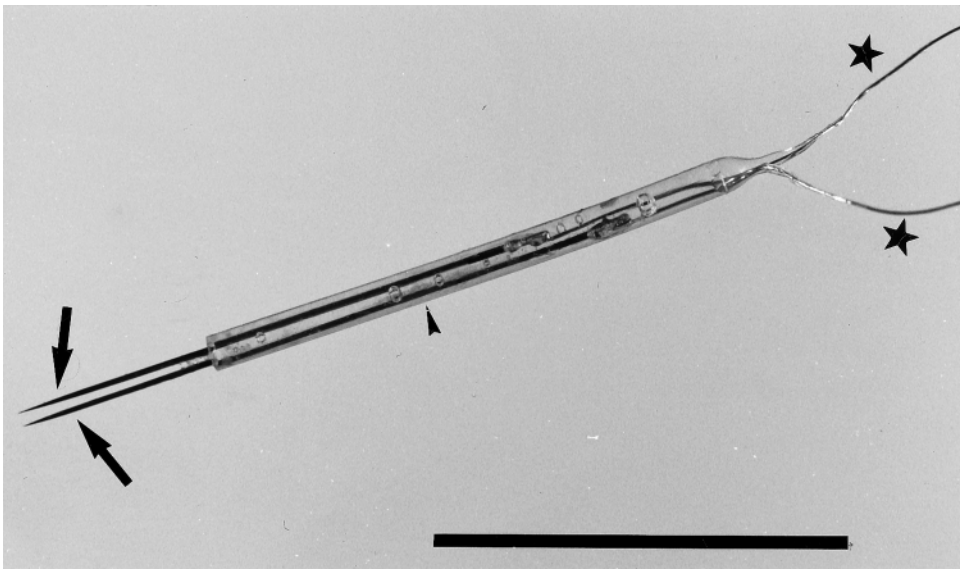

FIG. 1. Photograph showing the floating double microelectrode that has been designed to obtain unitary recordings in neurons in the human spinal dorsal horn. *Arrows* indicate the tungsten-in-glass microelectrodes, glued together in a rigid nylon sleeve *(arrowhead)* filled with silicon rubber. The two independent tips are separated by a distance of 300 µm. *Stars* denote 80-µm-diameter insulated copper connection wires. The electrode weighs 20 mg. Bar = 1 cm.

cording from several units and the size of the recorded spikes. 4) The whole system has to be sterile.

This new type of microelectrode has been developed to obtain intraoperative recordings in the dorsal horn of patients who suffer from persistent pain syndromes (due to a brachial plexus avulsion or a peripheral nerve trauma) or spasticity.

Clinical Material and Methods

This microelectrode was designed to obtain reliable data on the electrophysiological responses of the human spinal cord in different pathological conditions. Once it became operational it was possible to compare the neuronal activity in the dorsal horn in patients undergoing surgery to treat

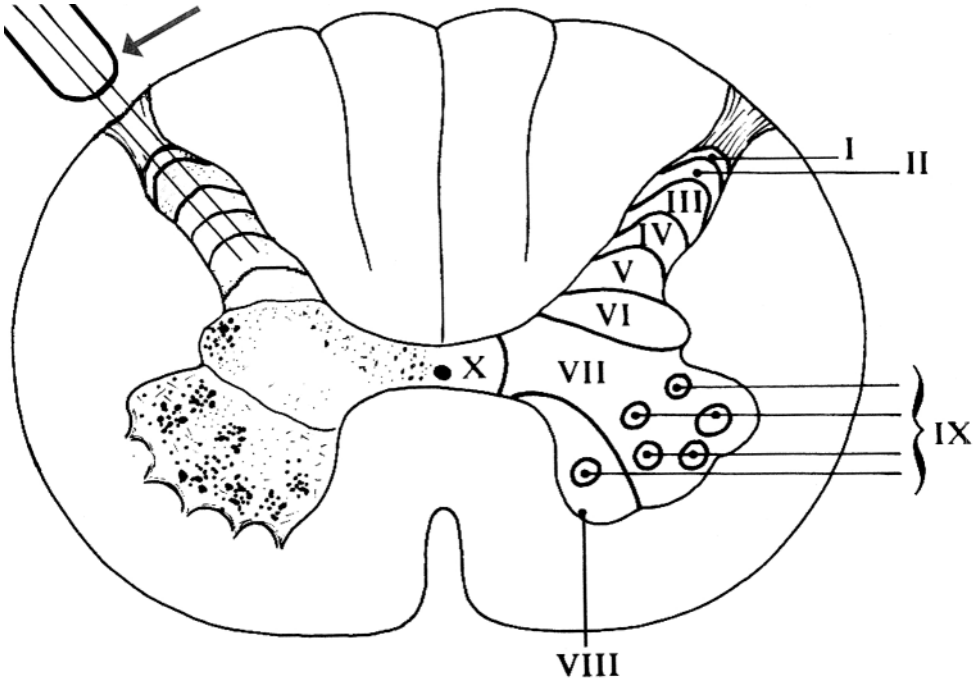

FIG. 2. Schematic drawing of the double microelectrode implanted in the axis of the dorsal horn. The silicon sleeve *(arrow)* is 5 mm away from the tips, making it possible to reach the L-1 lamina.

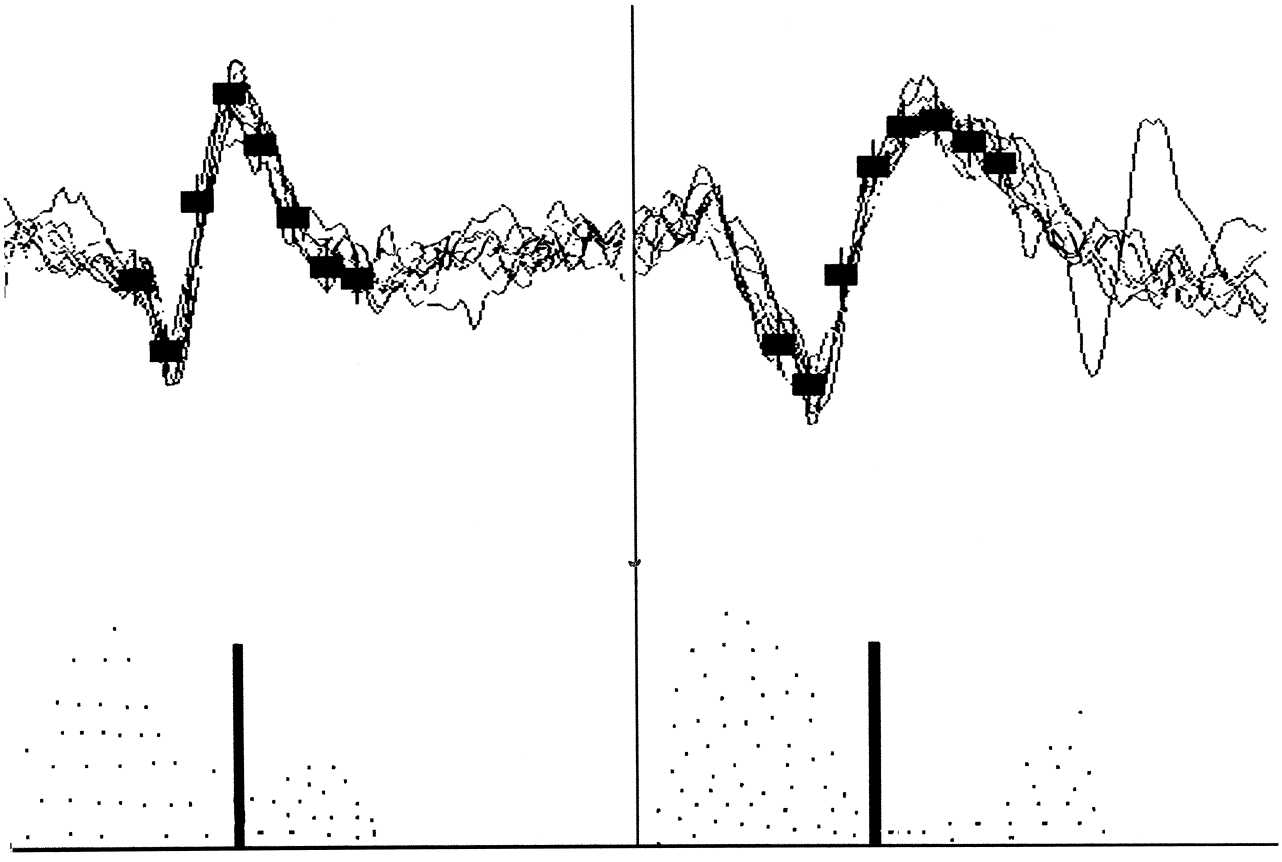

FIG. 3. Example of two different spikes recorded on the same tip, as displayed by the spike sorter. As a first step, a spike template is defined for events corresponding to the signal that crosses above a threshold level. Thereafter, every waveform compatible with this template is recognized as a spike. For each spike, the spike sorter accords a time stamp and calculates the sum of squares of the differences between the template and the waveform. Below the spikes are histograms showing the sums of squares of differences between the templates and the waveforms for many repetitions of the same spike. When the spike cannot be isolated, the histogram shows a continuous unimodal shape; when the isolation is good, an isolated mode separated from the rest of the histogram is observed (hump shape at the left of the vertical bar. The size of this mode is used to quantify the isolation index).

a persistent pain syndrome with those who were being treated for spasticity. Indeed, all patients in this study underwent the same operation, namely a dorsal root entry zone (DREZ) rhizotomy, which provided easy access to the dorsal horn. The study was approved by the local ethics committee, and all patients provided informed consent.

We used our double microelectrode to obtain unitary recordings in the dorsal horn of 17 patients. Five patients underwent DREZ rhizotomy for a persistent pain syndrome caused by a brachial plexus avulsion (deafferented dorsal horns), and 12 patients underwent DREZ rhizotomy to treat disabling spasticity or for a persistent pain syndrome caused by peripheral nerve trauma.

A total of 61 penetration sites were made (two–five per patient) in various parts of the dorsal horn: 19 at the cervical level and 42 at a lumbosacral level. The mean recording time for each site was 52 seconds.

Description of the Electrode

The basic elements of our microelectrode are classic tungsten-in-glass microelectrodes (Merril and Ainsworth type, 1972), designed to obtain extracellular unitary recordings. Two of these tungsten-in-glass microelectrodes are inserted and glued together in a rigid nylon sleeve that is filled with silicon rubber, thus resulting in a double microelectrode (Fig. 1).

This double microelectrode is 2 cm long and weighs 20 mg. Consequently, it can be manipulated by means of a simple microsurgical forceps and can be kept stable in the dorsal horn for many minutes without need of a micromanipulator. The device is easy to handle and to insert directly in the dorsal horn under the surgical microscope.

Because the two tips are separated by a distance of 300 µm, they cannot record in the same neuron; thus, it is possible, with certainty, to distinguish spikes (recorded on one tip) from electrical artifacts (recorded simultaneously on the two tips). The tip length is 20 µm, and the impedance before use varies from 800 to 1200 Ohms.

This single-use double microelectrode is sterilized by means of ethylene oxide.

Implantation Technique

During each surgical procedure, the double microelectrode is implanted "free hand," under a surgical micro-

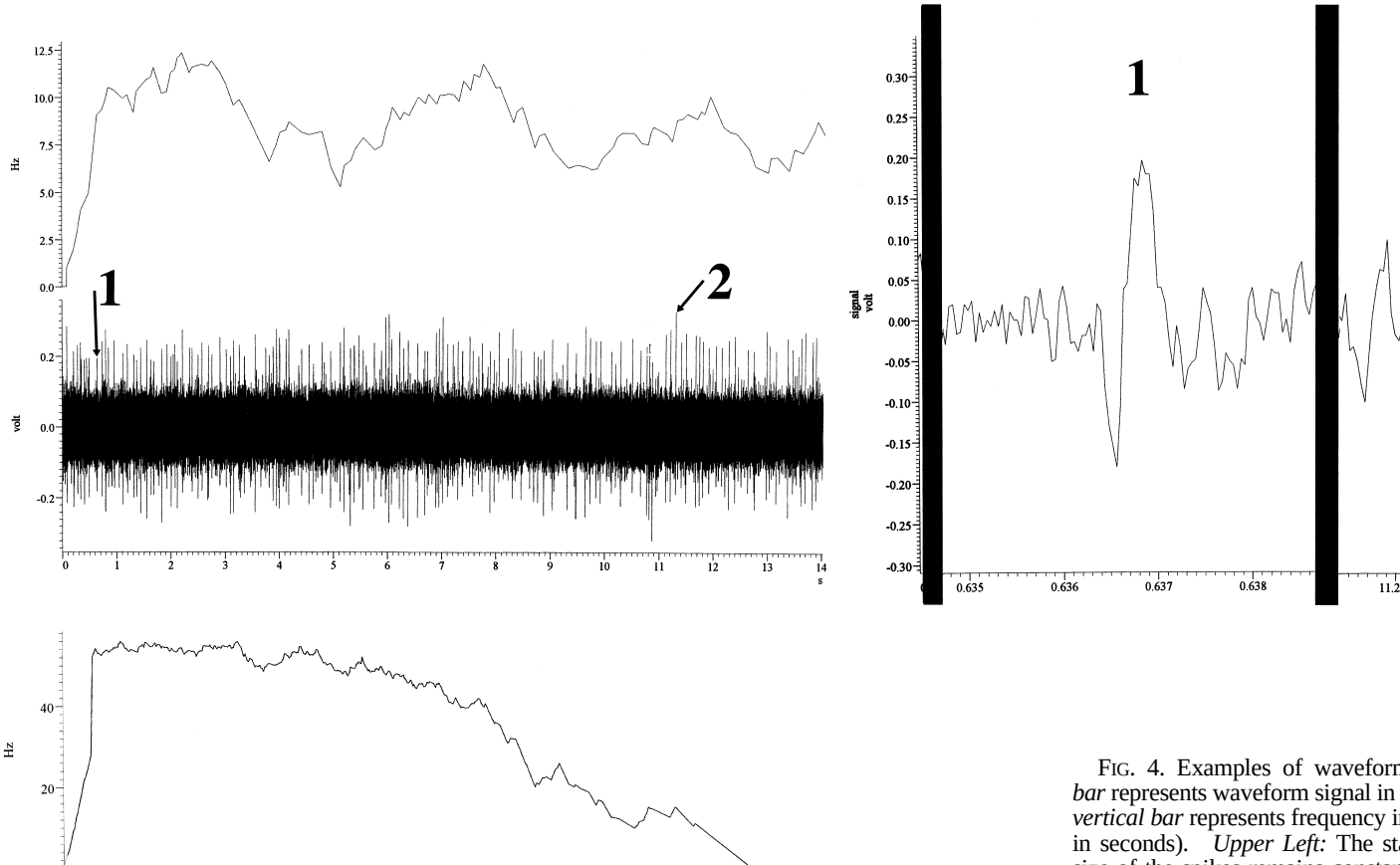

FIG. 4. Examples of waveform
bar represents waveform signal in
vertical bar represents frequency i
in seconds). *Upper Left:* The st
size of the spikes remains constan
firing rate. *Numbers* indicate the l
shown below in detail. *Upper R*
signal as shown in image at left,
scale to show the individual spik
spikes of this unitary recording var
file. Despite this, the spike sorter i
spike, because the histogram of th
similar to those shown in Fig. 3.
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decreases and finally the spikes dis

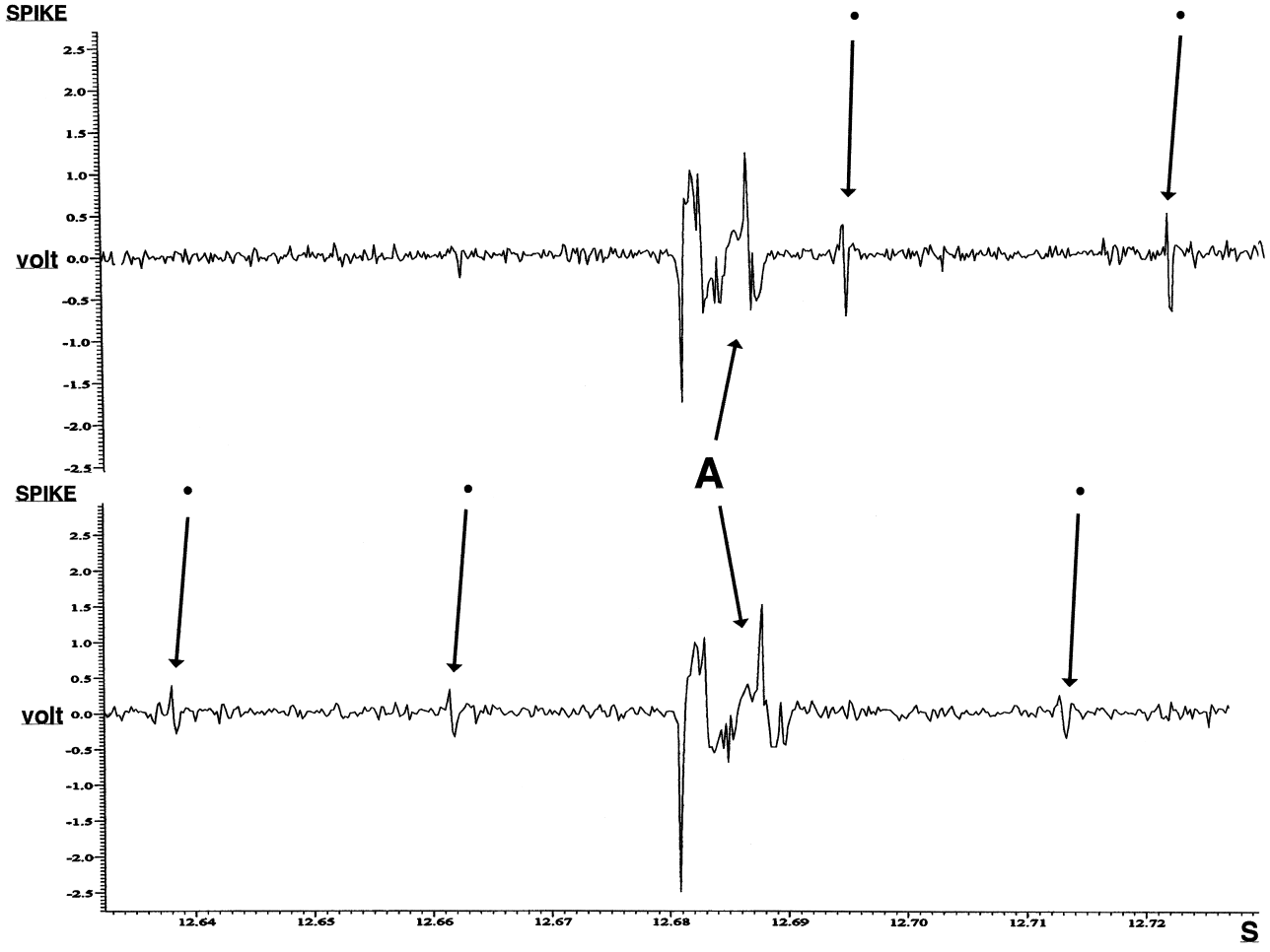

FIG. 5. Example of an easy discrimination between spikes and artifacts generated by the two independent tips. The artifacts *(A)* are visualized on both channels at the same time, whereas spikes *(arrows)* are visible only on one channel at a time.

scope, in the dorsal horn, by means of a simple microsurgical bipolar forceps. The electrode is implanted just prior to undertaking the microsurgical DREZ rhizotomy itself, which is performed according to standard surgical technique.[11,25,26] For insertion of the microelectrode, the axis of penetration is exactly the same as that usually chosen when inserting the bipolar coagulation device to perform the DREZ rhizotomy, namely 35 to 45° medially and ventrally (Fig. 2). The penetration depth is 4 mm and can be controlled under direct vision, because the surgeon knows that the silicon sleeve is 5 mm away from the tips. One-minute recordings at three to five sites in the dorsal horn can thus be successively obtained without tip deterioration.

Recording Technique

Each microelectrode is connected to a cathode follower, protected by a sterile envelope, and placed near the surgical opening. The connecting wires are very thin (80-µm-diameter and 15-cm-long insulated copper wires) to avoid applying force on the microelectrode. The cathode follower is connected to an amplifier (× 10000) and a signal filter (900–15000 Hz). The signal is visualized in the operating room on an oscilloscope, and it is recorded on a digital cassette recorder, at 20-Hz sampling frequency, for further off-line analysis.

Data Analysis

The data analysis is performed after obtaining recordings by means of two computerized tools. A spike sorter is used to isolate single units from the recording that sometimes contains activities of several neurons on one tip (Fig. 3). This hardware enables the discrimination and isolation of single spikes from multiunit recordings.

For each spike the spike sorter provides a time stamp that is transmitted to the computer hardware and software, which is used to calculate frequencies, as well as the interspike intervals.

Finally, several parameters can be quantified. 1) The stability of the recording is estimated as "good" if the size of the spikes is invariant along the recording file. If the size of the spikes gradually increases or decreases along the recording file, the stability is considered "poor" (Fig. 4). 2) The quality of isolation of each neuron is estimated by an isolation index given by the spike sorter and is quot-

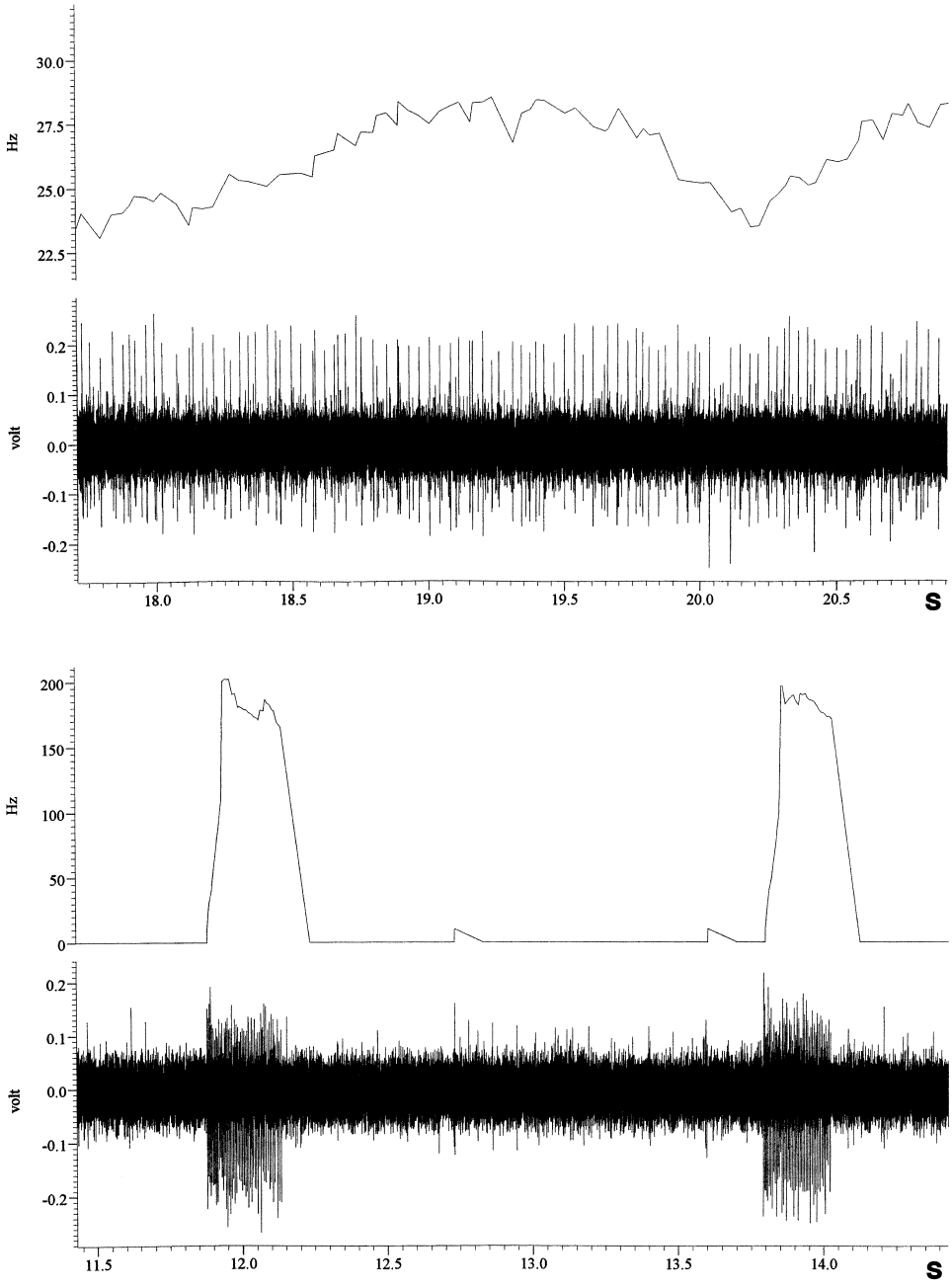

FIG. 6. Examples of waveform signals recorded in patients with different pathological conditions. *Upper:* Example of neuronal activity observed in a spastic dorsal horn. *Lower:* Example of deafferented dorsal horn (brachial plexus avulsion) displaying a burst activity (signal in volts [gain = 10,000], time in second[s]). In the upper line, frequency is measured in Hertz.

ed to range from + to +++ (see Fig. 3). 3) The mean frequency is calculated by dividing the total spike count by the duration of the recording. 4) Possible presence of bursts in the file is determined. We defined a burst as the presence of more than three spikes in 0.01 seconds. Other definitions have been reported.[6,9,12]

Sources of Equipment

We acquired the intravenous cannula from Portex Ltd. (Kent, UK). The double microelectrode that we developed is manufactured by Alan Ainsworth Inc. (Northamptshire, UK). Both the cathode follower and the signal filter are produced by Digitimer Neurolog Ltd. (Hertfordshire, UK). Phillips (Eindhoven, The Netherlands) manufacturers the oscilloscope used in our procedures. The digital cassette recorder was obtained from Cygnus Technology, Inc. (Delaware Water Gap, PA), and the bipolar forceps, used to handle the microelectrode, was acquired from Codman (Issy les Moulineaux, France). Alpha Omega Engineering

(Nazareth, Israel) manufactures the spike sorter. Both the computer hardware (CED 1401) and the software (CED spike 2) were obtained from Cambridge Electronic Design Ltd. (Cambridge, UK).

Results

We recorded in a total of 57 neurons at 61 penetration sites in the dorsal horns of 17 patients. Only 31 of the 61 penetration sites demonstrated one or more spike. Consequently, the chance of recording a neuron during one penetration is approximately 50%. Multiple units were recorded at nine penetration sites (18 neurons recorded by pairs on the same tip), and single-unit recordings were obtained in all the remaining cases. According to the criteria previously described stability was found to be good in 75% and poor in 25% of cases. In the 57 neurons the isolation index was +++ in 31 (54%), ++ in 18 (32%), and + in eight (14%) of the cases (Fig. 3).

Our microelectrode was able to record spikes in 15 (88%) of 17 patients. The cases of failure, defined by the absence of spikes in all the recording files obtained in a patient, were all due to a totally flat signal. Problems with electrical artifacts were most serious during the initial adjustments of the double microelectrode. Of the 17 patients in whom electrode readings were obtained, artifacts were a source of difficulty in fewer than 15% of the penetrations. They could be easily recognized by means of the two independent electrode tips (Fig. 5).

The electrophysiological results obtained with this electrode will be presented in a separate report. Some preliminary electrophysiological results (Fig. 6) have already been described.[7]

Discussion

Our custom-designed floating dual microelectrode has proven to be an effective and reliable tool for the electrophysiological study of neurons in the human dorsal horn. To achieve our purpose, certain problems had to be solved, among which two points were of particular importance: 1) to distinguish between spikes and artifacts and 2) the precious help provided by the spike sorter for the data analysis. As for the former point, because of the surgical conditions, we expected to encounter a greater number of difficulties in distinguishing between spikes and artifacts in our study than those encountered in all the previous studies in animals.[3–5,15,17] The two tips separated by 300 µm provided the only efficient solution to this problem of artifact recognition. Moreover, the two-tip design doubles the chances of recording a neuron, which is a very important point. Furthermore, by slightly modifying the electrode, we can envision the possibility of using smaller tip separations that would allow the study of synchronization of neighboring neurons. As to the second point, the considerable help provided by the spike sorter is related to our choice of tip length. Indeed, we had to achieve a compromise between a small tip size (5–15 µm) that provides rare but well-isolated spikes, and a large tip size (15–30 µm) that records in many neurons but provides a poorer isolation. We finally opted to use a tip length of 20 µm, because it allowed us a greater number of chances to record neurons, even if some of the spikes were small. It is not feasible to sort the spikes on-line because of lack of time; thus, use of the spike sorter proved to be the only way to identify and count with certainty the small or medium spikes.

The choice we made in favor of a floating microelectrode proved to be satisfying. The handling of the microelectrode by using a simple neurosurgical bipolar forceps never caused tip deterioration, and the connection wires allowed for electrode movements during spinal cord movements linked to respiration and cardiac pulsations. Moreover, these electrodes are relatively inexpensive (approximately $90 each).

The latest version of the microelectrode was able to collect spikes in more than 85% of the patients (15 of 17 in this series), without encountering artifacts. The two cases of failure (in which only totally flat signals were recorded) might have been caused by faulty electrodes or connections or by silent neuronal populations. Studies are currently being conducted using this reliable tool to highlight the unitary electrical activity in the human dorsal horn in particular pathological conditions such as a persistent pain syndrome. Further simple adjustments will make this microelectrode useful intraoperatively to study other sites of the gray matter, such as the cerebral cortex.

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