Spiral nerve cuff electrode for recordings of respiratory output

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Sahin, Mesut, Musa A. Haxhiu, Dominique M. Durand, and Ismail A. Dreshaj. Spiral nerve cuff electrode for recordings of respiratory output. J. Appl. Physiol. 83(1): 317–322, 1997.—The feasibility of using the spiral nerve cuff electrode design for recordings of respiratory output from the hypoglossal (HG) and phrenic nerves is demonstrated in anesthetized, paralyzed, and artificially ventilated cats. Raw neural discharges of the HG nerve were analyzed in terms of signal-to-noise ratios and frequency spectra. The rectified and integrated moving average activity of the HG nerve had a peak value of 1.74 ± 0.21 µV and a baseline value of 0.72 ± 0.11 µV at elevated respiratory drive induced by increases in CO2 or oxygen deprivation when recorded with 10-mm-long cuffs. The frequency content of the HG electroneurogram extended from several hundred hertz to 6 kHz. Spiral nerve cuff recordings without desheathing of the nerve provided large enough signal-to-noise ratios that allowed them to be used as a measure of respiratory output and had much wider frequency bandwidths than the hook electrode preparations. A major advantage of the cuff electrode over the hook electrode was its mechanical stability, which significantly improved the reproducibility of the recordings both in terms of signal amplitudes and frequency contents.

nerve recording; phrenic nerve; hypoglossal nerve; hook electrode; power spectrum analysis

MATERIALS AND METHODS
Spiral nerve cuff electrode fabrication. The details of spiral nerve cuff fabrication have been described earlier for electrical stimulation applications (12). The spiral nerve cuff electrode consists of two layers of Silastic sheet (Dow Corning) bound together and platinum-foil bands placed between the layers to provide electrical contact with the nerve (Fig. 1A). Platinum-foil bands (in this design, thickness = 5 µm and width = 1.5 mm) were welded to Teflon-insulated multistrand stainless steel (316 LVM) lead wires for electrical connection. The bands were aligned on top of an unstretched sheet of Silastic and lightly secured by using Silastic adhesive (Medical Adhesive Silicon Type A, Dow Corning). Curing agent (MDX4–4210, Dow Corning) was spread over the sheet and the platinum bands. Another layer of Silastic sheet was stretched and placed on the top. The sandwich was cured between heated pressure plates. The cuff coils in the direction parallel with the platinum bands and takes a cylindrical shape after it is cut out from its surrounding (Fig. 1B). Windows (1 mm wide) were cut inside the cylinder over the platinum bands to make electrical contacts with the nerve for recordings. The final cuff diameters were ~1 and 0.5 mm, which are the sizes of the HG and Phr nerves in the cat, respectively. In this design, three platinum-foil bands located 5 mm apart from each other (total cuff length = 10 mm) were used. These bands were connected to the preamplifier with the lead wires configured in either tripolar or bipolar modes (Fig. 2).

Experimental preparation. In three anesthetized, paralyzed, and artificially ventilated animals with intact carotid sinus nerves, HG and Phr nerve ENGs were recorded with spiral nerve cuff and conventional hook electrodes. Cats were anesthetized with α-chloralose (50 mg/kg ip). Supplemental doses of anesthesia were given every 60 min (10 mg/kg of α-chloralose). A low tracheostomy was performed, and a tracheal tube was inserted. Cats were paralyzed with gallamine triethiodide (Flaxedil, 4 mg/kg iv) and mechanically ventilated. Animals were allowed to periodically recover from
paralysis. If a withdrawal response to nociceptive stimuli was present, an additional dose of \( \alpha \)-chloralose was given before paralysis. For the recordings of the HG nerve with the cuff electrode, \( \sim 2 \) cm of the nerve length were carefully dissected. The cuff electrode was placed around the main trunk of the HG nerve proximal to the bifurcation point of the branches to the muscles of the tongue. For the hook electrode recordings, the standard preparation was used as described earlier (6, 7, 9). Briefly, the nerve (HG or Phr) was cut, desheathed, and covered with Vaseline. The hook electrodes had arbitrary lead separations (4–8 mm). The recordings were made starting from implantation of the nerve cuff electrode for a period of 8–10 h.

Experimental protocol. The recordings were obtained at different levels of respiratory drive. The respiratory drive was increased by incremental increases in arterial CO\(_2\) by rebreathing method (3% CO\(_2\) in O\(_2\)) and normocapnic hypoxia (8% O\(_2\) in N\(_2\)). A decrease in the respiratory drive was induced by reducing the end-tidal CO\(_2\) or switching the animal from hypoxic to hyperoxic gas mixture.

Data acquisition. Recording hardware consists of a custom-design preamplifier (head stage), a commercial laboratory amplifier with a band-pass filter (model 113, EG&G PARC), data-acquisition board/software (NB-M1O-16P-5L, Labview, National Instruments), and a personal computer. A low-noise integrated instrumentation amplifier (AMP-01, Monolithic Precision) is used in the design of the preamplifier. The experimental noise is primarily due to 1) the resistivity of the tissue (Johnson noise) and 2) the preamplifier. The contamination from the power lines is reduced by using an optical isolation stage (4N27, Texas Instruments) between the preamplifier and the amplifier, and the remaining contamination is removed by the low-frequency stop band of the band-pass filter (300 Hz) available on the commercial amplifier. The raw data are recorded breath by breath for study of the frequency characteristics of the neural activity. Data are sampled at 30,000 samples/s after band-pass filtering (300 Hz–10 kHz) to prevent aliasing. For integrated moving average ENGs, the nerve's electrical activity is first rectified and integrated by using a 200-ms electronic averager, in addition to filtering (300 Hz–3 kHz), and then digitized at 40 samples/s. The electrode configurations utilized are shown in Fig. 2.

Data analysis. The signal-to-noise ratio is defined as the peak value of the integrated moving average signal divided by the baseline value measured immediately before the start of the inspiratory phase (see Fig. 4B). The peak and baseline values are measured at the maximal respiratory level in each animal. Signal-to-noise ratios are calculated in each animal separately. Then, the mean and SD of each parameter are calculated across all the animals. The electronic noise due to the preamplifier is estimated by making a recording with the input of the amplifier short circuited. Power spectra are calculated by using the Welch method of power spectrum estimation. The sampled version of the time sequences consisting of samples (n) are divided into overlapping (50%) sections (K) of M points, where M is a power of two. Successive sections are filtered with a Hanning window, transformed by using fast Fourier transform, and averaged.

RESULTS

Integrated ENGs. An example of integrated nerve activity recorded during change in respiratory drive in a cat with intact carotid sinus nerves is shown in Fig. 3. The animal was first ventilated with O\(_2\) at end-tidal CO\(_2\) above apneic threshold (PO\(_2\) = 359 Torr, PCO\(_2\) = 40.7 Torr, pH = 7.393). Switching to hypoxic gas mixture (8% O\(_2\)-balance N\(_2\)) was associated with an increase in Phr nerve activities recorded by both hook and nerve cuff electrodes as well as an increase in HG nerve discharge. When the animal was switched from a hypoxic to a hyperoxic gas mixture (indicated by the arrow in Fig. 3), the activities of both nerves were decreased and then gradually returned to their prehypoxic exposure levels.

Raw ENGs. A typical HG nerve ENG recorded by using tripolar configuration is shown in Fig. 4A. The phasic component of the HG nerve activity is modulated by the respiratory activity. Under hypoxic conditions, the recorded amplitudes increased and were \( \geq 10 \) \( \mu \)V (peak to peak) during inspiration in all three animals. The peak and baseline values in integrated...
traces (Fig. 4B) were 1.74 ± 0.21 and 0.72 ± 0.11 µV (n = 3), respectively. The maximum signal-to-noise ratio averaged for all the animals was 2.44 ± 0.18 (n = 3). The electronic noise gave a baseline value of 0.43 ± 0.02 µV in the integrated traces.

Power spectra. The power spectra calculated from 1-s-long epochs taken during the inspiratory phase and a preinspiratory phase are shown in Fig. 5. During inspiration, most of the power is found between 500 Hz and 6 kHz. There is a considerable difference in power between inspiratory and expiratory (baseline) phases. The power spectrum of the electronic noise is also shown.

In Fig. 6, the power spectra of the HG nerve activities recorded with hook and cuff electrodes from four separate electrode-nerve preparations during increased respiratory drive are shown. Both cuff electrode recordings have a much wider frequency band compared with that of the hook electrodes (100 Hz-2 kHz vs. 500 Hz-6 kHz).

In Fig. 7, the power spectra of the HG nerve activity recorded by configuring the spiral nerve cuff electrode in tripolar and bipolar modes are compared. The overall frequency bandwidth for both spectra is approximately between 500 Hz and 4 kHz. The spectrum shown for the bipolar cuff is bimodal with the higher mode (2.5–4 kHz), which is similar to the spectrum from the tripolar electrode. However, the lower frequency components (500 Hz-2.5 kHz) have much higher amplitudes.

DISCUSSION

Signal-to-noise ratios. The signal-to-noise ratios of the HG nerve recordings obtained with the cuff electrode are in an acceptable range and can detect modulations of nerve activity by changes in respiratory drive (Figs. 3 and 4). The baseline value of the integrated signals is only slightly above the electronic noise level (0.72 ± 0.11 vs. 0.43 ± 0.02 µV). The fact that the tonic activity level is so small can be attributed to anesthesia (11). In unsedated cats, significantly higher levels of
tonic discharge of the genioglossus, which is innervated by the HG nerve, were found (8).

The cuff length (i.e., electrode separation) is one of the important parameters that determine the signal amplitude. The amplitudes of the recorded signals first increase as the cuff length increases and then reach saturation (16). Faster fibers require longer cuffs for saturation. Thus we consider only the largest fibers for evaluation of the cuff length. The largest fibers in the cat HG nerve have a diameter of 11.5 µm (1). The estimated conduction velocity for a myelinated fiber of this caliber is 64 m/s (10). Although not saturated, the signal amplitudes are large when the activity of a fiber of this diameter is recorded with a 10-mm-long cuff from the cat sural nerve, which has a size similar to the HG nerve (16). Thus the cuff length, which was limited by the dissectable length of the nerve, was chosen to be 10 mm in these experiments. In hook electrode preparations, Vaseline is applied to the nerve/electrode, and it is very difficult to determine the length of the restricted extracellular space surrounding the nerve. For this reason, one can expect large variations in the signal amplitude within an experiment as well as between experiments. Temporal variations in the degree of nerve dehydration and the damage introduced to the nerve complicate the issue further.

The signal amplitude is also dependent on the electrical configuration of the recording electrode (Fig. 7). When configuration is switched from tripolar to bipolar mode on the same cuff electrode, the integrated peak signal amplitudes were increased (1.95 vs. 2.42 µV). This increase was possibly due to the large components added in the lower frequency range of the bipolar spectrum.

Another important factor that determines the signal amplitude is the thickness of the extraneural medium inside the cuff that shunts the electrical potentials to be recorded. The fluid from the surrounding tissue fills this space in acute experiments. A snugly fitting cuff gives considerably larger amplitudes compared with a cuff that has a relatively larger diameter (data not shown). An advantage of the self-coiling cuff is that it squeezes the fluid out and increases the resistivity of the extraneural space within the cuff, thus increasing the signal amplitudes.

Frequency content of recordings. The power spectra shown in Fig. 6 for hook and cuff electrodes differ considerably. The frequency bandwidth of the plots for the hook electrodes is much narrower than that of the cuff electrodes. A possible explanation is the difference in the transfer function of the electrodes. When whole nerve recordings are obtained with the cuff (or hook) electrodes, the frequency spectrum of the nerve activity is modified by the following transfer functions: 1) the nonlinear, spatial frequency-dependent transfer func-

![Fig. 5. Power spectra (n = 30,000, M = 128, 50% overlap; see MATERIALS AND METHODS for description) of HG nerve activity during inspiration (1-s-long epoch at peak activity) and baseline (second before next breath starts) recorded by using nerve cuff electrode in tripolar mode. Third trace (dashed line), power spectrum of electronic noise (n = 30,000, M = 128, 50% overlap).](image1)

![Fig. 6. Power spectra (n = 30,000, M = 128, 50% overlap; see MATERIALS AND METHODS) of HG nerve activity recorded with tripolar cuff and bipolar hook electrodes. Each spectrum is obtained from a separate electrode-nerve preparation. Each plot is normalized with respect to its own peak for comparison.](image2)

![Fig. 7. Power spectra (n = 1,020, M = 512, 50% overlap; see MATERIALS AND METHODS) of short HG nerve recordings (10 ms) acquired by configuring spiral nerve cuff electrode in tripolar and bipolar modes. Raw data epochs are acquired one immediately after another to avoid changes in respiratory drive level. Data are sampled at 100 kHz after filtering with 300-Hz to 10-kHz band filter. In this trial, tripolar and bipolar modes gave peak values of 1.95 and 2.42 µV, respectively, in rectified and integrated versions of recordings.](image3)
tion of the nerve trunk and the surrounding medium as a volume conductor, including the restrictions on the extraneural space, i.e., the cuff (or Vaseline with the hook electrodes) (3, 19); and 2) the filter function determined by the location (separation) and the electrical configuration of the metal contacts (discussed below).

The transfer function of the volume conductor can be altered by restricting the extraneural space, e.g., surrounding the nerve with a nonconductive material such as Silastic, Vaseline, paraffin, or mineral oil. Because the restricted space provided by a nonsolid material like Vaseline is prone to mechanical disturbances, the frequency response of the recording system will vary throughout the experiment. Moreover, the extent of the extraneural restriction space can vary from experiment to experiment because the length of insulation is not constant. This may adversely affect the reproducibility of the recordings, especially in long trials. Mechanical stability and rigidity provided by the nerve cuff electrodes eliminate these problems.

The design parameters of the cuff electrode, i.e., separation and electrical configuration of the metal contacts, also affect the overall transfer function of the recording system. The tripolar configuration is used for its superior immunity to electrical disturbances from surrounding muscles and power lines (17), which may not be the primary concern in acute recordings conducted under anesthesia. Bipolar configuration is more common with the hook electrodes in acute experiments for practical reasons. The tripolar cuff provides the second spatial derivative of the extraneural potentials, whereas the bipolar configuration gives the first spatial derivative (18). Thus the nerve cuff electrode is, in fact, a linear filter in the spatial frequency domain, with a transfer function determined by the separation and the configuration of the metal contacts (simulation data not shown). These spatial transfer functions will be transformed into the temporal frequency domain after being scaled with the propagation velocity of the action potentials. The higher the conduction velocity, the further the transfer function spectrum is spread over higher frequencies. Thus the temporal frequency spectrum of the recordings should also be a function of the cuff length and the contact configuration. This is supported by the plots shown in Fig. 7. Although the overall frequency range occupied by both recordings is approximately the same, the bipolar recording has much larger components at the low end of the spectrum than does the tripolar recording. This suggests that the bipolar configuration has higher gains in the lower frequency range.

Finally, the bimodal spectra of the recordings in Fig. 7 could be explained by desynchronization of the fiber activity. It has been shown that as a result of desynchronization in the fibers’ activation, dips can exist in the power spectrum of compound action potentials and that the frequencies of dips would depend on the degree of desynchronization (2).

We conclude that the signal-to-noise ratios obtained with the spiral nerve cuff electrode recordings from intact HG and Phr nerves are large enough to allow one to use them as a measure of respiratory output under different respiratory drive levels. The mechanical stability provided by the cuff electrode can be crucial for the stability of the transfer function of the nerve-electrode system, and hence, the reproducibility of the recordings. The frequency content and the signal amplitude of the recordings depend on the cuff length (contact separation) and the electrical configuration of the metal contacts. The bandwidth of the signals obtained with our cuff electrodes was much broader than that of the hook electrodes.

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