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# BRIEF COMMUNICATION

# New Multi-purpose Chemitrodes for Electrical and Chemical Stimulation or Localized Perfusion of the Brain[1]

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LEROUX, A. G. AND R. D. MYERS. *New multi-purpose chemitrodes for electrical and chemical stimulation or localized perfusion of the brain.* PHARMAC. BIOCHEM. BEHAV. 3(2) 311–315, 1975. – The design and construction of two sizes of bipolar chemitrodes are described for stimulating directly a single site in the brain of a rat, cat, monkey or other animal. These chemitrodes are used for the injection of a drug at the same time that electrical stimulation is applied, or for the localized push–pull perfusion of the same locus. They also permit the recording of electrical potentials at the tip of the guide tube. The chemitrodes may be implanted chronically for the purpose of examining the relationship between chemically and electrically elicited responses in the awake and unrestrained animal.

Electrical stimulation  Chemical stimulation  Drug stimulation of CNS  Push–pull perfusion  Brain locus

THE direct stimulation of a single site in the brain with both a chemical substance and electric current offers several distinct advantages for the study of behavior [14]. To illustrate, after a reliable pattern of responding is established by means of repeated electrical stimulation of a specific locus, the neuronal activity of the same region can be modified simultaneously by an injection of a neurotransmitter or other humoral substance into the site. Similarly, the sensitivity of the locus to electrical stimulation can be enhanced or attenuated by a pharmacological agonist or antagonist injected locally before the pulses are delivered [14]. In such a way, a relationship can be established between the neuronal response to electrical excitation and localized chemical modification.

In 1937 Masserman [9] introduced to the field of neurophysiology a bipolar electrode through which a drug or electrical pulse could be delivered at the tip. Subsequently, Liljestrand [5] devised a diminutive monopolar electrode–cannula by drawing a silver wire into a fine glass capillary tube. In the last 20 years, a number of electrode–cannula devices, now termed chemitrodes, have been designed for simultaneous electrical or chemical stimulation, recording of electrical potentials, exploring tissue at different depths and other studies [1, 2, 3, 6, 10].

This paper describes the methods for constructing two types of chemitrodes. Each can be fabricated inexpensively, with ease, and used for independent or simultaneous electrical and chemical stimulation of the brain. The smaller of the chemitrodes is designed for the rat or other laboratory animal of similar size. The larger chemitrode, used for the cat or monkey, not only delivers a chemical or a series of electrical pulses but the internal dimension of the shaft also permits the insertion of a push–pull cannula assembly for the localized perfusion of the region.

## CONSTRUCTION

### *Chemitrode for Small Animal*

The shaft of the chemitrode for the rat or other small animal is fashioned from 23 ga thin-wall stainless steel tubing cut to a length of 18 mm. This serves as a chronically implanted guide tube which accommodates a 27 ga stilette cut to the same length. Both guide and stilette are beveled at the tip to an angle of 30°. Should the option of a push–pull perfusion be desired, a 20 ga guide tube can be substituted so as to accommodate a 23 ga or even smaller push–pull cannula assembly which is now used routinely in the rat [7, 8, 13].

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Each of the two stimulating electrodes consists of 0.008 in. teflon-coated platinum wire (Medwire Corp., Mount Vernon, N.Y.), which is cut to the appropriate length by sharp scissors. Thus, the stimulating surface of the implanted portion of wire is just that portion of the exposed end bared by the scissors' cut. The insulation at the external ends of both wires is carefully scraped away. Then these ends are soldered into or crimped onto two 4 mm lengths of 22 ga stainless steel tubing which serve as the female socket for a twin lead male plug.

As shown in Fig. 1, the two wires are positioned against the side of the guide cannula. They are then cemented with a special epoxy cement (Hardman, Inc., Belleville, N.J. 07109) which is biologically nontoxic and dries to a perfectly smooth surface within 3 to 5 minutes at 75°F. The electrodes can be aligned so that their axis of implantation falls either in the coronal or longitudinal plane. Figure 1 illustrates the final position of the electrodes dressed against the shaft of the guide tube and into the sockets. While the epoxy glue is applied over the surface of the chemitrode, and during the drying process, the two tubes which serve as the female socket are held temporarily in place by a male connector plug which acts as a jig. The connector assembly is fastened to the guide cannula at an angle of 30°, so that an injector needle can be inserted into the guide tube and a solution injected at the same time that the male plug is connected to the chemitrode. Figure 2 illustrates a completed chemitrode that is ready to be implanted into the brain of a rat.

The injector needle to be lowered through the guide cannula is cut from 28 ga stainless steel tubing to a length which depends on the site at which one intends to inject the chemical. The overall depth to which the injector needle is lowered into the brain can be controlled by a stainless steel collar of approximately 3 mm in length which can be crimped temporarily onto the tube.

*Chemitrode for Large Animal*

For a larger animal such as a cat or monkey, an array of up to three chemitrodes is arranged on a single base as shown in Fig. 3. Although the base can be constructed of Plexiglas, teflon or other easily workable material, we have found an amphenol rack and panel plug, Model 223 Tiny Tim, to be of ideal dimensions and easily adapted for a base and connector. The amphenol plug (No. 223–1109) contains 9 holes; 3 holes are used to hold the cannula guides; and through the remaining 6 holes the 3 pairs of respective electrodes are fed.

Each of the three 18 ga stainless steel guide tubes is cut to a length of 45 mm or other desired length and beveled to a 45° angle at the end to be implanted. Arranged in the longitudinal plane, the tubes are pressed through the three adjacent holes, and because of the extremely tight fit, they are held firmly in place by friction. Although their position can be varied according to the depth of the structure to be stimulated, the tips of the guide tubes are extended as much as 20 to 25 mm beyond the amphenol base. For certain long-term studies, the length of the external portion of the guides can be reduced. One typical arrangement of the chemitrodes is depicted in Fig. 3.

Six Medwire teflon coated wires are soldered to each of 6 female connector pins which are inserted in the remaining 6 holes (Fig. 3, bottom) of the amphenol base. Each of the pairs of wires is then dressed along the external shaft of the

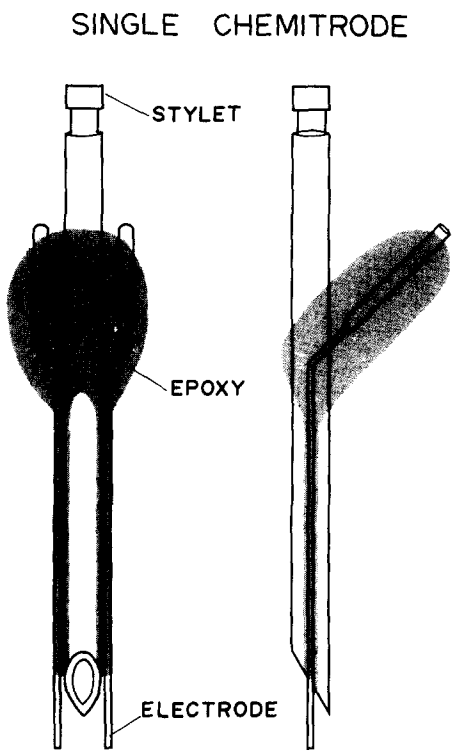


FIG. 1. Front and side views, not to scale, of a chemitrode designed for the rat. Teflon insulated wires are cemented to the sides of a cannula fitted with an indwelling stilette as shown. Wires are soldered onto the female connector tubes that are held in place by epoxy.

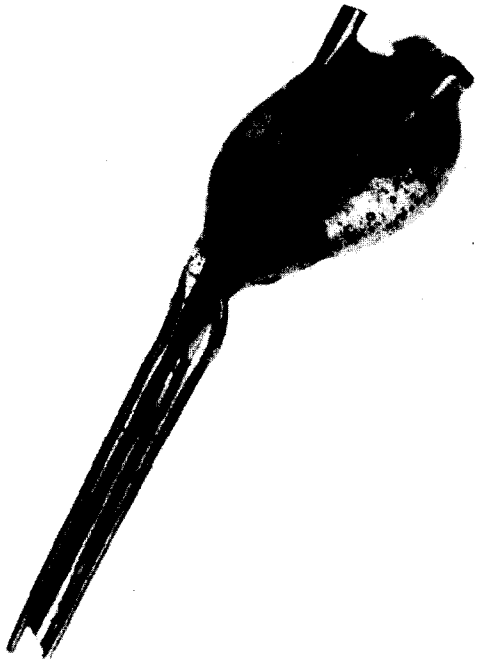

FIG. 2. A completed chemitrode for the rat. The photograph depicts the epoxy bead which bonds the connector plug and electrodes to the guide cannula.

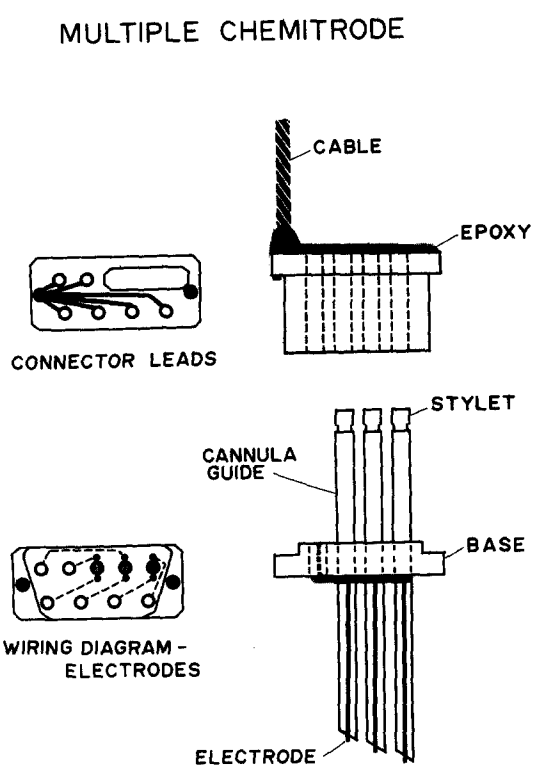


FIG. 3. Three-cannula chemitrode assembly. The amphenol connector to which the leads are wired (top, left) to a spirap-covered cable (top, right) fits onto the matching amphenol base. The electrode leads are soldered to the female connector pins as shown in the wiring diagram (bottom, left) and dressed along the shafts of the respective guide tubes on the underside of the chemitrode base (bottom, right).

respective guide tubes as illustrated. To affix the wires to the guide tubes, the quick-drying epoxy resin cement again is carefully applied over the wires as shown in Fig. 3. The tips of the paired electrodes are cut with a sharp scissors so as to extend only 0.5 mm beyond the beveled tip of the guide tube. Once again, the bared end of each wire serves as the stimulating surface. Stilette wire of 21 ga stainless steel is cut to match the length of the guide tube and inserted in each of the guide tubes.

The amphenol receptacle (No.223–1209) which mates with the plug is used as the connector for the multi-lead cable that is hooked up to the stimulator. The male pins which are supplied with each receptacle are soldered to the 6 wire leads. Then the pins are forced into the holes whose position corresponds exactly (Fig. 3, top) to the 6 female electrode pins located in the plug base (Fig. 3, bottom).

In order that the external portion of the cannula array (Fig. 4B) can pass through the connector when it is fastened to the base during stimulation of the brain, a window is drilled out of the receptacle which is just large enough to accommodate the passage of the 3 guide tubes. Thus, an injector needle can be lowered into a guide tube after the receptacle is connected to the base. The position of this window is shown in Fig. 4A. The stimulator leads are dressed to one side of the top of the receptacle (Fig. 4C and D), and held firmly in place by epoxy cement packed over the wires and around a stainless steel anchoring screw inserted into the end-hole of the receptacle (Fig. 4A). To form a cable for the wires, Spiroband (Electrovent, Mount Vernon, N.Y.) is wrapped around the leads, the ends of which are connected to the terminals of the stimulator. Figure 4D shows the connector in position to be plugged into the base.

## SURGICAL IMPLANTATION

Both chemitrodes are implanted in the brain according to standard stereotaxic procedures [15]. The stereotaxic coordinates for the structure(s) beneath each chemitrode are determined before the surgery is begun. When the 3-chemitrode array is employed, the tip of either the most anterior or posterior guide tube is used to calculate the intended locus of stimulation in the appropriate horizontal, lateral and rostrocaudal planes.

After the initial surgical preparation is completed and a craniotomy hole has been trephined or drilled in the calvarium [12], the chemitrode is positioned over the meninges according to the predetermined coordinates. We have found that it is necessary to incise the dura mater in each case with a dura knife or BP 12 scalpel blade with precautions taken not to damage the underlying vessels on the surface of the cortex. As the chemitrode passes through the pial membrane, additional care must be taken that the tip of either platinum electrode which protrudes beyond the end of the guide tube is not bent or displaced.

Before the single chemitrode or an array of chemitrodes is lowered to the final horizontal coordinate, small strips of gelfoam sponge are placed within the craniotomy hole over the surface of dura so as to cover in its entirety the exposed meningeal surface. These sponges thus separate the chemitrode base from contact with tissue. Further, when cranioplast cement is packed around the chemitrode base, the gelfoam prevents the cement from flowing onto the dura or exposed neural tissue [12].

Around the craniotomy hole 3 or 4 anchor screws, to which the cement adheres, are placed equidistantly in order to hold the chemitrode firmly in place. For long-term experiments, it is advisable to place a polyethylene pedestal or other protective covering [12] over the chemitrodes.

## APPLICATIONS

In addition to the well-known usage of a chemitrode to contrast the effects of electrical with chemical stimulation, the immediate utility of this chemitrode consists of being able to attenuate the local effect of electrical pulses by a pharmacological agent or other substance [4]. Conversely, with other substances such as the endogenously occurring amines, it is possible to enhance whatever action the locally applied current may bring about. Another of the main advantages of the chemitrode designed for the smaller animal is that its diminutive size creates a lesion which is not perceptibly larger than an ordinary micro-injection needle or standard bipolar electrode made of twisted wire.

Not only does the larger chemitrode assembly possess these same experimental advantages, but several other applications are readily apparent. Since the internal diameter of the guide permits the insertion of a concentric push–pull cannula assembly [11], it is now possible to collect by discrete perfusion those specific substances that are present at the tip of the chemitrode or elaborated as the result of

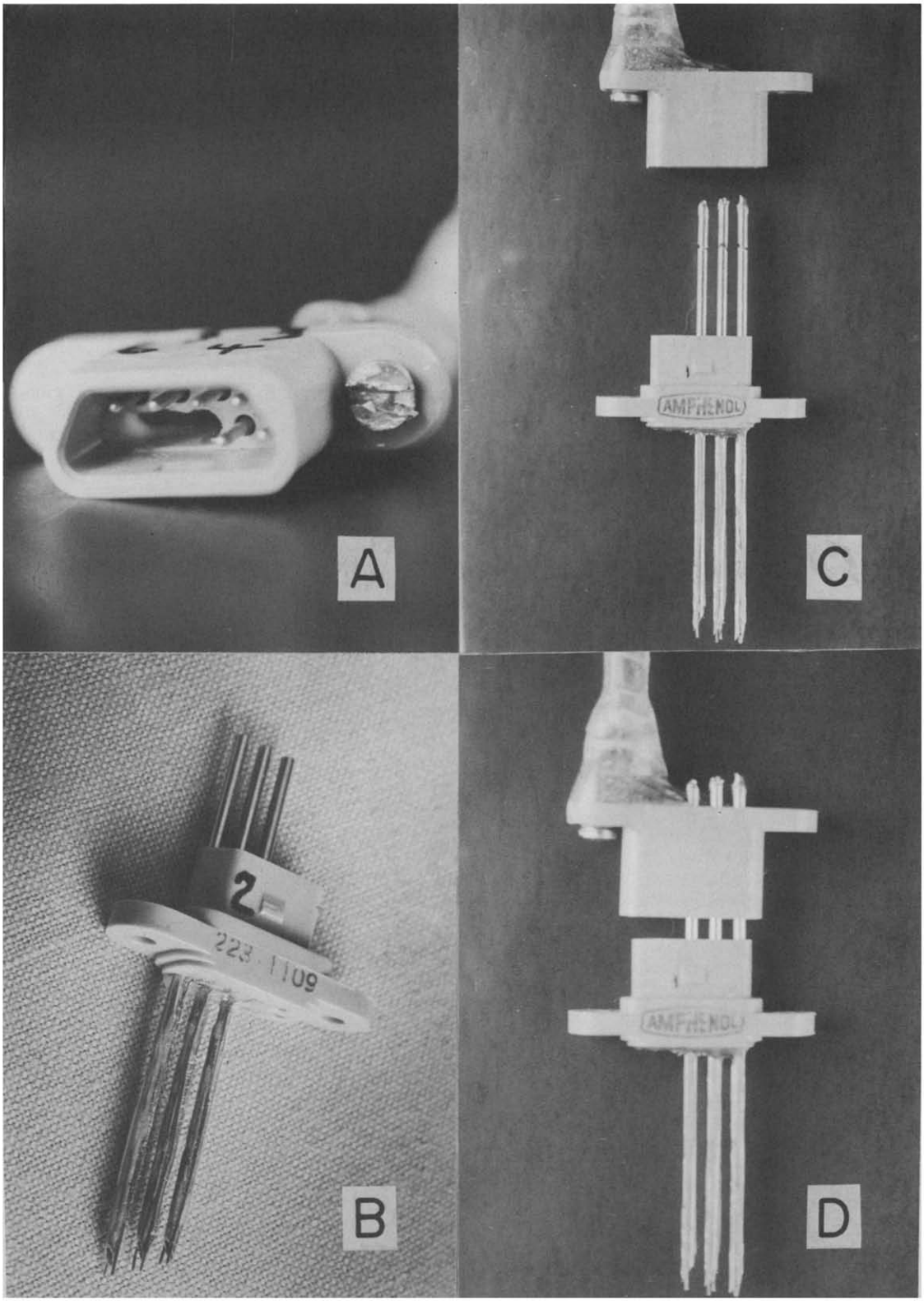


FIG. 4. (A) End view of connector receptacle showing window through which the cannulae pass, the male pins, and the cable anchoring screw; (B) Completed base showing three cannulae with the stimulating electrodes extending beyond each tip; (C) Alignment of amphenol connector to chemitrode base; (D) Connector being passed through the three cannulae.

electrical stimulation. Whether their release, turnover or metabolism is influenced by electrical stimulation can thus be determined.

Another very useful aspect of the larger chemitrode is the recording of the electrical activity at the tips of a set of electrodes or across the tips of a combination of two or more electrodes. To do this, we have connected the external leads which are not being used for electrical stimulation to the input of one or more channels of an electroencephalograph. Then EEG recordings can be made intermittently during the course of an experiment in which a chemical injection or electrical stimulus is given.

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