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Simple Cannula for Repeated Intracerebral Drug Administration in Rats[1]

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CRANE, L. A. AND S. D. GLICK. *Simple cannula for repeated intracerebral drug administration in rats.* PHARMAC. BIOCHEM. BEHAV. **10**(5) 799–800, 1979.—A simply constructed cannulation system for chronic implantation in rats is described. The guide cannula, stylet and injection cannula are all made from stainless steel tubing, require little time to construct, and are designed for minimum brain damage and atraumatic infusion into unanesthetized rats.

Intracerebral cannula Chronic implantation Drugs

NEUROPHARMACOLOGICAL studies often require direct administration of chemical substances into specific brain regions of unanesthetized animals. This need is fulfilled through surgical implantation of a cannulation system. The cannula itself must be of small enough diameter to produce minimal brain damage; it must contain an easily removable stylet to retain patency; and it must easily accept a preconstructed injection cannula. Most chronically implanted cerebral cannulation systems described to date [2, 3, 4, 5, 6] are complicated in structure, take much time to construct and demand a variety of parts and tools. The following system has been designed for quick and simple construction, minimal brain damage, and atraumatic infusion into unanesthetized rats.

Materials

Parts for the cannula system itself consist of lengths of 26 ga, 32 ga, and 33 ga stainless steel hypodermic tubing, and PE 10 plastic tubing. Only two tools are required for construction: a Dremel emery wheel for cutting and filing the hypodermic tubing and a pair of needle nose pliers for holding the cannulae during construction. A 25 ga hypodermic needle is necessary to open the ends of the hypodermic tubing after cutting and epoxy cement is used in assembling the injection cannulae.

Construction

The cannulation apparatus consists of a permanently implanted guide cannula, a removable stylet and a separate injection cannula, all made from stainless steel hypodermic tubing. For the guide cannula (Fig. 1a) the Dremel emery wheel is used to cut and polish the ends of a 20 mm length of 26 ga hypodermic tubing. Both ends of the tube are opened by rotating the point of a 25 ga hypodermic needle within its lumen.

A 24 mm length of 32 ga tubing is cut next and the ends polished in the same manner. Since this will form the stylet (Fig. 1b), no liquid need pass through it and the ends remain closed. (Solid stainless steel wire of the same gauge proved too soft for use as a stylet since constant removal and replacement within the guide cannula caused it to bend.) The stylet is then fitted inside the guide cannula with 2 mm protruding from each end. Holding the top 2 mm of the guide cannula at a 10° angle against the emery wheel, a notch (Fig. 1c) is cut into the side of the tubing. During this process the outer edge of the stylet may be scraped. This damaged end should be grasped with pliers and the stylet pulled a mm or two farther out of the guide cannula until the shiny surface of the stylet shows at the notch. The stylet is then bent at a 45° angle away from the guide cannula over the notch and the damaged part cut off, leaving about 2 mm of stylet overhanging the notch (Fig. 1d). Bending the stylet at any greater angle away from the vertical stresses the metal and the handle may break off during removal of the stylet. The opposite end of the pair of tubes (Fig. 1e) is sharply bevelled with the emery wheel until the total length is 16 mm. The result of this process is the outer guide cannula and its stylet, with a sharpened point for penetration of the dura. The notch prevents rotation of the stylet within the guide cannula, keeping the bevels perfectly matched, and the handle allows easy removal and replacement of the stylet. Finally, the outer surface of the guide cannula is slightly roughened with the emery wheel for adhesion of dental cement during implantation.

The injection cannula (Fig. 1f) is made from a 30 mm length of 33 ga hypodermic tubing with the ends polished, lumen opened, and outer surface roughened along one third its length with the emery wheel. An 8 mm cuff of 26 ga tubing is slid onto the roughened end and glued in place with epoxy (Fig. 1g). This cuff acts as a stop when the injection cannula is placed in the guide cannula. A 40 cm length of PE 10 tubing is pushed about 3 mm down over the cuff and glued in place (Fig. 1f). Once the glue has dried the injection cannula is cut

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to a length of 17 mm from the edge of the cuff to the tip of the cannula. The lumen is again opened with a 25 ga hypodermic needle and water injected through the cannula to check for patency and leaks.

Implantation

Using a stereotaxic atlas (e.g. Pellegrino and Cushman) the appropriate site of injection is located and coordinates for the locus of cranial penetration, angle, and depth of cannula implantation are chosen. Myers [4] suggests that the guide cannula be implanted 1 mm above the actual injection site. Therefore, the injection cannula has been cut one mm longer than the guide cannula to insure injection of chemicals into healthy brain tissue rather than into the fibrous tissue that will grow around the end of the guide cannula after implantation.

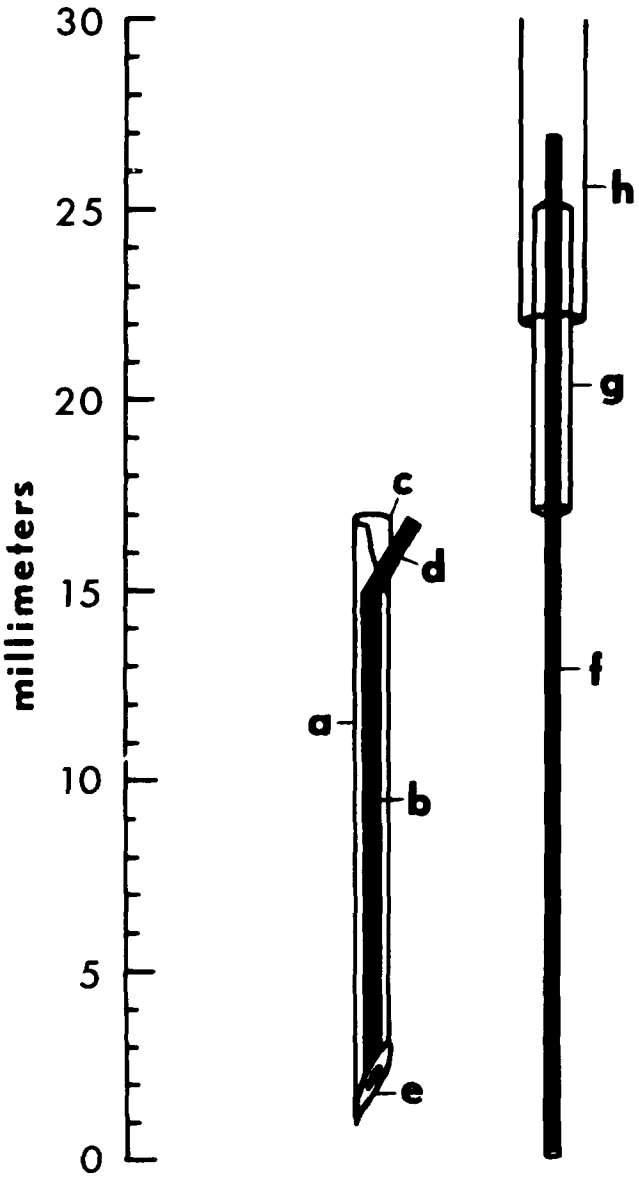

FIG. 1. Cannulation apparatus for chronic cerebral implant and injection: a. guide cannula, b. stylet, c. notch in guide cannula, d. stylet handle, e. bevel, f. injection cannula, g. stainless steel cuff, h. PE 10 tubing.

Rats are anesthetized with 50 mg/kg Brevital (Methohexital sodium) and the dorsal surface of the head is closely shaved. The head is placed in a Kopf stereotaxic apparatus, cleaned with zephiran chloride, and the skin opened directly above the site of cannula implantation. Connective tissue is scraped away from the skull and surrounding tissue swabbed with a small amount of adrenalin to retard bleeding.

The site of cranial penetration is located and a hole only slightly larger than the guide cannula diameter is drilled through the skull with a dental drill. Two support screws are fixed to the skull adjacent to the hole and the guide cannula, complete with stylet, is then lowered into the brain. A small amount of dental cement is placed around the screws and cannula until the screws are covered and the cannula held firmly in place. Once the cement has hardened, antibiotic cream (e.g. bacitracin/neomycin/polymyxin ointment) is applied around the implant. (Infection erodes and destroys the skull, loosening the implant.) The skin is then closed with wound clips so that only the cannula protrudes through the incision.

Discussion

This cannula system has been used in more than 200 rats in this laboratory [1] and has proved to be both expedient and reliable. Two dozen guide cannulae with stylets can be produced within two and one half hours and the implantation procedure for one cannula takes as little as twenty minutes.

The few parts and tools are easily accessible and inexpensive. Dremel tools and plastic tubing are available from many laboratory supply houses and the hypodermic tubing can be ordered from Small Parts, Inc., 6901 N.E. 3rd Ave., Miami, Florida.

Injection cannulae of varying lengths may be used to stimulate loci at different depths through a single guide cannula. The small size of the entire cannula implant allows several cannulae to be placed close together within the same brain. Depending upon the site of stimulation, the length of the guide cannulae may be adjusted as well, so that a minimal amount of tubing extends above the dental cement, thus reducing the risk of bent cannulae. Removal and replacement of stylets and injection cannulae can be done quickly, allowing for totally atraumatic injections into unanesthetized rats. This is obviously an important consideration in behavioral studies of drug effects.

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