A simple and inexpensive method for the intracerebral administration of drug solutions to the conscious rat

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Many different cannula systems have been designed to allow the direct application of drugs to discrete brain areas of conscious animals (Myers, 1971; Harvey & Stevens, 1975). The major technical problem lies in securing the device to the skull and consequently many of the cannula systems are complex and hence expensive. The system detailed here is both inexpensive and simple to construct.

Cannula guides consist of 23 swg stainless steel tubing cut to the required length and electrochemically cleaned of burr. The length of each guide is obviously dictated by the topographical location of the brain area under investigation but certain minimum requirements are apparent. Thus, 4 mm is sufficient to allow positioning in the stereotaxic cannula-guide carrier and a further 4 mm for cementation. This portion carries a small ball of epoxy-resin (2–3 mm diameter) which acts as guide anchorage and prevents movement of the tube in the vertical plane. The remaining part of the cannula guide which lies below the cranium is of length such that the tip rests 2–3 mm above the area under investigation.

Stilettes, which remain within the cannula-guides at all times other than when injecting, are also simply constructed. Stilette shafts of 30 swg, non-ferrous wire are coated with a water repelling agent (dimethyldichlorosilane) and bent, at one end, over a 3–4 mm length of polythene tubing (I/D 0.86 mm) and secured in place with a 3 mm ball of epoxy resin. This facilitates removal of the stilette from the guide, and the cylinder of polythene, which fits closely over the guide tube provides anchorage and prevents access of foreign material into the underlying tissue. The tip of the shaft lies flush with that of the cannula guide.

The cannula guides are stereotaxically positioned and then secured to the surface of the cranium with polymethyl methacrylate. Sufficient cement is used such that both the guide anchorage and the whole of the incised area are covered. The cement is dried by a stream of warm air for 3–4 min before unclamping the guide from the stereotaxic apparatus. Stilettes are then fitted and the animals housed individually for 5 days before experimentation.

Drug solutions are injected through a 30 swg cannula at a rate of 0.47 µl/min and in a volume of 0.5 µl. Injection placements have been histologically verified following the infusion of 0.5 µl of 1% methylene blue and 4 days storage of tissues in 8% formyl saline at 4°C. Placements were found to be consistently reproducible.

References

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Central and peripheral inhibition of the milk-ejection reflex: studies with µ-adrenoceptor antagonists

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Most species of mammal fail to milk eject when they are anaesthetized and suckled by their young. This could be the result of high circulating levels of adrenaline, either blocking the release of oxytocin from the neurohypophysis or preventing the action of the hormone on the mammary gland (Cross, 1955). Rats are an exception and will milk eject when anaesthetized (Lincoln, Hill & Wakerley, 1973), though an appreciable number, too many for some forms of experimental study, still fail to respond to the suckling stimulus. The rat mammary gland is sensitive to the actions of adrenaline, but the effects can be eliminated by β-adrenoceptor antagonists (Bisset, Clark & Lewis, 1967). Thus we have questioned whether central or peripheral adrenoceptor stimulation might explain the failure, or partial failure, of some anaesthetized rats to milk eject when suckled.

Rats, at day 7–10 of lactation and separated from their young for 16 h, were anaesthetized with urethane (1.2 g/kg, i.p.), and two teat ducts were cannulated for the measurement of intramammary pressure. Three hours later, and while the animals were still deeply anaesthetized, 10 pups were applied to the uncannulated nipples. Each milk ejection in the next 3 h was recorded; each ejection was associated with