Brain Scan in Cerebral Ischemia

AN EXPERIMENTAL MODEL IN THE RAT

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Abstract:
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A rapid embolic method for consistent induction of stroke in the rat is described. Brain scans were performed using a micro-pinhole collimator system, and the value of the model for studies in localization of radiopharmaceuticals in cerebral ischemia is demonstrated.

Additional Key Words
• stroke
• cerebrovascular embolism
• radiopharmaceutical localization

Many experimental models of cerebral infarction are available, but no convenient technique for the study of radionuclide localization has been described. This report outlines a rapid reproducible method for the induction of stroke in the rat which allows investigation of technetium 99m pertechnetate distribution related to time after an ischemic insult.

Methods
Thirty Sprague-Dawley retired male breeders (average weight: 700 gm) were anesthetized with 350 to 400 mg chloral hydrate intraperitoneally. Intramedic PE tubing 7400 (I.D. 0.011" X O.D. 0.024") was charged with Microflit (MU 117) by capillary action to prepare a 1 cm rubber plug. After setting overnight the embolus was loosened by pressure on a tuberculin syringe connected via a 27-gauge needle. The tube was then cut to length, beveled and introduced under direct vision into the internal carotid artery via the common carotid. The embolus was flushed with saline, and in more than 75% of animals it was arrested in the cerebral circulation (fig. 1), the only other available path being via the pterygopalatine artery in the skull (fig. 2).

Neurological deficit was apparent immediately on recovery from anesthesia and often increased over the next 24 hours. Intraperitoneal atropine and perchlorate premedication and 7 mCi technetium 99m pertechnetate were given, and three hours later scanning was performed under Metofane sedation at 24 and 48 hours after surgery.

A 1 mm pinhole collimator was machined from a lead generator plug to be interchangeable in the standard Nuclear-Chicago gamma camera pinhole shield. The pinhole collimator was evaluated using a rat brain phantom (fig. 3) constructed in lucite with a single 4 mm loop of PE tubing (I.D. 0.011") for a “lesion” and a larger “sagittal sinus” tube in continuity. The gamma camera with pinhole collimator in position for brain scanning is shown in figures 4 and 5. The phantom “lesion” was well demonstrated with technetium 99m pertechnetate (fig. 6).

The animals were killed after demonstrating a positive brain scan (fig. 7), and the brains were removed immediately, frozen and sectioned in a cryostat for autoradiography. Alternate sections were taken for histopathological correlation and will be the subject of a subsequent paper.

Results
Neurological deficit was produced in 22 of 27 animals. Of these, seven had complete left hemiplegia, six had moderate left hemiparesis, and nine had mild left hemiparesis. Three animals died in the immediate postoperative period before neurological assessment could be made. There were no further deaths until the second 24 hours following operation, when a high yield of positive brain scans may be expected.

Discussion
Standard animal models of cerebral ischemia cannot be applied conveniently for scanning studies. Direct intracranial artery ligation introduces craniotomy artifact, small particle embolization cannot be confined to one hemisphere, and experiments using anoxia or exploiting anatomical deficiencies in cerebral collateral circulation, such as in the gerbil, are not comparable to the human situation.

The circle of Willis in the rat is similar to that of humans and also may be affected by atherosclerosis as shown by Wexler in male breeders. Bilateral carotid ligation in rats yields variable results, and unilateral ligation alone is usually regarded as relatively innocuous. Hypotension of about 30 mm Hg may be maintained for over ten minutes by a single intravenous dose of methacholine after unilateral carotid ligation, and even when attempts are made to compromise cerebral collateral circulation by serotonin (induced spasm), no consistent neurological deficit is achieved (unpublished data).

The effective embolic method described in this report is a modification of Molinari’s technique of...
An embolus lodged in the right middle cerebral artery (arrow) in the ventral view, and evident on the lateral aspect of the brain.

stroke induction developed in the dog and monkey. Chloral hydrate anesthesia is convenient and safe, and avoids the possible protective action of barbiturates against cerebral ischemic injury. The operative procedure in rats is quick and offers a good yield of hemiparetic animals for study at relatively low cost.
MAIN SCAN IN CEREBRAL ISCHEMIA

Gamma camera with pinhole collimator in position for brain scanning.

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References

Another view of the gamma camera with the pinhole collimator in position for brain scanning.

A technetium scintiphoto of the phantom.

Technetium pertechnetate scintiphotos of rat brains: (a) normal, (b) abnormal. The midline is indicated and increased activity is evident over the right cerebral hemisphere.
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