EFFECTS OF HYPOTHERMIA ON LOCAL BLOOD FLOW AND METABOLISM DURING CEREBRAL ISCHEMIA AND HYPOXIA*

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The recent use of hypothermia to prevent anoxia during temporary occlusion of cerebral blood vessels allows a more satisfactory approach to many neurosurgical procedures, particularly in cases of intracranial aneurysms, cerebrovascular malformations and vascular tumors.\(^2,3,9–11\) It is possible that, with a better understanding of its mechanism, hypothermia may have wider therapeutic application in the treatment of cerebral ischemia, hypoxia, trauma and increased intracranial pressure.

We wish to report here polarographic changes in oxygen tension of cerebral cortex and brain stem resulting from temporary respiratory anoxia before and after hypothermia. In addition, clinical observations have been made which give information concerning the functional state and metabolism of the cerebral neurones during hypothermia. Observations have been made on 7 cats and 3 monkeys (Macacus mulatta). Some preliminary observations on human cerebral cortex are included.

METHODS

a) Experimental Animals. Concurrent records have been made of the local oxygen availability in several small areas of cerebral cortex and brain stem by the modification of the polarographic method described in earlier studies.\(^13–15\) A silver-silver chloride anode is used in the form of a silver wire coated with silver chloride. The active electrode (cathode) consisted of finely tapered and exposed tips of 0.01-in. platinum wires insulated with Teflon. The exposed point is 1 mm. in length, tapering to a point. The principle of the method requires a potential of 0.6 V. supplied to the anode by a potentiometer. The platinum electrode is connected to the negative pole of the potentiometer through a resistance of 1.2 million ohms. On either side of this resistance, leads are taken to the input of a vacuum-tube micro-ammeter. The output of this instrument is recorded on bromide paper with a kymographic camera. Changes in cortical temperature are measured by a calibrated microglass thermistor bead used as a sensitive resistance thermometer.\(^13,14\)

Concurrent records were made of the cortical temperature, rectal and axillary

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temperatures, the cortical pH, electroencephalogram and steady potential, together with the blood pressure, electrocardiogram and respirations. In some experiments the intracranial pressure was also recorded with a strain gage screwed into a trephine hole in the skull. The technique of recording these parameters in situ has been described previously.\textsuperscript{13,14}

In some experiments the corneal, pinna, tendon and pupillary light reflexes were tested at various temperatures. The cortical stimulation threshold was also measured before and after hypothermia, using a Grass stimulator model S4B.

The animals were anesthetized with Nembutal, 0.5 mg. per kg. of body weight, and, in several instances, chlorpromazine, 2 mg. per kg., was also given. Recordings were made in the steady state at normal body temperature (35\textdegree{}–37\textdegree{}C.). Observations were then made of the effect of brief occlusion of each carotid artery for measured periods of time. In some experiments the middle cerebral artery was occluded. Occlusion was produced by light traction on silk ligatures previously passed around these vessels. The effects of brief breathing of nitrogen and carbon monoxide were recorded, also the effects of breathing oxygen and 7 per cent CO\textsubscript{2} and oxygen mixtures.

The body temperature was then lowered by partially immersing the animal in an ice-water bath and the above observations were repeated for purposes of comparison at different body temperatures.

Measurements were also made of the diameter of cortical arteries and veins with a microscope at various temperatures, using techniques which will be described in a later communication.\textsuperscript{14} In 5 animals the brains were immediately removed in the hypothermic state, fixed in 10 per cent formalin and stained with the Nissl and the benzidine methods.\textsuperscript{6}

b) Studies in Man. In the neurosurgical operating room the principal observations noted in the cat and monkey have been confirmed in man. For example, polarographic records were made during the course of an operation for excision of an arteriovenous malformation of the frontoparietal cortex in a patient who had suffered from repeated episodes of subarachnoid and intracerebral bleeding. Premedication consisted of 50 mg. each of chlorpromazine, Phenergan and Demerol. Anesthesia was maintained with endotracheal administration of a mixture of oxygen, nitrous oxide and ether. The body temperature was lowered in the operating room with a refrigeration blanket. Axillary, cortical and rectal temperatures were recorded together with the blood pressure, electrocardiogram and electroencephalogram. The effects of occlusion of the common carotid artery on local availability of cortical oxygen and electroencephalogram were compared at temperatures of 37\textdegree{}C. and 29.8\textdegree{}C. The artery was occluded in the neck for periods of 50 sec. by means of a Blalock clamp.

In the operating room the polarograph anode and three platinum electrodes were mounted on a Grass cortical electrode holder.* The electrodes and electropolarograph were constructed along lines similar to those used in the animal experiments. Teflon insulation of the electrodes permitted them to be autoclaved. The micro-ammeter readings were recorded by hand on graph paper at 4-sec. intervals. An adjustable microglass thermistor bead was also mounted on the electrode holder so that measurements could be made of any small changes in cortical temperature.\textsuperscript{13} Cortical electrograms were made with a Grass Electroencephalograph Model III-D.

\textsuperscript{* Grass Instrument Company, Quincy, Massachusetts.