Monoventricular Hypothermic Perfusion
Cortical Electric Responses to Analeptic Agents*

MAURICE COSTAL, M.D., JAMES AUSMAN, M.D., SABBO WOLDRING, M.D.,
AND GUY OWENS, M.D.
Department of Neurosurgery, Roswell Park Memorial Institute, Buffalo, New York

In a recent report from this laboratory, the effects of hypothermic perfusion of the cerebral ventricular system were described. It was reported that diminished cortical electric activity during the cooling period was similar to that observed during total-body hypothermia. However, it seemed likely that more detailed information about cortical electric responses might be obtained by limiting perfusion to selective cerebral ventricular segments, thereby cooling the related brain areas surrounding the perfused ventricles. By so doing, further information might be obtained regarding the reticular activating system. Since analeptic agents are needed in this type of exploration, it was our purpose to compare the seizure-producing effects of these agents during cerebral hypothermia by the ventricular-perfusion method with the effects observed by Owens in 1958 during whole-body hypothermia. He reported prolonged seizure activity in experimental animals following intravenous administration of various analeptic agents during total-body cooling.

Methods

Thirty adult mongrel dogs were anesthetized (Nembutal 30 mg./kg.), intubated, and placed in a head holder. Polyethylene cannulae were placed in 15 dogs in a lateral ventricle through threaded fittings so that a closed entrance-and-exit system was established. In an additional 15 animals, the 3rd ventricle was cannulated through the corpus callosum (to be used as a route of entrance) and a catheter was inserted in the cisterna magna (for a pathway of exit). Continuous monitoring of electroencephalogram, blood pressure, electrocardiogram and temperatures of brain, esophagus, and rectum was employed. Normal blood pressures were maintained at all times. Brain temperatures were measured bilaterally from frontal, temporal, and occipital areas at a depth of 1 cm. Cerebellar temperatures were measured through the vermis just above the roof of the 4th ventricle. Entrance-and-exit temperatures of the perfusate also were recorded. A cooling, circulating device described previously was then employed. Rates of flow ranged between 2 and 20 cc./min. These rates of flow were reached by monitoring intraventricular pressures which varied from -5 to +5 cm. H2O at the entrance and from -10 to -15 cm. H2O at the exit. The vacuum effect created by maintaining the pressure at exit lower than the pressure at entrance served mainly to prevent distention of the ventricular wall and electroencephalographic spike activity by intraventricular pressures above normal. Metrazol, strychnine, and Megimide were administered intravenously in amounts sufficient to produce cortico-electric spike and/or seizure responses under normothermic conditions. The same quantities of the drug then were given during hypothermic ventricular perfusion. Diodrast was given intra-arterially following cannulation of the internal carotid arteries on one or both sides. The animals were sacrificed at the end of the procedure. No pathologic studies were performed.

Results

Unilateral ventricular perfusion with initial temperatures of perfusate on the order of 5°–20°C. was associated with decreased frequency and amplitude of electroencephalographic waves on the perfused side. Seizure responses to administered drugs (intravenous Megimide, strychnine, Metrazol, and intra-arterial Diodrast) were absent on the cooled side, but appeared in the noncooled cortex. Rapid rewarming often was accompanied by the appearance of cortical dysrhythmia in the perfused hemisphere. Fig. 1 demonstrates these observations following the use of Megimide.

On cooling of the 3rd and 4th ventricles to intraventricular temperatures ranging between 5° and 15°C., an immediate reduction

Received for publication January 23, 1963.

* Supported in part by United Health Foundation of Western New York.
of cortico-electric activity was observed. With rewarming, return of the base-line cortico-electric pattern was possible. Following administration of an analeptic agent at normal brain temperatures bilateral cortical burst activity was recorded. This seizure activity was abolished by resuming hypothermic 3rd and 4th ventricular perfusion to the ranges noted above although the cortical temperatures remained normal. Again, rewarming by perfusion allowed for the reappearance of seizure activity. Fig. 2 records the electroencephalographic response of one animal (Dog 20) to Metrazol before, during, and after hypothermic perfusion. It was possible to eliminate within 60 sec. cortical seizure responses and within 90 sec. all cortical electrical activity by cooling the structures adjacent to the 3rd and 4th ventricles. Simultaneously recorded cortical temperatures were maintained at ranges between 34°–36°C, while temperatures recorded in the roof of the 4th ventricle ranged around 15°–20°C. Systemic temperatures were not affected significantly by hypothermic perfusion, unless the cooling was prolonged for periods of several hours. Electrocardiographic and respiratory alterations consisting of diminished cardiac and respiratory rates were observed; however, the blood pressure remained unchanged during the local hypothermia.

Discussion

Our work indicates that cooling of the 3rd and 4th ventricles to temperatures of 5°–15°C abolishes the cortico-electric activity. From the low cerebellar temperatures recorded, it can be assumed that similar reductions in temperature were effected in brain areas surrounding the perfused ventricles.

![Fig. 1. Electroencephalographic record from dog whose left cerebral ventricle was perfused (B) with hypothermic normal saline. At C the effects on the electroencephalogram of Megimide are recorded. Right-sided seizure activity was quite apparent in contrast to the perfused side. At D, the bilateral seizure activity is recorded after raising the temperature of the ventricular perfusate.](image)