Cerebrospinal Fluid Production During Temperature Stress and Feeding in the Conscious Monkey[1]

The rate of production of cerebrospinal fluid (CSF) depends upon several important factors, two of which are intracerebral blood pressure and the hydrostatic pressure within the ventricular lumen[2]. Although the rate of formation of CSF is relatively low in terms of the capacity of the ventricular system[3], we have found that the rate of elaboration of the fluid in the monkey will change significantly if the physiological state of this primate is altered.

Six male rhesus monkeys, weighing 5–7 kg, were acclimated to special primate restraining chairs equipped with feeding and watering systems and constructed so that the ambient temperature of the chair chamber could be varied rapidly. Each animal was implanted under rigid aseptic conditions with an 18 gauge, chronic intraventricular cannula placed on mid-line in the anterior portion of the 3rd cerebral ventricle rostral to the massa intermedia. The cannula was positioned stereotaxically and held in place by cranioplast cement according to procedures described previously[4]. So that blood temperature could be monitored continuously, a thermistor bead was inserted against the sagittal sinus about 1 cm caudal to the cannula.

Following post-operative recovery, the ventricle of the monkey was tapped, and CSF flowed through a PE-50 drain tube positioned so that the end was 3 cm below the level of the 3rd ventricle. A calibrated 1 ml reservoir was used to collect the CSF, and volume measures were taken at 5 min intervals throughout the period of CSF drainage. Usually, 40–50 min base-line, flow-rate measurements (i.e., 8–10 samples) were taken before the experimental procedure began.

To cool the monkey, dry ice was placed in the chair chamber and after 10 min the temperature dropped to $-5°$ to $-10\,°C$. To heat the monkey, a stream of warm air was blown into the chair chamber until a maximum temperature of 50–55 °C was reached. In the feeding experiments, the monkey was simply given its normal morning food ration of biscuits following the base-line CSF flow. During the cooling, heating or feeding experiments, 10–12 samples were obtained, and following the termination of each of the conditions, the flow rate measurements were continued for an additional 50–60 min. As is shown in the Table, the mean CSF production rate decreased substantially when the monkeys were cooled, heated, or fed. In each case, the flow rate declined to almost less than half of that of the base-line rate. The post-experimental CSF flow rate rebounded significantly and in the case of the feeding experiment, returned virtually to the same level as the base-line production. The flow rate in the control non-altered state simply showed a slight decrease in overall mean production during consecutive 5 min intervals.

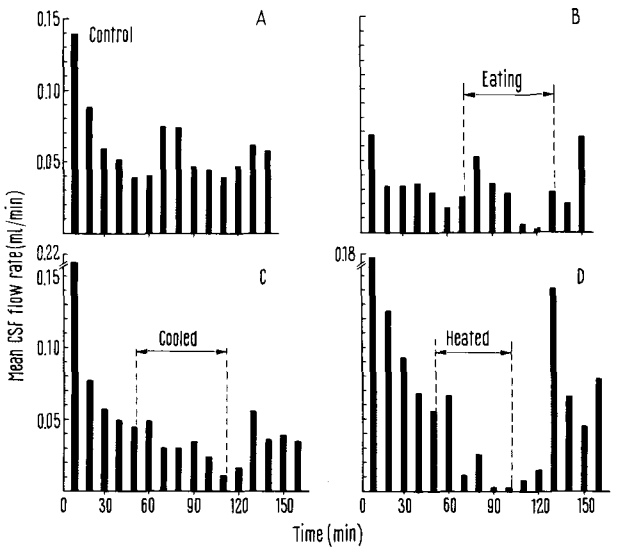
The Figure illustrates representative experiments for 4 monkeys under 4 conditions: control (A); eating (B); cooling (C); and heating (D). In these experiments, the reduction in CSF flow rate (mean ml/min) is clearly seen. Following cooling or heating, the recovery of the normal CSF production did not occur until usually 30 min after exposure to the temperature stress was terminated. This flow rate recovery interval is directly correlated with the time required for the restoration of the monkey's normal thermoregulatory responses after being heated or cooled. In the cooling experiment, the animal continued to shiver for 30 min following removal of the ice; vasodilatation and drowsiness continued in the heated monkey for approximately the same amount of time, after heating was discontinued.

The high initial output of CSF (see Figure) was due to the release of fluid pressure at the level of the 3rd ventricle. Because of the interrelationship between pressure and flow rate[5], these results are particularly remarkable because the decline in CSF production occurred independent of the loss of pressure. In fact, alterations in CSF flow were produced by feeding, cooling or heating even though the fluid pressure within the third ventricle was virtually zero because of the position of the brain tube.

Of particular importance is the fact that CSF elaboration decreased even when the functional states of the

Mean cerebrospinal fluid (CSF) production rates (ml/min) in conscious rhesus monkeys during body cooling, heating or while the animal was eating its morning meal. Each period represents flow rate for 40–60 min

	Baseline rate	During condition	Post rate
Cooling	0.064	0.033	0.039
Heating	0.063	0.029	0.043
Feeding	0.041	0.023	0.046
Control	0.066	0.056	0.052



The mean rate of cerebrospinal fluid (CSF) production as measured continuously at the level of the 3rd ventricle in unanesthetized monkeys during 4 conditions: control (A); feeding (B); cooling (C); and heat exposure (D). Each solid bar represents the volume of CSF collected during a 10 min interval.

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monkey were totally opposite. When heated, the animal exhibited vasodilatation and other peripheral heat loss signs, whereas cooling produced vasoconstriction, vigorous shivering and apparent agitation. Because feeding produced a similar decline in CSF flow rate, it is difficult to explain this finding on the basis of a functionally nonspecific stress due to the profound alteration in ambient temperature. It is possible that although the elaboration of CSF from the choroid plexus might have remained essentially constant, the secretion of extracellular fluid into the ventricular lumen[6] could have diminished significantly. If the ventricular lumen does act as a cellular 'sink'[7], then the physiological changes in some way could affect the release, exchange and concentration of electrolytes or other constituents of extracellular fluid. In any event, CSF flow rate at other levels of the primate's ventricles, including the lateral and 4th ventricles must, be ascertained for a more complete understanding of the fluid dynamics of the cerebral ventricular system.

Zusammenfassung. Das Flüssigkeitsvolumen des Ventrikelliquors wurde in Affen (im 3. Ventrikel kanuliert) gemessen. Die Produktion von Ventrikelliquor verringerte sich stark während 40–50 min, und zwar bei Nahrungsaufnahme, bei Erwärmung oder Abkühlung. Hernach Rückkehr des normalen Liquorvolumens.

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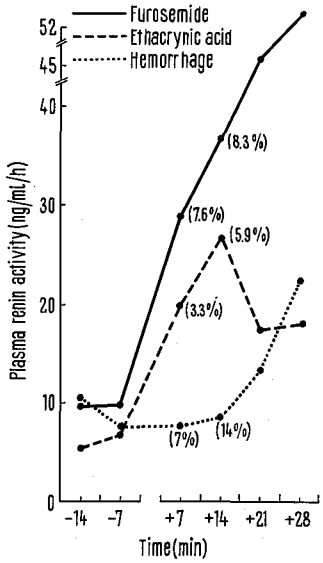
Re-Evaluation of the Role of Hypovolemia on the Release of Renin[1]

It is generally accepted that reduction of blood volume increases the release of renin[2]. It was considered of interest to study the variations of plasma renin activity (PRA) induced by blood volume reductions of similar importance but of different origins. 22 male rabbits weighing 2650 ± 150 g were anesthetized with sodium ethylmethylbutyl barbiturate (mebubarbital, Abbott 50 mg/kg, i.v.), tracheotomized, mechanically ventilated, and placed on a heating table. In a first set of 16 rabbits, reduction of blood volume was induced by i.v. injection of ethacrynic acid (Edecrin, Merck, Sharp and Dohme; 10 mg/kg, 7 rabbits) or of furosemide (Lasilix, Höchst; 10 mg/kg, 9 rabbits); these rabbits were hydrated by i.v. infusion of isotonic saline solution, given at the rate of 0.35 ml/min during the 45 min preceding the experiment. In a second set of 6 rabbits, the reduction of blood volume was accomplished by a slow arterial bleeding. In all experiments, 2 basal periods were followed by 4 experimental periods, each period being of 15 min duration. Determinations of inulin, sodium excretion, plasma volume, arterial blood pressure, and PRA were performed as already described elsewhere[3]. Central venous pressure was measured through a catheter inserted in the external jugular vein, the tip of the catheter being in the superior vena cava. Heart rate was estimated during the recording of pulse pressure with a strain gauge manometer (Telco, E.D. 26).

Results and discussion. As shown in Table I and in the Figure, ethacrynic acid significantly increased PRA, the increase being obvious in the 7th min following the injection (mid-point of the first experimental period); plasma volume was reduced by 3.3% in the first, and by 5.9% in the second experimental period. The increase of PRA observed after furosemide injection was greater than that observed after ethacrynic acid; the reduction of plasma volume seen in the first experimental period is 7%, and 8.3% in the second one. As indicated in Table II, the rate of arterial bleeding performed in the second experiment was adjusted by a screw placed on the arterial catheter so that the reduction of plasma volume was 7% for each experimental period; PRA measured on an aliquot fraction of arterial blood sampled at the mid-point of each period did not vary significantly during the 2 first experimental periods. The increase of PRA observed in the 2 last periods was significant, but inferior to that observed in the diuretic experiments (Figure). These results demonstrate that blood volume reduction



Variations of mean plasma renin activity after ethacrynic acid, furosemide and after hemorrhage. The percentage of mean plasma volume reductions observed in each experiment are indicated in brackets.

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