Short communications

Effect on body temperature in dogs of perfusion of cerebral ventricles with artificial CSF deficient in calcium or containing excess of sodium or calcium

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In anaesthetized dogs at room temperatures of 28–33° C, the cerebral ventricles were perfused with artificial CSF from the left lateral ventricular to the aqueductal cannulae. The animals' temperatures were recorded from the rectum. Addition of Ca^{++} in excess to the artificial CSF perfusing the ventricles produced hyperthermia and addition of Na^{+} in excess produced hypothermia. Perfusion with medium deficient in Ca^{++} and containing sodium edetate produced hypothermia. The temperature effects of Na^{+} or Ca^{++} in excess were mutually antagonistic.

In cats, rabbits and monkeys perfusion of the cerebral ventricles with a physiological solution containing excess of Na^{+} or Ca^{++} produces hyperthermia and hypothermia respectively, and perfusion with physiological solution devoid of Ca^{++} produces hyperthermia (Feldberg, Myers & Veale, 1970; Feldberg & Saxena, 1970; Myers & Yaksh, 1971).

In our laboratory, during an investigation in dogs of the role of calcium in mediating noradrenaline release which follows the intraventricular injection of γ-aminobutyric acid, the cerebral ventricles were perfused with artificial CSF containing sodium edetate and lacking in calcium (Dhumal, Gulati, Raghunath & Sivaramakrishna, 1974). This resulted in marked hypothermia. In view of the recent reports cited above, this was unexpected. The present communication describes the effects of perfusion of dog cerebral ventricles with artificial CSF deficient in calcium or containing excess of sodium or calcium.

Methods.—The experiments were performed in mongrel dogs of either sex weighing 6–10 kg and anaesthetized with pentobarbitone sodium (30 mg/kg i.v.). The details of perfusion of the cerebral ventricles from ventricular to aqueductal cannulae and of recording rectal temperature are reported elsewhere (Dhumal *et al.*, 1974). Unless otherwise specified, the room temperature ranged between 28–33° C. The ventricles were perfused with the artificial CSF of Merlis (1940) at a rate of 0·4–0·5 ml/minute. The NaCl and $CaCl_2$ concentrations in this solution were 138·4 mM and 1·25 mM, respectively. To examine the effect of increasing the concentration of Na^{+} or Ca^{++} selectively, these ions were added to the artificial CSF in the form of their chloride salts. The effect of calcium deprivation was studied by removing calcium from the artificial CSF and by adding to it sodium edetate (B.D.H.) (1 mM) during the first hour of perfusion. A solution of sucrose, double the isotonic concentration (18·5%), was perfused into the ventricles as a control for the possible effects of hypertonicity.

Results.—*Calcium excess.* Perfusion of ventricles with artificial CSF containing 11·8 mM Ca^{++} in excess had no effect on temperature (1 experiment). Solutions containing 23·9 mM and 47·8 mM Ca^{++} in excess produced rises in temperature. The rise with 23·9 mM Ca^{++} in excess (2 experiments) ranged between 1·0–1·5° C and began within 10 min of the start of perfusion, reached a peak within 20–100 min and was sustained at this level during the remainder of the perfusion (Figure 1a). The rise with 47·8 mM Ca^{++} in excess (1 experiment) started within 40 min, reached a peak in 80 min and was maintained at this level during the rest of the perfusion. Hyperthermia was associated with shivering. Solutions containing 105 mM Ca^{++} in excess (2 experiments) produced hypothermia (0·5° C) and the animals died within 60–120 min of starting the perfusion.

At a room temperature of 21° C, the solution containing 23·9 mM Ca^{++} in excess produced hypothermia beginning at 3 min and reaching a peak (2·5° C) at 32 min after the start of the perfusion (1 experiment).

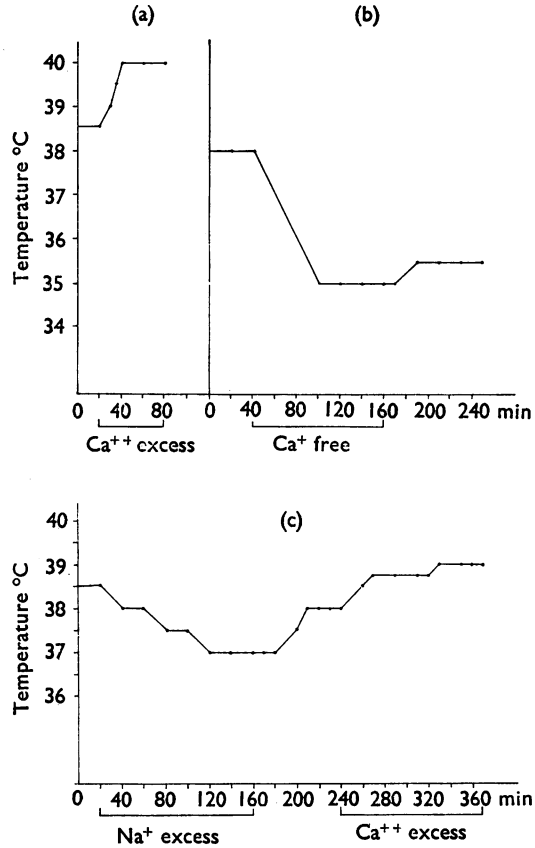

FIG. 1. Records from dogs (under pentobarbitone sodium (30 mg/kg, i.v.) anaesthesia) of rectal temperature during perfusion of cerebral ventricles, from left lateral ventricular to aqueductal cannulae, with artificial CSF (room temperature, 28–33° C). The bracket in (a) indicates when the ventricles were perfused with artificial CSF containing Ca^{++} in excess (23·9 mM). The bracket in (b) indicates when the ventricles were perfused with Ca^{++}-free artificial CSF; the fluid also contained sodium edetate (1 mM) during the first hour of perfusion. In (c) the first bracket indicates when the ventricles were perfused with artificial CSF containing Na^{+} in excess (34 mM) and the second bracket indicates when the ventricles were perfused with artificial CSF containing Ca^{++} in excess (23·9 mM). The records shown in the three panels were obtained from single but different dogs.

Calcium deficiency. In four experiments, the ventricles were perfused with calcium-free artificial CSF containing sodium edetate for one hour followed by perfusion with calcium-free artificial CSF. This produced a fall in temperature (1·5–4·0° C) starting within 10–20 min of perfusion, reaching a peak within 40–60 min and lasting for the remainder of the perfusion with calcium-deficient solution (Figure 1b). Figure 1b also shows that replacement of calcium-deficient solution by normal artificial CSF resulted in a partial restoration of temperature. During perfusion with sodium edetate there was profuse salivation, lacrimation, generalized twitching of muscles, and tremors. After sodium edetate was omitted from the solution, the associated symptoms disappeared.

The calcium-deficient solution containing sodium edetate was perfused intraventricularly in two dogs at a room temperature of 21° C. In one dog, after an initial fall in temperature (0·5° C) at the end of 5 min, the temperature started rising, a maximum effect (2·0° C above the control) occurring at the end of 25 minutes. In the other dog, the temperature decreased by 0·5° C at the end of 5 min, remained at this level for another 10 min and then started rising, reaching maximum (2·5° C above the control) at the end of the next 10 minutes.

Physiological saline. During perfusion of the ventricles with a 0·9% w/v NaCl solution, there was a fall in temperature (0·5–2·5° C, 5 experiments). The hypothermia began within 20–60 min of the start of perfusion, reached a maximum within 45–140 min and persisted during the subsequent period of perfusion. The hypothermia was associated with twitching of muscles which began in the lower extremities and later became generalized.

Sodium excess. Perfusion of the ventricles with artificial CSF containing excess of Na^+ (34 mM) resulted in hypothermia (1·5–2·5° C ; 3 experiments) starting within 20 min, reaching a peak within 100–120 min and remaining at this level as long as the perfusion lasted (Figure 1c).

A solution of sucrose, double the isotonic concentration was perfused for 80 min and had no effect on rectal temperature.

In one experiment, 40 min after attaining peak hypothermia with a solution containing excess of Na^+ (34 mM), the ventricles were perfused with artificial CSF for 60 minutes. This produced a rise in temperature of 1° C. The ventricles were then perfused with artificial CSF containing excess of Ca^{++} (23·9 mM). There was a further 1° C rise in temperature (Figure 1c). Hyperthermia induced with calcium excess (23·9 mM) could similarly be reversed by sodium excess (34 mM ; 1 experiment).

Discussion.—At ambient temperatures ranging from 28–33° C, perfusion of the dog cerebral ventricles with artificial CSF, deficient in Ca^{++} or containing excess of Ca^{++} or Na^+, produced effects which are the reverse of those reported previously for cats, rabbits and monkeys (Feldberg *et al.*, 1970 ; Feldberg & Saxena, 1970 ; Myers & Yaksh, 1971). At an ambient temperature of 21° C, Ca^{++} in excess or Ca^{++} lack produced effects which are in accord with observations reported in the literature for ambient temperatures of 22–25° C (Myers & Yaksh, 1971). Perfusion of cat cerebral ventricles with normal saline produces hyperthermia which is due to Ca^{++} lack (Feldberg *et al.*, 1970). In the present study perfusion with normal saline, or artificial CSF with Na^+ in excess or deficient in Ca^{++}, was associated with hypothermia. These opposite results could be explained by the probable differences in ambient temperature between different laboratories. A change in Ca^{++} concentration acting through a posterior hypothalamic site (Myers & Veale, 1971 ; Myers & Yaksh, 1971) might be expected to produce opposite effects on rectal temperature depending upon whether the animals are actively attempting to lose heat or actively producing or conserving heat.

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