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Title : CEREBRAL PROTECTIVE EFFECT OF LOW GRADE HYPOTHERMIA

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Introduction. Induced hypothermia is a well-established method of preventing hypoxic brain injury. The mechanism is not completely understood, but has been related to the reduced rates of biochemical reactions and hence of oxygen demand. Reduction of body temperature to 32°C in rats has been shown to abolish virtually all the cerebral metabolic changes induced by severe hypoxia, while an equi-depressant dose of barbiturates only has a minimal effect.[1] However, in clinical practice the use of this degree of hypothermia is impractical. Spontaneous decrease of 2-3°C in body temperature frequently occurs in anesthetized patients, who are not actively protected against heat loss. To study the possible cerebral protective effect of low grade hypothermia we used an hypoxic-oligemic experimental model, that previously has been shown to produce metabolic and histopathological signs of neuronal damage in the normothermic animal.[2-3]

Methods. Male Wistar rats were mechanically ventilated with 70% N_2O in O_2 via a tracheostomy. Blood pressure and temperature were recorded and arterial blood gases were sampled intermittently. One carotid artery was dissected free. Following a stabilization period, during which the rectal temperature was either kept at 37°C or allowed to fall to 36° or 34°C, F_{IO_2} was reduced and the carotid artery clamped. The animals were then maintained on 5% O_2, 25%N_2 in N_2O to give a p_aO_2 of 20-30 torr (corrected for temperature) for 20 minutes. A small amount of CO_2 was added to prevent an excessive fall in $PaCO_2$. An additional group was kept normoxic and normothermic, but otherwise identically treated. The brains were then frozen *in situ* with liquid N_2 for subsequent analysis of cortical concentrations of ATP, phosphocreatine (PCr) and lactate (La). Protection was evaluated by the preventive effects of hypothermia on the changes in metabolite levels produced. Student's t-test was used for statistical evaluation and p 0.05 was considered a significant difference.

Results. The 34° group had significantly higher arterial blood pressure, PO_2 and pH than the normothermic hypoxic group, while only pH was higher in the 36° group. Cerebral cortical metabolite concentrations from the hemisphere ipsilateral to the ligated carotid artery are given in table. The ATP concentrations in the hypothermic groups are higher than the normothermic hypoxic value, and the same as that of the normoxic animals. In the hypoxic groups the PCr increases and lactate decreases as the temperature falls, but the concentrations are still different from the normoxic values.

Discussion. This experimental model with a comparable degree of hypoxia causes energy failure (and neuronal death) in the hemisphere ipsilateral to the ligated carotid artery in about 70% of normothermic animals.[3] These results were duplicated in the present study. However, with a slight decrease in body temperature, the energy balance of the brain was maintained and the metabolic signs of tissue hypoxia decreased with progressive hypothermia.

It can be concluded that, in this model, low grade hypothermia has a significant effect on the preservation of the cerebral energy balance which could be of value in the clinical practice.

References.

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Hypoxia	n	ATP	PCr	La
37°C	10	1.21 ±0.32	1.27 ±0.53	25.7 ±3.7
36°C	8	2.44[x] ±0.05	2.08 ±0.28	16.1[x] ±1.0
34°C	12	2.42[x] ±0.03	2.81[x] ±0.13	10.7[x] ±1.4
Normoxia 37°C	6	2.41[x] ±0.05	3.56[x] ±0.07	3.5[x] ±0.6

Values $um.g^{-1}$ S.E.M.

* p 0.05 Student's t-test