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Effect of drugs used in status-epilepticus on the potassium fluxes of cerebrospinal fluid in the conscious dog

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Zuckerman & Glazer (1968) demonstrated that localized high concentrations of potassium in the region of the inferior horn of the lateral ventricle could cause convulsions originating in the hippocampal system.

The potassium concentration in the cerebrospinal fluid (C.S.F.) is maintained within narrow limits independent of large alterations in plasma concentrations (Kemeny, Boldizsar & Pethes, 1961). The mechanisms whereby this is achieved have been investigated and characterized by ventriculo-cisternal perfusion techniques (Heisey, Held & Pappenheimer, 1962; Cserr, 1965; Katzman, Graziani & Ginsberg, 1968; Bradbury & Stulcova, 1970). In the experiments described here, drugs useful in the treatment of status epilepticus were investigated for their effect on the potassium fluxes of C.S.F.

Ventriculo-cisternal perfusions were performed in adult beagle dogs with chronically implanted guide tubes, using inulin and ^{42}K contained in a sterile salt solution which was comparable to dog C.S.F. The perfusion fluid was pumped into one lateral ventricle and out of the cisterna magna at a rate of 0·3 ml/min using two equally calibrated modules of a multichannel pump. The experiments were carried out while the animals were conscious and free moving, and pressure alteration within the cerebrospinal fluid system still appeared to be governed by normal physiological variables such as head movement, respiration and blood pressure. The effluent from the perfusion system was collected by means of a fraction collector and the samples were subsequently analysed for inulin, ^{42}K and total potassium. This data, in conjunction with the results of comparable analyses on the inflowing fluid, allowed calculation of bulk flow of C.S.F. from the system and the appropriately corrected rate constants (meq/min) governing the influx and efflux of C.S.F. potassium. All these parameters could thus be assessed on a continuous basis throughout the experiments.

When a stable base line of control values had been established after a period of at least 90 min, the drug under study was administered by either intravenous or intramuscular injection. Of the drugs investigated, the barbiturate anaesthetics, sodium thiopentone and sodium pentobarbitone, when given in doses sufficient to achieve light anaesthesia, had the most striking effects, producing highly significant decreases of up to 40% in both potassium rate constants. Phenytoin and diazepam both produced significant decreases of between 6–14% in efflux and influx rates of C.S.F. potassium in subanaesthetic doses while paraldehyde, even when given in sufficiently high doses to produce light anaesthesia, had no significant effect on potassium fluxes.

These preliminary results would seem to indicate that while the potassium fluxes of

C.S.F. can be reduced by drugs with anaesthetic or anticonvulsant action, these states can be induced by paraldehyde without any significant alteration in C.S.F. potassium.

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Can drugs replace hypoxic drive in respiratory depression?

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The respiratory control of cats deeply anaesthetized with pentobarbitone or with chloralose depends on hypoxic drive from the arterial chemoreceptors. Changing their inspired gas from air to pure oxygen will severely depress or even arrest the respiratory movements. We have compared the effectiveness of suberyl dicholine diiodide (SDC) with that of nikethamide in this situation. SDC stimulates the arterial chemoreceptors, and does not act centrally (Mikhel'son, Rybovlev, Gorelik & Dardymov, 1957).

Five cats were anaesthetized with chloralose. The anaesthetic solution was slowly infused intravenously until their P_{a,CO_2}, while breathing air, rose to between 55 and 60 torr (about twice the level for unanaesthetized cats). SDC (50 μg/min) and nikethamide (12·5 mg/min) were infused in turn for periods of 5 min, allowing 30 min for recovery after each drug infusion. The results are shown in Table 1.

TABLE 1. *Mean results from five cats (female, 2–3 kg) under chloralose*

	Breathing air			Breathing 100% oxygen		
	Control	SDC	Nikethamide	Control	SDC	Nikethamide
$\dot{V}$ ml/min	436±74	577±84	674±95	273±46	394±46	376±79
Tidal volume ml	53±6	69±6	47±6	42±8	51±9	32±5
Respiratory rate breaths/min	8·5±1	8·5±1	14·1±1	7·4±2	8·9±2	12·9±2
P_{a,CO_2} torr	58±5	50±6	49±5	70±6	52±4	60±5

SDC infused at 50 μg/min and nikethamide at 12·5 mg/minute.

The results were analysed by paired t tests ($P<0{\cdot}01$ being taken as significant).

SDC increased ventilation ($\dot{V}$) by an effect on tidal volume, with no significant effect on respiratory rate. SDC was significantly more effective in lowering P_{a,CO_2} during oxygen breathing than during air breathing, although the increases in $\dot{V}$ were similar.

Nikethamide increased $\dot{V}$ by an effect on respiratory rate with no significant effect on tidal volume. Nikethamide was significantly less effective in increasing RMV during oxygen breathing than during air breathing.