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.

For a given increase in $\dot{V}$, SDC was more effective than nikethamide in lowering P_{a,CO_2}. This would be expected of a drug acting on tidal volume rather than respiratory rate.

The response to SDC was sustained during infusions lasting 30 minutes.

We conclude that SDC may have advantages over centrally acting drugs for the replacement of hypoxic drive, making it possible for pure oxygen to be breathed in respiratory depression.

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Evidence for an active uptake of noradrenaline in the guinea-pig isolated trachea

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Tracheae were incubated for 15 min in Krebs solution at 37·5°C containing ^{14}C-sorbitol (16 nmol/ml) or H^3-L-noradrenaline (50 or 6,400 pmol/ml.) After transfer to a washing solution which was changed at intervals over 60 min the tissue radioactivity showed a double exponential decay. The first decay corresponded with the loss from a rapidly exchanging compartment which was virtually cleared within 30 minutes. The second decay corresponded with the loss from a slowly exchanging compartment.

Tracheae were incubated for 3·75 or 7·5 min with H^3-L-noradrenaline (20–10,000 pmol/ml) and washed for 30 minutes. The concentration of radioactive material in the tissue was measured and used to estimate the initial velocity of uptake into the slowly exchanging compartment. This uptake was attributable to a saturable and a non-saturable mechanism. The saturable mechanism predominated at substrate concentrations of 20–500 pmol/ml, obeyed Michaelis-Menten kinetics and showed a K_m similar to that seen in other tissues ($0{\cdot}53 \times 10^{-6}$ M) but a very low V_{max} (70 (pmol/g)/min). The non-saturable mechanism predominated at substrate concentrations of 1,600 to 10,000 pmol/ml.

TABLE 1. *Effect of modifications of the incubation medium on the concentration of radioactive material in the trachea after exposure for 15 min to 50 pmol/ml H^3-L-noradrenaline and 30 min of washing*

Incubation medium	Concentration mean ± S.E.M. (pmol/g)	*n*	*P* Two-tailed
Krebs solution	65·0 ± 4·4	13	—
Low Na^+ solution (63 mEq/l)†	54·0 ± 4·1	10	≃0·1
Low Na^+ solution (25 mEq/l)†	30·0 ± 0·7	10	<0·001
K^+-free solution	47·5 ± 1·5	5	<0·005
Ouabain (10^{-4} M)	9·6 ± 0·6	5	<0·001
2,4-Dinitrophenol (10^{-3} M)	72·4 ± 5·9	5	>0·1
Bubbled with 95% N_2/5% CO_2	85·4 ± 13·9	4	>0·1
Glucose-free solution	60·4 ± 6·8	4	>0·1
Glucose-free solution bubbled with 95% N_2/5% CO_2	13·4 ± 1·0	4	<0·001
NaF (2×10^{-2} M)	25·3 ± 3·7	5	<0·001

Most preincubations were for 1 h but glucose-free conditions were maintained for 3 h and bubbling with N_2/CO_2 for 30 min: preincubation conditions were maintained during exposure to radioactive material and during washing. †Tonicity maintained with sucrose.