In conclusion, our electrophysiological data confirm the hypotheses based on psychophysical studies[2,3] in two ways: short-wavelength flashes, after switching off a yellow adaptation light, are 'seen' by the green cones rather than by the blue cones; and the inhibition of the blue cones can probably be located at the horizontal cell level.

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# Rapid effect of change in cerebrospinal fluid sodium concentration on salt appetite

THIRST can be evoked within 1–2 min by intracarotid infusion of hypertonic NaCl. In contrast, the onset of a specific appetite for sodium salts as a result of rapid loss of body sodium is slow. A parotid fistula in naive sheep can produce a significant Na deficit (200–700 mmol) within 1–3 d but a Na appetite usually develops after 2–5 d (ref. 1). With large urinary water and Na loss induced by frusemide, water intake occurs within an hour but Na appetite is delayed until 24 h (ref. 2). Moreover, in the Na-depleted sheep or goats, increase in the Na concentration of cerebral arterial blood by 10–30 mmol $l^{-1}$ by slow intracarotid infusion of 4 M NaCl for 7 min before or during presentation of Na solution does not reduce Na intake[3,4]. However, rapid intravenous infusion of significant amounts of isotonic and 2–4 M NaCl solutions in Na-deficient sheep substantially reduces Na appetite after 40–120 min[5,6]. In the rat, tissue fluid sequestration produced by subcutaneous polyethylene glycol injection causes water drinking within an hour, but onset of salt appetite is delayed by 6–10 h.[7] This delay also occurs in salt appetite produced by peritoneal dialysis[8], tourniquet release[9] and formalin injection[10,11]. New data indicate the powerful effects of the hormones involved in the reproductive process in inducing salt appetite. With pregnancy and lactation in Na-replete rabbits, avid salt appetite develops with a daily turnover of 50% or more of extracellular fluid (ECF) Na (ref. 12). This is caused by the combined action of oestradiol, cortisol, ACTH, prolactin and oxytocin[13]. ACTH seems to act directly on the brain[14]. Recent experimental data provide new information on the central nervous system control mechanism. Weisinger *et al.*[15] reported that in Na-depleted sheep, the systemic influx of hypertonic NaCl significantly reduced motivation for salt within 10–20 min. In the light of these data, we decided to evaluate the effect on Na appetite of increasing the cerebrospinal fluid (CSF) Na concentration or osmolality in Na-deficient sheep. We now report the first experiments to show that it is feasible to induce salt appetite within an hour or less by a physiological procedure.

Sheep with a parotid fistula were trained to bar press for 600 mM $NaHCO_3$ (15 ml per delivery = 9 mmol Na). They were allowed to bar press for 2 h daily (1200–1400 h), and thus had been deprived of Na for 22 h (deficit of 350–450 mmol) when the bar press was made available. On the day of the experiment, the infusion (1 ml $h^{-1}$) into a lateral brain ventricle was begun 1 h before and continued until the end of the 2-h bar press period. The composition of artificial CSF has been described previously[16,17]. CSF was sampled immediately after the end of infusion and analysed for [Na], [K] and osmolality. Data were analysed by a two-way analysis of variance with subsequent *t*-tests.

The results (Fig. 1, $n = 6$) show that within 10 min, intraventricular infusion of CSF [Na, 500 mM] caused a significant decrease in Na intake relative to infusion of CSF [Na, 150 mM]. When an infusion of 0.7 M mannitol–CSF[Na, 150 mM] was used to test the effect of increasing CSF osmolality without increasing CSF [Na], Na intake was almost doubled (Fig. 1). The increase relative to the CSF [Na, 150 mM] infusion was significant within 60 min and thereafter. In experiments where no i.v.t. infusion was given, the intake was similar to that with CSF [Na, 150 mM]. In five animals tested Na appetite was significantly increased within 60 min whether the mannitol infusion was begun 60, 15 or 0 min before the bar press period. No significant increase in water intake occurred. The effect of mannitol infusion on Na intake was the same whether water was concomitantly available to the animal or not.

Relative to infusion of CSF[Na, 150 mM], CSF (Na, 500 mM) increased CSF [Na] and therefore osmolality and decreased CSF [K]. Infusion of 0.7 M mannitol–CSF[Na, 150 mM] decreased CSF [Na] and [K], and increased CSF osmolality (Table 1).

The question of whether hypertonic mannitol would induce a Na appetite in Na-replete sheep was then examined. Naive Na-replete sheep with no known history of Na deficiency were given continuous access to water. Two-hour access to a bin containing 600 mM $NaHCO_3$ was given daily for a control period of 2–4 weeks. After two or three control infusions of artificial CSF[Na, 150 mM], which had no significant influence on $NaHCO_3$ intake (Fig. 2), the animals ($n = 5$) were infused on three consecutive occasions with 0.7 M mannitol–CSF[Na, 150 mM] (Fig. 2). This was usually done on three consecutive weeks. A 3-h infusion (1 ml $h^{-1}$) into a lateral brain ventricle was begun 1 h before access to Na.

Na intake increased in all animals on each of the three mannitol–CSF infusion days relative to the mean Na intake on the two days preceding the infusion ($P < 0.01$) in all experiments (Fig. 2). The following day intake was basal or below. A small increase in water intake occurred during the first hour of infusion on trial 3 ($P < 0.02$) but was never increased during the 2-h period when $NaHCO_3$ was available. In 18 other experiments with a cafeteria of Na, K and Mg salts the specificity of choice of Na salts was clearly shown (300–500 mmol increase,

**Table 1** Effect of a 3-h i.v.t. infusion of various solutions on CSF composition

| Condition | Na (mM) | K (mM) | Osmolality (Mosmol) |
|---|---|---|---|
| CSF[Na, 150 mM] | 151.2 ± 0.4 (25) | 2.84 ± 0.03 (25) | 297 ± 1.3 (15) |
| 0.7 M Mannitol CSF[Na, 150 mM] | 129.9 ± 1.4‡ (28) | 2.52 ± 0.02‡ (28) | 379 ± 7.8‡ (17) |
| 0.3 M Mannitol CSF[Na, 0 mM] | 127.0 ± 2.8‡ (5) | 2.72 ± 0.11 (5) | 319 ± 7.2‡ (5) |
| CSF[Na, 500 mM] | 177.2 ± 13.7‡ (4) | 2.47 ± 0.08‡ (4) | |

CSF was sampled from the ipsilateral ventricle immediately after the end of infusion. Statistical comparisons with CSF[Na, 150 mM] value by Student *t*-test (*$P < 0.05$, ‡$P < 0.01$; ‡$P < 0.001$). Numbers in parentheses indicate the number of animals tested.

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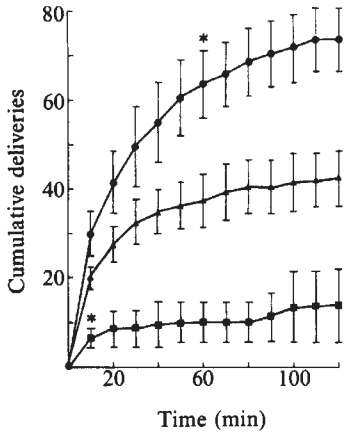


**Fig. 1** Effect of i.v.t. (lateral ventricular) infusions on bar pressing for $NaHCO_3$ solution. The sheep were Na depleted as a result of parotid salivary loss for 22 h. Cumulative mean (±s.e.m.) number of deliveries (15 ml 0.6 M $NaHCO_3$ = 9 mmol) over the 120-min period in the various conditions: ■, 3 h i.v.t. infusion (1 ml $hr^{-1}$) of artificial CSF [Na, 500 mM]; ▲, artificial CSF[Na, 150 mM]; ●, 0.7 M mannitol–artificial CSF[Na, 150 mM]. Infusion was started 1 h before the bar press period. $n = 6$ Na-deficient sheep. *Significantly different from CSF[Na, 150 mM] values, $P < 0.05$.

$P < 0.01$), although a small increase in $KHCO_3$ sometimes occurred.

With i.v.t. hypertonic mannitol the decrease in CSF [Na] and [K] was presumably due primarily to the osmotic withdrawal of water from the choroid plexus and surrounding brain tissue capillaries. A decrease of CSF [Na] with less water movement was obtained by infusion of 0.3 M mannitol–CSF[Na, 0 mM] ($n = 7$) (Table 1). The Na appetite induced was similar to that with 0.7 M mannitol–CSF[Na, 150 mM] (Fig. 2). No increase in water intake occurred.

The results of these experiments indicate that a change in the composition of CSF involving an increase or decrease in [Na] may rapidly alter salt appetite drive. A rapid induction, within 60 min or less, of a large Na appetite has been shown.

The induction of a Na appetite in the naive Na-replete sheep, augmentation in the moderately deplete animal, the demonstration by both voluntary intake and operant behaviour and the inhibition of appetite as a result of increase of CSF [Na] in the Na-deficient animal strengthen the inference that altered CSF [Na] affected the physiological control system. In all cases, the experimentally induced changes in CSF [Na] were in the physiological range. The absence of significant water drinking despite an increased osmotic pressure may be due to concurrent decrease of CSF [Na][17,18]. With i.v.t. CSF [Na, 500 mM] infusions, if water was available during the whole infusion, or in the period 0–120 min when Na $HCO_3$ was available, drinking of 1–2 l occurred.

The results are consonant with the suggestion by D.A.D. that reduction in intracellular [Na] of the hypothalamic nerve cells subserving Na appetite is the basic mechanism for the genesis of this specific drive[19]; however, further experiments are required to confirm this. Whether the time interval for CSF changes to induce behaviour is too short for a transcription mechanism is also a matter for further investigation. Intracellular ionic change could act at the level of translation[20]. A change in brain ECF [Na] may also have a direct effect on the membrane. The fact that the large salt appetite in the Na-replete animal during reproduction is generated by a sequence of steroid and peptide hormone actions[21], presumably by the same neural mechanisms which respond to body Na deficit, is consistent with the idea that a complex neurochemical mechanism underlies the genesis of salt appetite.

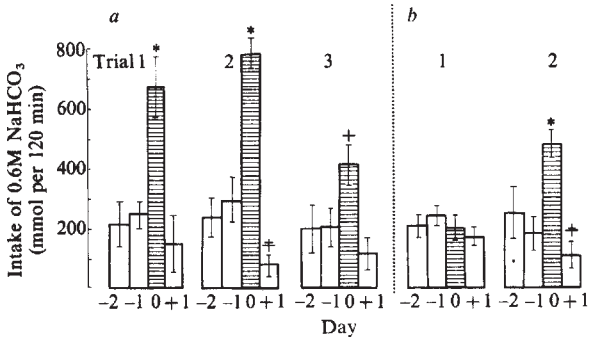


**Fig. 2** *a*, Effect of 3 h i.v.t. infusion (1 ml $h^{-1}$) of 0.7 M mannitol–artificial CSF[Na, 150 mM] on voluntary intake of 0.6 M $NaHCO_3$ by 5 Na-replete sheep. Infusion was started 1 h before the 2 h access period on day 0. No infusion on days −2, −1 or +1. Water was continuously available. The effect of infusion on Na intake on three trials on consecutive weeks is shown. *b*, Effect in the same conditions of infusion of artificial CSF[Na, 150 mM] (1), 23 experiments in 13 sheep, and 0.3 M mannitol–artificial CSF[Na, 0] (2), 7 sheep. *$P < 0.001$; †$< 0.01$; ‡$P < 0.02$.

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# Immunisation of guinea pigs and cattle against ticks

IXODID TICKS attach to the skin of their host and remain there for several days, engorging on blood and intermittently passing salivary secretions into the host[1]. Several species of Ixodid ticks transmit pathogenic microorganisms along with their saliva into the host, and tick-borne diseases are of great economic importance, particularly in cattle in subtropical and tropical areas[2]. The control of cattle ticks by chemical acaricides has become increasingly difficult due to the emergence of acaricide-resistant strains of ticks[3]. An apparently novel immunological method of tick control in guinea pigs and cattle is reported here. Hosts were immunised with antigens extracted from the gut and

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