stimulation. The problem has been re-examined using a modification of the cortical cup technique (Mitchell, 1963) since it seemed likely that previous failure was due to artifacts associated with the use of push–pull cannulae.

Adult rabbits were anaesthetized with urethane, the frontal cortex removed to facilitate the placement of bipolar stimulating electrodes on the olfactory tract, and both olfactory bulbs exposed. A Perspex cup (7 mm i.d.) containing 0·25 ml Krebs-phosphate solution at 37°C was then applied to both bulbs, and the system made leakproof by the infiltration of paraffin wax (M.P. 37°C) around the cup. Radioactive (±)-noradrenaline (7-^{3}H or methylene-^{14}C, 5 μCi) with either ^{14}C-urea (20 μCi) or ^{3}H-γ-aminobutyric acid (2,3-^{3}H, 5 μCi) (^{3}H–GABA) was then added to the cup fluid and left for 1 hour. Thereafter the Krebs solution contained metaraminol (10^{-5} M). The bulbs were washed twice, and successive 10 min samples taken for estimation of activity of the two differently labelled substances by liquid scintillation counting. The spontaneous and evoked electrical activity in the bulbs was monitored with a unipolar electrode inside the cup.

Initially there was a large spontaneous efflux of the labelled compounds which declined rapidly over 1·5 hours. Thereafter the radioactivity declined more slowly and stimulation studies were made in this latter period. Continuous stimulation of one medial olfactory tract (0·5 ms duration pulses, 6 mA, 15–25 Hz) or direct stimulation of the bulbs for periods of 7 min caused an increase in the efflux, attributable to labelled NA, to levels about 50% greater than in the preceding period. Characteristically these increases did not coincide with the period of stimulation, but followed immediately after. The neurally evoked release of ^{3}H–NA appeared to be calcium dependent and was not accompanied by an increase in the efflux of the marker substance ^{14}C-urea. It could be repeated 3 or 4 times within an experiment, and the size of the release was related to the intensity and rate of stimulation. In preliminary experiments the increased release of ^{14}C-NA, following stimulation of one olfactory tract, was invariably accompanied by an increased release of ^{3}H–GABA.

These results suggest that a neurally evoked specific release of labelled NA from the olfactory bulb can be achieved *in vivo*, and this technique may be of use in analysing the role of NA in synaptic inhibition in the olfactory bulb.

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Effects of an anticonvulsant, acetazolamide, on the sodium gradient and xylose uptake of cerebral cortex slices

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The kinetics of uptake of D-(+)-xylose by the non-raffinose compartment of guinea-pig cerebral cortex slices incubated in a bicarbonate medium suggest that xylose interacts with a membrane component (carrier) during its transport (Gilbert, 1966). The

concentration of xylose in the non-raffinose compartment exceeds that of the medium (1 mM) after incubation for 10 min and this accumulation against a concentration gradient depends upon the sodium concentration of the medium. Under these conditions a gradient of sodium ions from the raffinose to the non-raffinose compartment could be detected.

The uptake of xylose has been determined in a phosphate medium and not only was there no accumulation of xylose by the non-raffinose compartment but also no sodium gradient could be detected across the two compartments. These results suggest that the active transport of xylose in the bicarbonate medium may depend on asymmetries of the transport system due to interaction between the carrier and sodium ions. Of particular importance might be the effects of sodium ions upon the apparent dissociation of the carrier-xylose complex at the inner and outer edges of the membrane independently.

Acetazolamide can influence xylose uptake by the slices (Gilbert, Gray & Heaton, 1971). It has also been reported to increase the sodium gradient (Na_0/Na_i) in brain (Woodbury, Koch & Vernadakis, 1958). If the accumulation of xylose by cerebral cortex slices results from asymmetries induced by sodium ions then acetazolamide might be expected to increase the degree of accumulation. In fact, acetazolamide (20 μM) prevented the active transport of xylose and it also prevented xylose from equilibrating with the total slice water over a 15 min incubation period (medium xylose concentration 1 mM). However, determinations of the sodium contents of slices incubated in the bicarbonate medium showed that, in contrast to the observation of Woodbury, Koch & Vernadakis (1958), acetazolamide (20 μM) did not significantly alter the sodium gradient. Initial velocity studies of xylose uptake indicated that the drug altered both the apparent dissociation constant of the carrier-xylose complex and the maximal transport rate in a manner compatible with previous observations (Gilbert, Gray & Heaton, 1971) and with the inhibition of xylose uptake from a medium containing 1 mM xylose.

A high concentration of acetazolamide (200 μM) did not inhibit the active transport of xylose by the tissue but significantly increased the sodium gradient. These results are compatible with the concept that active xylose transport depends to some extent on the sodium gradient and further suggest that the membrane component involved in xylose transport has separate sites for interaction with xylose and sodium. Acetazolamide may interact with the sodium site effectively only at the high concentration whereas the sugar site may be sensitive to the low concentration and probably also to the high concentration of the drug.

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Possible role of dopamine-containing neurones in the behavioural effects of cocaine

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Cocaine and drugs of the imipramine group are believed to act on sympathetic postganglionic neurones through inhibition of the noradrenaline neuronal uptake