Using the technique of iontophoretic injection, the dose ratios, compared with dopamine, of N-methyldopamine, adrenaline and noradrenaline, were similar to those obtained by addition to the bath.

It is concluded that, in the neurones studied in this investigation, the receptor for dopamine resembles a true dopamine receptor rather than an α-adrenaline receptor.

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Dual effect of noradrenaline on incorporation of ^{32}P into phospholipids of rat brain

P. M. KEEN and J. M. SNEDDON*, *Department of Pharmacology, University of Bristol, Bristol BS8 1TD*

Noradrenaline (NA) is present in brain, where it possibly functions as a chemical transmitter or as a modifier of nervous function. Noradrenaline might change neuronal activity by an effect on membrane phospholipids ; to test this possibility we have investigated the effect of NA on the incorporation of ^{32}P into phospholipids of rat brain *in vitro*.

Rat brain stems were homogenized (10%w/v) in sucrose-Tris-EDTA (0.25 M–10 mM–0.5 mM, pH 7.4). The homogenate was centrifuged at 1,000 *g* for 10 min, the

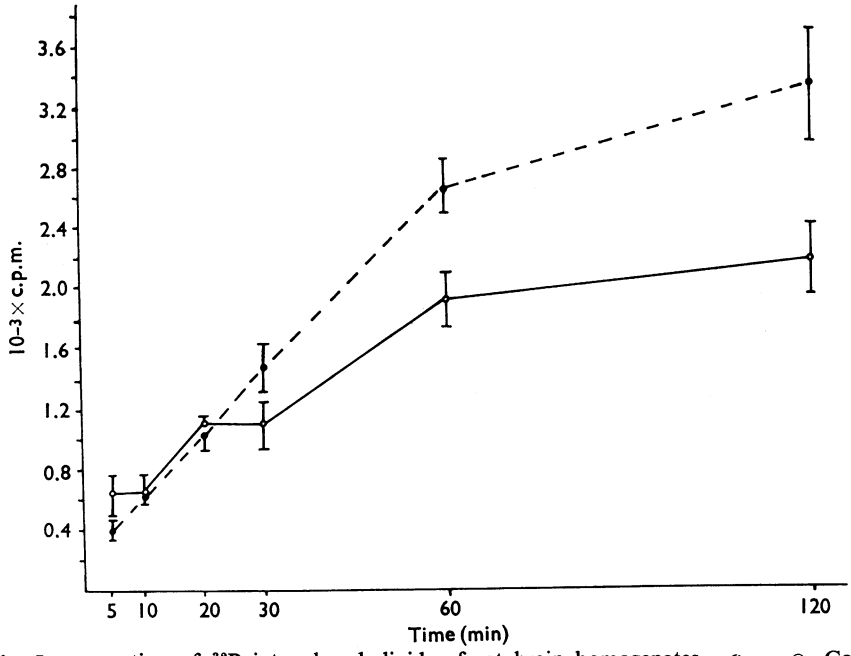

FIG. 1. Incorporation of ^{32}P into phospholipids of rat brain homogenates. ○——○, Control; ●- - - -●, 5×10^{-6} g/ml. (—)-noradrenaline bitartrate. Radioactivity expressed as ^{32}P incorporated into total phospholipids per mg homogenate protein. Vertical bars represent S.E. Means of five experiments.

pellet was discarded and the supernatant centrifuged at 100,000 *g* for 30 min. The final pellet was resuspended in Krebs-Henseleit bicarbonate incubation medium without phosphate and containing 1.24 $\times 10^{-4}$M EDTA, 5×10^{-5}M pargyline and 1.14×10^{-3}M ascorbic acid) to a final protein concentration of 3–5 mg/ml. Aliquots (3 ml.) of this suspension were incubated at 37° under O_2–CO_2 (95 : 5) with 25 μc [^{32}P] orthophosphate. Phospholipids were extracted by the method of Hokin & Hokin (1958) and the incorporation of ^{32}P was measured by liquid scintillation counting.

The effect of NA on ^{32}P incorporation is shown in Fig. 1. NA caused a significant decrease in the incorporation of ^{32}P at 5 min ($P<0.05$) and a significant increase at 30, 60 and 120 min ($P<0.001$). Thymoxamine, which blocks peripheral α-receptors (Birmingham & Szolcsanyi, 1965) inhibited the stimulatory effect of NA on ^{32}P incorporation at 4×10^{-5} g/ml. The β-receptor blocking agent, propranolol (4×10^{-5} g/ml.), itself increased incorporation of ^{32}P into phospholipids and so potentiated the effect of noradrenaline. The possible significance of these findings will be discussed.

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Analgesic activity after intracerebral injection in the mouse

SHEILA L. HANDLEY* and P. S. J. SPENCER, *Department of Pharmacy, The University of Aston, Birmingham 4*

It has been reported that the sympathomimetic agent, adrenaline (Leimdorfer & Metzner, 1949), and the parasympathomimetic, oxotremorine (Haslett, 1963), possess analgesic activity. Consequently, these and related compounds have been examined for analgesic activity in the mouse following their intracerebral injection (Brittain & Handley, 1967).

Analgesic activity was determined in A_2G albino male mice, using the hot-plate method of Woolfe & Macdonald (1944). ED50 values were determined 15 min after intracerebral injection, the criterion of analgesia being a response time at least twice that in control mice. When tested in this way, morphine had an ED50 of 0.07 (0.05–0.10) μg/mouse. Oxotremorine was equipotent with morphine, while both noradrenaline and adrenaline were 1/5 as active, and dopamine was 1/100 as active as morphine. Acetylcholine was only weakly active, although its activity was increased 20-fold by physostigmine (20 μg/kg subcutaneously). Intracerebral injections of histamine, 5-hydroxytryptamine, amphetamine and angiotensin were almost completely inactive. Subcutaneous injections of noradrenaline were completely inactive.

Next, an examination was made of the effects of noradrenaline and oxotremorine in the presence of other drugs. Atropine (0.8–2.0 mg/kg subcutaneously) significantly reduced the analgesic activity of both noradrenaline and oxotremorine, while