The ouabain-induced hypothermia and behavioural depression were rapidly and completely reversed by the intraperitoneal injection of dexamphetamine (10 mg/kg). Similarly, intraperitoneal desipramine reduced (5 mg/kg) or abolished (10 mg/kg) these effects. In contrast, nialamide (20 mg/kg intraperitoneally 2 h beforehand) produced no reversal. In a recent report (Abdulla & Hamadah, 1970) successful treatment of clinical depression by anti-depressant drugs was shown to be accompanied by increased levels of urinary cyclic adenosine monophosphate. In the present experiments the intracerebral injection of a mixture of ouabain (0·3 μg) and dibutyryl cyclic adenosine monophosphate (25 μg) produced a level of depression and hypothermia significantly less than the same dose of ouabain administered alone ($P<0.05$). Finally, the effects of intracerebral ouabain on whole-brain amine levels were determined. Using a spectrophotofluorimetric assay (Spencer & Turner, 1969) ouabain increased dopamine levels by 103% ($P=<0.01$), while noradrenaline and 5-hydroxytryptamine remained unchanged.

The pharmacological effects of centrally-administered ouabain show a number of similarities to peripherally-administered reserpine, but there seems to be no depletion of brain amines. Although nialamide was unable to antagonize ouabain, the antagonistic effects of dexamphetamine and desipramine suggest that the effects of ouabain are mediated through central adrenergic mechanisms. It is possible that centrally administered ouabain might prove to be an alternative tool to reserpine in the evaluation of potential anti-depressant drugs.

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Some effects of muscarine on the central nervous system of chickens

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The central effects of cholinergic drugs have been little studied in avian species. In the present investigations, cholinergic drugs were introduced into the third ventricle of adult fowls in volumes of 10 μl or micro-infused intracerebrally in 1 μl volumes for 30 s using chronically implanted cannulae (Marley & Stephenson, 1968a) in 12 to 20 day old chicks.

Muscarine (0·0067 μmol) within 4 min of intraventricular injection induced marked electrocortical arousal in drowsy birds, lasting 60–90 min; in alert birds, arousal

was intensified. Behavioural changes were minimal during the first 30–40 min, and involved head jerking and increased nictitating membrane movements. Thereafter, the bird developed tachypnoea (up to 200/min) and stood with neck and wings extended. The minimal effective dose was 0·0017 μmol. Electrocortical and respiratory effects of muscarine (0·0017 μmol) were potentiated by intraventricular eserine (0·006 μmol), itself ineffective on these parameters. The large amplitude, slow frequency electrocortical activity observed in mammals after hyoscine (Bradley & Elkes, 1957) was not evoked in fowls, but intravenous hyoscine (10 μmol/kg) prevented the effects of muscarine; a similar dose of pempidine had no antagonistic action. In fowls anaesthetized with chloralose, intraventricular muscarine (0·0133 μmol) raised blood pressure 30 to 60 mmHg for 2 min and larger doses (0·067 μmol) elicited reproducible increases in electromyographic activity of neck muscles.

Muscarine (0·0033 μmol) micro-infused into various sites in the prosencephalon of young chicks elicited, within 4 min, intense electrocortical arousal lasting 30–90 min. Behavioural changes were marked, the chicks exhibiting alternating bouts of quiescence and violent motor activity. Muscarine micro-infused into the hypothalamus or given intraventricularly did not alter temperature. Muscarine (0·0033 μmol) micro-infused unilaterally into the telencephalon evoked ipsilateral electrocortical arousal; behavioural changes were minimal. None of the respiratory or postural changes seen on intraventricular injection were observed even with muscarine micro-infused into the brain-stem. Behavioural and electrocortical effects were prevented by hyoscine given intravenously (100 μmol/kg) or directly into the brain (0·15 μmol), but once established were reversed with difficulty.

Clearly, areas sensitive to muscarine are widely distributed in the brain of fowls. Muscarine evoked marked behavioural and electrocortical changes not only when given intraventricularly but also when micro-infused into a small area of brain. Average diffusion of a 1·0 μl injection of various dyes into rat diencephalon was a sphere 1·9 mm in diameter (Myers, 1966). An action on descending and diffusely projecting ascending pathways in the chicken brain (Jones & Levi-Montalcini, 1958) could explain the marked effects of even localized muscarine injections, particularly since there is widespread uniform distribution of true cholinesterase in the chicken nervous system (Cavanagh & Holland, 1961). This widespread responsive area to muscarine contrasts with that for catecholamines, the only site at which they are effective when micro-infused into the brain being the hypothalamus (Marley & Stephenson, 1968b, 1969).

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