Failure of autonomic and central nervous system blocking agents to antagonize the gross behavioural effects of tubocurarine injected intraventricularly in conscious cats

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Tubocurarine injected into the cerebral ventricles of unanaesthetized cats produces a variety of autonomic and motor phenomena (Feldberg & Sherwood, 1954; Feldberg & Fleischhauer, 1965). Perfusion of the cerebral ventricles with tubocurarine causes the release of dopamine and its metabolite homovanillic acid into the fluid bathing the cat caudate nucleus (Portig, Sharman & Vogt, 1968). The possibility exists that tubocurarine also releases other neurotransmitters which contribute to the gross behavioural responses. In the experiments described here, the effects of intraventricular injections of drugs affecting the autonomic nervous system (acetylcholine antagonists, adrenoceptor blocking drugs, 5-hydroxytryptamine antagonists and antihistamines) or the central nervous system (antiepileptic agents and inorganic ions) on the central actions of tubocurarine were studied.

Cats of either sex (2·3–3·5 kg) were anaesthetized with pentobarbitone sodium (30–40 mg kg^{-1} i.p.) and a cannula (Feldberg & Sherwood, 1953) was screwed into the skull through which injections were subsequently made. Postoperatively, penicillin was administered intramuscularly. An interval of 5–7 days elapsed before the cats were used for the experiments. All drugs were dissolved in sterile 0·9% sodium chloride solution. The solutions, warmed to 37°, were injected slowly under aseptic conditions in volumes of 0·1–0·2 ml and washed in with 0·1 ml of 0·9% saline. The cats were observed continuously for 2–8 h and intermittently for 24–48 h.

Intraventricular injections of tubocurarine in conscious cats elicited characteristic and reproducible alterations in behaviour. Tubocurarine hydrochloride, in doses from 0·02–0·1 mg, caused emotional behaviour (miaowing, restlessness and fear-like responses), autonomic changes (mydriasis, hippus, nystagmus, widening of palpebral fissures, withdrawal of nictitating membranes, tachypnoea, dyspnoea, salivation, lacrimation, piloerection, defaecation and micturition) and motor phenomena (ataxia, tremor, swallowing movements, circling, myoclonic jerks, rigidity, spasticity and clonic-tonic convulsions). Gross behavioural effects of various single doses of tubocurarine were dose-dependent. The characteristic effects of tubocurarine in doses from 0·05–0·1 mg were convulsions. Clonic-tonic convulsions appeared within 10–20 min. The convulsions were preceded by an initial period of restlessness with signs of fear, salivation, defaecation, dyspnea, piloerection, tremor, mydriasis and bouts of loud calling.

Atropine sulphate (0·5 mg), hyoscine hydrobromide (0·5 mg), hexamethonium bromide (0·4 mg), tetraethylammonium chloride (0·4 mg), nicotine hydrogen tartrate (0·4 mg), phenoxybenzamine hydrochloride (1·0–2·0 mg), yohimbine hydrochloride (0·2–0·5 mg), propranolol hydrochloride (1·0–2·0 mg), practolol hydrochloride (0·1–·02 mg), antazoline chlorhydrate (0·5 mg), chlorpyramine (Synopene-Geigy; 1·0–0·2 mg), phenobarbitone sodium (3·0–5·0 mg), calcium chloride (1·0–2·0 mg) or magnesium chloride (1·0–2·0 mg) did not themselves cause detectable changes in behaviour and after 20 min did not antagonize the gross behavioural effects of tubocurarine (0·05–0·1 mg).

Methysergide bimaleate (0·2 mg), injected intraventricularly, caused slight hippus, slight piloerection and slight tremor, but after 15–20 min did not antagonize the gross behavioural effects of tubocurarine (0·05–0·1 mg). Trimethadione (1·0–2·0 mg) and ethosuximide (1·0–2·0 mg), applied intraventricularly, evoked scratching, slight myoclonic jerks and swallowing movements, but did not antagonize the gross behavioural effects of tubocurarine (0·05–0·1 mg).

The results showed that, in the doses used, acetylcholine antagonists, adrenoceptor blocking substances, 5-hydroxytryptamine antagonist, antihistamines, antiepileptic drugs, calcium or magnesium injected intraventricularly failed to block the emotional behaviour, autonomic changes, and motor phenomena including clonic-tonic convulsions produced by intraventricular injection of tubocurarine. It thus appears that the gross behavioural effects of tubocurarine are not mediated through the release of acetylcholine, noradrenaline, 5-hydroxytryptamine or histamine.

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