thesis and turnover of dopamine (Nybäck & Sedvall, 1972) is confirmed and the suggestion that several of the metabolites have antipsychotic properties (Lal & Sourkes, 1971; Nybäck & Sedvall, 1972) is further supported.

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Evidence for α-methyl-*m*-tyramine as a false dopamine-like transmitter

We have shown previously that after administration of α-methyl-*m*-tyrosine (αMMT), its decarboxylation product, α-methyl-*m*-tyramine (MMTA), accumulates specifically in the corpus striatum of rats and rabbits concomitant with a lowering of dopamine content in that brain region, while metaraminol, the β-hydroxylated product of MMTA, accumulates in noradrenaline-containing areas of the brain (e.g., hypothalamus) while at the same time the level of noradrenaline is lowered in these areas (Dorris & Shore, 1971a). A false transmitter role for the noradrenaline analogue, metaraminol, in noradrenergic neurons has been well established (Muscholl, 1966). The specific localization of the dopamine analogue, MMTA, in a dopamine-rich area of the brain and its release by (+)-amphetamine (Dorris & Shore, 1971b), a drug which releases dopamine (Carlsson, Fuxe & others, 1966) suggests that, like metaraminol in noradrenergic neurons, MMTA acts as a false transmitter in dopaminergic neurons (Dorris & Shore, 1971a, 1971b). This report presents further evidence for this hypothesis.

Apomorphine induces a compulsive gnawing activity in rats, apparently by stimulation of striatal dopamine receptors (Ernst, 1967), and the drug retards the decline of brain dopamine content after blockade of tyrosine hydroxylase (Andén, Rubenson & others, 1967). This effect of apomorphine is thought to result from a reflexly decreased impulse flow in dopaminergic neurons after dopamine receptor activation by the drug (Andén & others, 1967). Haloperidol, on the other hand, by blocking

Table 1. *Effect of apomorphine, haloperidol, or their combination on rat striatal MMTA concentration.*

Treatment	Striatal MMTA $\mu g/g \pm$ s.e.	Decline (%)
αMMT 17 h	0·75 ± 0·04 (4)	—
αMMT 26 h	0·42 ± 0·01 (6)	44
αMMT 26 h .. .. .. + apomorphine 9 h	0·71 ± 0·02[a b] (6)	5
αMMT 26 h .. .. .. + haloperidol 9 h	0·18 ± 0·01[a] (6)	76
αMMT 26 h .. .. .. + apomorphine 9 h + haloperidol 9 h	0·32 ± 0·01[c] (6)	57

[a] Significant difference from 26 h control ($P < 0·001$).

[b] No significant difference from 17 h control.

[c] Significant difference from haloperidol only ($P < 0·001$).

Figures in parentheses denote number of experiments.

striatal dopamine receptors, reflexly increases impulse flow, thus accelerating the rate of dopamine depletion after catecholamine synthesis blockade (Andén, Corrodi & others, 1971). Haloperidol also blocks the apomorphine-induced gnawing behaviour (Ernst, 1967) as well as the retardation of dopamine levels after synthesis blockade (Andén & others, 1967). We have used these actions of apomorphine and haloperidol as models to test further the hypothesis that MMTA is a false dopamine-like transmitter in the striatum.

Female Sprague-Dawley rats were given (±)-αMMT (100 mg/kg, s.c.). Some rats were killed 17 or 26 h later. At the 17 h time, other αMMT-treated rats were given either haloperidol (1 mg/kg, i.p.) or apomorphine (2 mg/kg, s.c.) or a combination of these two drugs with the apomorphine administered 10 min after haloperidol. The apomorphine injections were repeated hourly. All rats were killed 26 h after the αMMT injections. Striatal MMTA concentrations were measured according to Shore & Alpers (1964) and Dorris & Shore (1971a).

The results are summarized in Table 1. The decline of striatal MMTA in control rats was about 44% during the interval between hours 17 and 26. This decline was virtually abolished by apomorphine, an effect in harmony with the action of apomorphine on dopamine decline after synthesis blockade, while haloperidol strikingly accelerated the decline of MMTA from the striatum, a finding consistent with the effect of this drug on striatal dopamine. Furthermore, the lowering of MMTA by haloperidol was partially blocked by simultaneous treatment with apomorphine, an observation also consistent with a similar interaction of the two drugs on striatal dopamine content (Andén & others, 1967).

The marked antagonistic effects of apomorphine and haloperidol on striatal MMTA concentrations thus support the notion that MMTA acts as a false dopamine-like transmitter. The results further suggest that this system should be a valuable tool in studies of drugs activating or blocking striatal dopamine receptors.

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Reduction of acetylcholine output from the indirectly stimulated rat diaphragm preparation by some carbamates and phenols

During a comparative study of some cholinesterase inhibitors on the extra-cellularly recorded endplate potential of the rat phrenic diaphragm preparation it was observed that 3-isopropylphenylmethylcarbamate (OMS 15) caused a slower rate of rise of the endplate potential than paraoxon, eserine, 2-methyl-2-methylthiopropion aldehydeo-(methylcarbamoyl)oxime (OMS 771) or 2-oxo-1,3-dithiolane *O*-(methylcarbamoyl) oxime (OMS 744) when tested in concentrations which gave a similar degree of cholinesterase inhibition. It was thought likely that this difference could be due to a relative reduction of acetylcholine output from the phrenic nerve terminals in the presence of the phenylcarbamates.

Phrenic-diaphragm preparations from male rats 200–250 g, were set up as described by Bülbring (1946) in a Perspex bath containing 7·0 ml Krebs solution at 37°. In every experiment paraoxon 10^{-4} M was added to the bath 20 min before stimulating to ensure complete inhibition of cholinesterases.

All the compounds tested, and paraoxon, were made up as concentrated solutions in acetone and a small volume added to the diaphragm bath to give the desired concentrations. It had previously been established that the maximum concentration of acetone used in the bath did not itself reduce acetylcholine output.

Preparations were stimulated at 50 Hz for 15 min then the bath fluid was removed by pipette and assayed for acetylcholine within 5 min using the leech dorsal muscle preparation (Murnaghan, 1958). Responses to the test solutions were matched with those elicited by standard solutions of acetylcholine perchlorate in Krebs also containing the same concentrations of drugs as the diaphragm bath fluid samples.

Three collections of acetylcholine were made from each preparation. (i) Paraoxon 1×10^{-4} M alone in the bath, (ii) paraoxon 1×10^{-4} M and the compound under test, (iii) paraoxon 1×10^{-4} M alone.

Acetylcholine output in the presence of paraoxon 1×10^{-4} M alone ranged from 21–84 ng with a mean of $44{\cdot}22 \pm 1{\cdot}73$ ng per 15 min stimulation period.

The percentage reduction of acetylcholine output was calculated by comparing the mean of periods (i) and (iii) with period (ii); see Table 1.

In view of the marked reduction of acetylcholine output with the phenylcarbamate OMS 15, the effects of 3-isopropylphenol and some other phenols were also tested; see Table 1. These results may appear to be at variance with those of Otsuka & Nonomura (1963), but their observations on the effects of phenol on the endplate potential only extended up to 7 min after adding the phenol compared with the 20 min incubation period used in these experiments.

The effect of OMS 15 on acetylcholine output may possibly be due to the formation of 3-isopropylphenol from carbamylated cholinesterase at motor nerve endings.