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Effects of morphine on uptake and release of dopamine in mouse and rat striatal synaptosomes

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There is a large species variation in locomotor responses following morphine. In the mouse, Rethby, Smith & Villareal (1971), Villareal, Guzman & Smith (1973), and Kuschinsky & Hornykiewicz (1974) report that morphine causes increase in locomotor activity, an effect which the latter authors found could be prevented by pretreatment with α-methyl-*p*-tyrosine, and which could be restored by treatment with L-DOPA. Kuschinsky & Hornykiewicz (1974) suggested therefore that the increase in locomotor activity in the mouse following morphine could be due to dopamine release. In the rat, Babbini & Davis (1972) and Smee & Overstreet (1976) found that morphine caused an initial decrease in locomotor activity, followed by hyperactivity, while Kuschinsky & Hornykiewicz (1974) only reported a catalepsy response. They suggested that in the rat, morphine causes decrease of dopamine release, and consistent with such a hypothesis, was the finding of Blundell, Crossman & Slater (1976), who found that morphine reduced the circling response to (+)-amphetamine in rats with unilateral 6-hydroxydopamine lesions in the striatum.

We have investigated the ability of morphine to inhibit uptake, or cause the release of [^{3}H]-dopamine ([^{3}H]-DA), in synaptosomes prepared from rat or mouse striatum, and also the ability of morphine to affect inhibition of uptake, or release of [^{3}H]-DA caused by (+)-amphetamine in similar synaptosomal preparations.

Uptake inhibition and release experiments were made as previously described (Kruk & Zarrindast, 1976).

In experiments to study the effects of morphine on inhibition of uptake or release of [^{3}H]-DA, 8 determinations were made at each of 6 concentrations in the range 10^{-9} M to 10^{-4} M. In neither mouse nor rat synaptosomes was there any evidence for either facilitation or inhibition of uptake or release of [^{3}H]-DA in the dose range of morphine examined.

(+)-Amphetamine was found to block [^{3}H]-DA uptake with IC_{50} values of 2×10^{-7}M (rat) and 3×10^{-8} M (mouse). Morphine, in the concentration range 10^{-9} M to 10^{-4} M, did not significantly affect the (+)-amphetamine induced inhibition of [^{3}H]-DA uptake.

(+)-Amphetamine caused release of [^{3}H]-DA with RC_{50} values of 7×10^{-7} M (rat) and 4×10^{-7} M (mouse). Morphine, in the range 10^{-7} M to 10^{-4} M did not significantly affect the (+)-amphetamine induced release of [^{3}H]-DA. Our results do not support the hypothesis of Kuschinsky & Hornykiewicz (1974) that morphine has a direct presynaptic action at dopamine nerve terminals in mouse and rat striatum.

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