The effect of morphine on turning behaviour in rats and mice with unilateral 6-hydroxydopamine lesions

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The acute administration of morphine to rats alters dopamine metabolism in the striatum (Kuschinsky & Hornykiewicz, 1974) and results in an indirectly mediated inhibition of dopamine receptor activity (Lal, 1975). We have examined the action of morphine in rats with unilateral 6-hydroxydopamine (6-OHDA) lesions of the substantia nigra since (+)-amphetamine-induced rotation of these animals is used to investigate the effects of drugs on dopamine release in the brain. Female Sprague Dawley albino rats (150 g) were injected unilaterally with 6-OHDA (8 μg in 4 μl) into the left substantia nigra (co-ordinates: A +2.0 mm; L 1.6 mm; H −2.3 mm, Konig & Klippel, 1963). After 21 days, ipsilateral circling induced by (+)-amphetamine (5 mg/kg i.p.) in groups of 8 rats was recorded for 1 hour. Morphine (2 or 4 mg/kg i.p.) when administered 48 h later together with (+)-amphetamine, caused a statistically significant reduction in the turning. Morphine (2 mg/kg) reduced the mean turning rate recorded between 15 and 60 min after the amphetamine injection by 45% from 19.8 ± 1.0 turns/min to 10.9 ± 1.0 turns/min ($P < 0.001$). The higher dose of morphine (4 mg/kg) caused a 68% reduction in the mean turning rate from 22.7 ± 0.8 to 7.2 ± 1.1 turns/min ($P < 0.001$). The rate of contralateral circling induced by apomorphine (2.0 mg/kg) in groups of 8 nigral lesioned rats was counted. After 48 h morphine (2 or 4 mg/kg) was administered followed 15 min later by apomorphine. In contrast to the results with (+)-amphetamine, apomorphine turning was not affected by 2 mg/kg of morphine but there was a significant 18% reduction in the mean turning rate following a dose of 4 mg/kg of morphine ($P < 0.01$).

Lesions were also produced in adult rats (240 g) by injecting 6-OHDA (40 μg) into the left striatum (co-ordinates: A +8.5 mm; L 2.6 mm; H −1.0 mm). After 14–21 days groups of 8 such rats circled when given (+)-amphetamine (5 mg/kg). Morphine (4 mg/kg) reduced the mean turning rate by 71% from 22.1 ± 0.9 turns/min to 6.4 ± 0.8 turns/min ($P < 0.001$). When given a larger dose of morphine (8 mg/kg) the animals stopped turning completely. The reduction in (+)-amphetamine-induced turning was entirely prevented by naloxone (2 mg/kg i.p.). Levorphanol (6 mg/kg) totally suppressed (+)-amphetamine-induced turning whereas dextrorphan (6 mg/kg) had no effect.

We investigated the action of morphine on turning induced by (+)-amphetamine in albino mice lesioned by injection of 6-OHDA (10 μg) into the left striatum. (+)-Amphetamine (5 mg/kg) caused ipsilateral circling with a mean rate of 9.9 ± 0.9 turns/min ($n = 12$). Morphine (4 mg/kg) had no effect whatsoever on the rate of turning or the total number of turns made over 45 minutes.

The results are consistent with the hypothesis of Kuschinsky & Hornykiewicz (1974) that one effect of morphine in the rat is to reduce the release of dopamine in the striatum but that morphine does not apparently have the same action in the mouse.

References

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