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Effects of morphine on acetylcholine release from the frog spinal cord

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Varying reports on the effects of morphine on acetylcholine (ACh) release from the cerebral cortex have been made. For example, in the cat morphine either depresses (Jhamandas, Phillis & Pinsky, 1971) or stimulates (Phillis, Mullin & Pinsky, 1973) ACh release. The opiate action on cortical cholinergic fibres is probably indirect but further experiments are needed to clarify this matter. To this end the frog spinal cord was chosen as an *in vitro* CNS preparation in order to study the effects of bath-applied morphine on spinal root potentials and endogenous ACh release with the method previously reported (Nistri, 1975). The effects of morphine on the ACh content of the frog brain and spinal cord *in vivo* have already been reported (Nistri, Pepeu, Cammelli, Spina & De Bellis, 1974).

The spontaneous ACh release from the frog cords was 7.3 ± 1.06 ng/ml every 10 min (mean \pm s.e. mean, $n = 28$). The effects of morphine were variable and related to the concentrations used. Ten minutes after the application of $1 \mu\text{M}$ morphine spontaneous ACh release was reduced by $29.7 \pm 5.5\%$; a similar decrease was also found in subsequent samples. However, with this dose of morphine a 10 min antidromic ventral root stimulation (1 Hz; 0.1 msec; supramaximal voltage) was accompanied by a $246.8 \pm 70.1\%$ increase in ACh output over preceding values whereas in untreated cords similar stimulation yielded a $177.7 \pm 50.7\%$ rise. The dorsal root potential produced by such stimulation was slightly reduced by $1 \mu\text{M}$ morphine. All these effects were reversible on washing. Ten minutes after $100 \mu\text{M}$ morphine was added to the bathing fluid a $142.2 \pm 43.2\%$ rise in unstimulated ACh output was seen; the increase persisted in the

following samples. However ventral root stimulation could not produce any further rise in ACh output. A small increase in ventral as well as dorsal root potentials was found. Naloxone ($100 \mu\text{M}$) slightly stimulated the spontaneous ACh release ($+ 51.4 \pm 15.3\%$), prevented the decrease in ACh output following $1 \mu\text{M}$ morphine and reduced the stimulation of ACh release after high doses of morphine.

In the frog spinal cord the motor axon collaterals are cholinergic fibres (Mitchell & Phillis, 1962) which can be directly activated by antidromic ventral root stimulation. Since small concentrations of morphine depressed spontaneous ACh output but failed to reduce the electrically-evoked ACh output, it is suggested that morphine reduced ACh release through an indirect mechanism probably mediated by interneurons. The stimulant action of high concentrations of morphine on spinal ACh release and root potentials might be one of the factors involved in the behavioural excitation seen in frogs after large doses of this opiate.

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