t-BPTBO was the most potent antagonist and convulsant and was approximately four times more potent than bicuculline. The reasonably close agreement between the CD_{100} values and the molar potencies as antagonists lends further support to the suggestion that the convulsant properties of the PTBO derivatives may be due to antagonism of the actions of synaptically-released GABA (Bowery *et al.*, 1976b).

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Influencing morphine self-administration in dependent rats

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Naive rats do not normally drink solutions of morphine, possibly because they are bitter tasting (to man) and possibly because of the post-ingestional effects of the drug. Rats can, however, learn to prefer such solutions (morphine HCl 0.5 mg/ml) to plain water if they are repeatedly 'forced' to drink them in order to relieve thirst. Once such preferences have been acquired, they are relatively stable and persistent and provide a useful animal model of dependence on morphine (Stolerman & Kumar, 1970). There are a number of conceptually distinct ways of trying to change patterns of behaviour that are maintained by pharmacological reinforcers. We report some experiments in rats with established preferences for morphine in which different 'treatment' procedures were compared for their ability to reduce or eliminate morphine-seeking behaviour.

Dependent rats ($n=9$) which received injections of saline 2 h before their daily choice tests continued to ingest about 60% of their daily fluid intake in the form of morphine solution; this corresponded to a daily dose of approximately 20 mg/kg. Other rats ($n=10$) were injected with morphine HCl (30 mg/kg), 2 h prior to their choice tests for 12 days and this treatment initially reduced the proportion of the daily fluid intake consumed as morphine solution from 63% to 43% ($P<0.005$). Increasing the daily doses of injected morphine up to 120 mg kg day did not further reduce the proportional intake of the drug.

Rats ($n=10$) treated with naloxone (initially naloxone HCl 1 mg kg^{-1} day^{-1} for 12 days, then increasing up to 8 mg kg^{-1} day^{-1}) 30 min before choice trials showed little change in their patterns of morphine consumption. It is possible that naltrexone, which is also a relatively 'pure' opioid antagonist but with more prolonged actions, might have altered morphine intake. However, both morphine and naloxone were clearly effective in the range of doses used since they inhibited normal growth—the linear trends for the drugged rats' body weights differed significantly from the saline-injected group ($P<0.01$). Thus, other important factors, apart from the need to relieve withdrawal symptoms or to obtain primary positive reinforcement, must be involved in sustaining morphine preferences.

When saccharin sodium (0.5 mg/ml) was added to the usual morphine solution and this novel taste was associated with an aversive state, naloxone-precipitated abstinence from morphine (cf. Pilcher & Stolerman, 1976), dependent rats ($n=10$) subsequently markedly avoided this mixture in preference tests; they took about 5% of their fluid as drug solution. This aversion was long lasting and it did not generalize either to solutions of morphine alone ($P<0.005$) or to saccharin alone ($P<0.01$). Control (non-averted) subjects showed clear preferences for morphine + saccharin solutions and the preference for this now familiar taste was resistant to the aversion procedure.

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