

EFFECT OF APOMORPHINE AND ITS *N*-PROPYL HOMOLOGUE ON ETHANOL WITHDRAWAL HEAD TWITCHES IN MICE

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Collier, Hammond & Schneider (1976) reported that apomorphine, given orally, decreased the incidence of head twitches induced by ethanol withdrawal. These results were confirmed in the present study. Moreover, the *N*-propyl homologue of apomorphine was about 45 times more potent than apomorphine in affecting head twitching.

Introduction Collier, Hammond & Schneider (1976) found that mice twitch their heads after ethanol withdrawal and that various drugs, including L-DOPA and apomorphine, inhibit this twitching. They suggested that some of the active drugs may be useful in the clinical management of alcoholism.

The purpose of the present study was to compare the potency of apomorphine and its *N*-propyl homologue in counteracting twitching. Although the

propyl compound was no more potent than apomorphine in some tests, results of most studies indicate that the propyl compound is considerably more potent than apomorphine in various tests in animals and in man (for review of results, see Ashton, Anlezark & Meldrum, 1976; Pearl, 1977).

Methods Male Swiss-Webster mice, weighing 18 to 22 g at the start of treatment, came from Taconic Farms, N.Y., U.S.A. The treatment was that of Collier *et al.* (1976) in which mice were dosed with 40% ethanol orally for 4 days (4 rising to 7 g/kg) and tested 24 h after ethanol withdrawal.

Apomorphine hydrochloride and its *N*-propyl homologue, which is *N*-*n*-propylnorapomorphine hydrochloride in the (R)-(-) form (Atkinson, Bullock, Granchelli, Archer, Rosenberg, Teiger & Nachod,

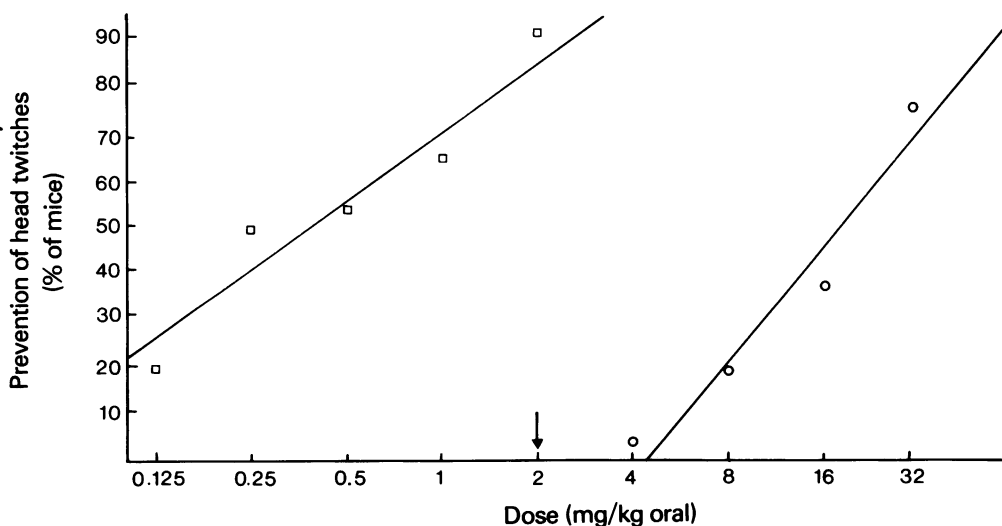


Figure 1 Log-probit plot of the effects of apomorphine and its *N*-propyl homologue in preventing head twitches after ethanol withdrawal in mice. Each point in the plot represents results from eight to 18 mice. For apomorphine (○) the ED_{50} and 95% confidence limits were 17.6 (11.0–40.8) mg/kg. For the *N*-propyl (□) compound the corresponding values were 0.39 (0.13–0.72) mg/kg. There was no statistically significant difference in the slopes ($P > 0.10$, Chi-sq test). The arrow indicates that apomorphine, 2 mg/kg, failed to prevent the reaction in any of the mice.

1975), were dissolved in distilled water and administered orally 30 min before testing. The 30 min interval was used because pilot work indicated that apomorphine exhibited peak potency 30 min as opposed to 60 min after medication. Doses are expressed in mg/kg of the free base.

Head twitches were counted for 8 min after transferring each mouse to a plexiglass box, 64 cm x 60 cm x 25 cm. The observer was unaware of the medications the mice received. A quantal, all or none method was used to compute ED_{50} values, 95% confidence limits and slope values (Finney, 1964). Because Collier *et al.* (1976) determined statistical significance by the nonparametric Mann-Whitney U test (Siegel, 1956), this test was used to supplement the analysis.

Results Nine (13%) of 67 control mice did not twitch after ethanol withdrawal. The mean number of twitches for the 67 mice was about 0.5/minute.

Figure 1 shows the effects of apomorphine and its *N*-propyl homologue on head twitching after ethanol withdrawal. Based on ED_{50} values, the *N*-propyl

compound was about 45 times more potent than apomorphine in preventing twitching. According to the Mann-Whitney U test, the lowest dose of apomorphine that produced a statistically significant ($P < 0.05$, two-tailed) decrease in the incidence of twitching was 8 mg/kg. The dose of the *N*-propyl compound that did so was 0.25 mg/kg.

The apomorphines did not produce conspicuous overt effects including stereotyped licking and gnawing in mice withdrawn from alcohol. However, 30 min after medication about 30 mg/kg of each apomorphine produced stereotyped behaviour in mice that had not received ethanol when the mice were tested in glass beakers.

Discussion Apomorphine inhibited head twitching in mice after ethanol withdrawal in accordance with the results of Collier *et al.* (1976). That the *N*-propyl compound was considerably more potent than apomorphine in preventing head twitching agrees with the majority of results of previous studies in which different tests were used (Ashton *et al.*, 1976; Pearl, 1977).

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