Drug effects on avoidance behaviour in selected strains of rats

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Roman High (RHA) and Roman Low Avoidance (RLA) strain rats were produced by selective breeding, using as selection criteria high or low rates of conditioning in a shuttle-box (Broadhurst & Bignami, 1965). Using conventional bioassay techniques we have found significant differences between the two strains in acetylcholine concentrations in the brain. RLA rats showed significantly higher concentrations than the RHA rats (2.06 ∓ 0.34 μg/g as compared to 1.73 ∓ 0.34 μg/g). When brain regions were examined the differences were most noticeable in the cortex and medulla. No differences were found in acetylcholinesterase activity.

We have also investigated the effects on conditioning behaviour in the two strains of drugs directly or indirectly affecting cholinergic mechanisms. Groups of 10 male RHA, RLA and Porton strain rats weighing 180-200 g were trained in a shuttlebox on 4 consecutive days, 15 min after treatment with either n-ethyl 3-piperidyl benzilate (NEPB, a potent atropine-like drug) 1.0 mg/kg i.p., physostigmine salicylate, 0.12, 0.06 or 0.03 mg/kg s.c. or (+) amphetamine 0.1 mg/kg i.p. NEPB facilitated avoidance conditioning in all 3 strains, but there were significant differences between the strains both in the intensity of effect and in retention of response. RHA and Porton rats showed a similar degree of enhancement, and avoidance responding was maintained when the drug was withheld for a fifth training session. RLA rats showed only slight facilitation of their normally-low responding rate, and when drug was withheld, performance returned to control levels. The rate of conditioning of all 3 strains was decreased by physostigmine; the effect on RLA rats was most marked, these animals actually showing a decreased avoidance with the lowest doses. In all strains (+) amphetamine produced facilitation similar to that seen after NEPB. When rats were given (+) amphetamine and NEPB simultaneously in doses (0.075 mg/kg and 0.75 mg/kg respectively) which alone produced no response, all strains showed facilitated avoidance.

The fact that differences in brain acetylcholine concentrations are found in strains of rats selected to display behavioural differences would support the hypothesis of a central cholinergic system controlling certain types of behaviour (Carlton, 1969) and such a hypothesis is further supported by the differential responses of the strains to NEPB and physostigmine. The observation that amphetamine also produces a differential response, despite the absence of strain differences in synthesis and turnover of catecholamines (Coyle, Wender and Lipsky, 1973) might further suggest that the cholinergic system may be activated by adrenergic neurones.

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References

BROADHURST, P.L. & BIGNAMI, G. (1965). Correlative effects of psychogenetic selection: a study of the Roman High and Low avoidance strains of rats. *Behav. Res. Ther.*, **2**, 273-280.

CARLTON, P.L. (1969). Brain acetylcholine and Inhibition. In: *Reinforcement: Current Research and Theories.* Ed. Tapp, J., New York: Acad. Press. 286-327.

COYLE, J.T., WENDER, P. & LIPSKY, A. (1973). Avoidance Conditioning in different strains of rats: neurochemical correlates. *Psychopharmacologia* (Berl.) **31**, 25-34.