LETTER TO THE EDITOR

REPEATED ADMINISTRATION OF ELECTROCONVULSIVE SHOCK TO RATS : EFFECT ON HALOPERIDOL- AND MORPHINE-INDUCED CATALEPSY AND ITS MODIFICATION BY CARBAMAZEPINE AND DIAZEPAM

Sir,

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The effects of repeated administration of electroconvulsive shock (ECS) to rats have been investigated from several viewpoints in past few years (see, 3, for review). This treatment leads to an enhancement of 5-hydroxytryptamine (5-HT)- and dopamine (DA)-mediated behavioural responses (2, 3, 5) and to an attenuation of cataleptogenic effect of haloperidol (4). One aim of our present study was to examine whether such a treatment can also alter morphine-induced catalepsy, an aspect which is hardly investigated. Some alteration was anticipated, since ECS-administration is known to increase met-enkephalin concentration in brain (5) and to activate selective endorphin system in rats (7), a species in which endogenous peptide analogues have been shown to be cataleptogenic (6). The other aim of the study was to see whether diazepam and carbamazepine, which can block the augmenting effect of ECS-administration of 5-HT- and DA-mediated behaviours (2), exert a similar or comparable influence on the effect of ECS on haloperidol- and morphine-induced catalepsy.

Male Charles Foster rats (10–15 animals per group) were daily given transpinnal ECS (50 H_z sinusoidal current, 150 V for 0.5 sec) on 10 consecutive days as detailed earlier (2). One of the two catalepsy tests was performed on day-11. (a) Haloperidol catalepsy; catalepsy induced by haloperidol (1.5 *mg/kg*, ip) was assessed at 3 hr and scored as described by Green *et al.* (4). (b) Morphine catalepsy; catalepsy induced by morphine sulphate (10 *mg/kg*. sc) was assessed at 1 hr and scored as described by Balsara *et al.* (1). These tests were also performed in unshocked rats for a comparison.

Additional groups were given either diazepam (2.5 *mg/kg*, sc; Sycocam Injection, Unichem Labs., India) or carbamazepine (Suhrid-Geigy, India; 40 *mg/kg*, po, as an aqueous suspension in 2% carboxymethylcellulose) every day for 10 days 1 hr after ECS as described earlier (2); control groups were given drugs alone without ECS. Mann-Whitney U test was used to assess differences between the groups.

After 10 days of ECS-administration haloperidol catalepsy was found to be significantly attenuated (Fig. 1) as described by others (4); in contrast, morphine catalepsy was found to be significantly enhanced. This latter finding, not described well so far, could simply mean that ECS-treatment leads to an increased central met-enkephalin function (see above), which can add up to the cataleptogenic effect of morphine. Diazepam or carbamazepine had no major effect on cataleptogenic potency of haloperidol or morphine in unshocked rats (Fig. 1). The attenuation of haloperidol catalepsy following ECS was abolished only by carbamazepine, while the enhancement in morphine catalepsy following ECS was not affected either by diazepam or carbamazepine.

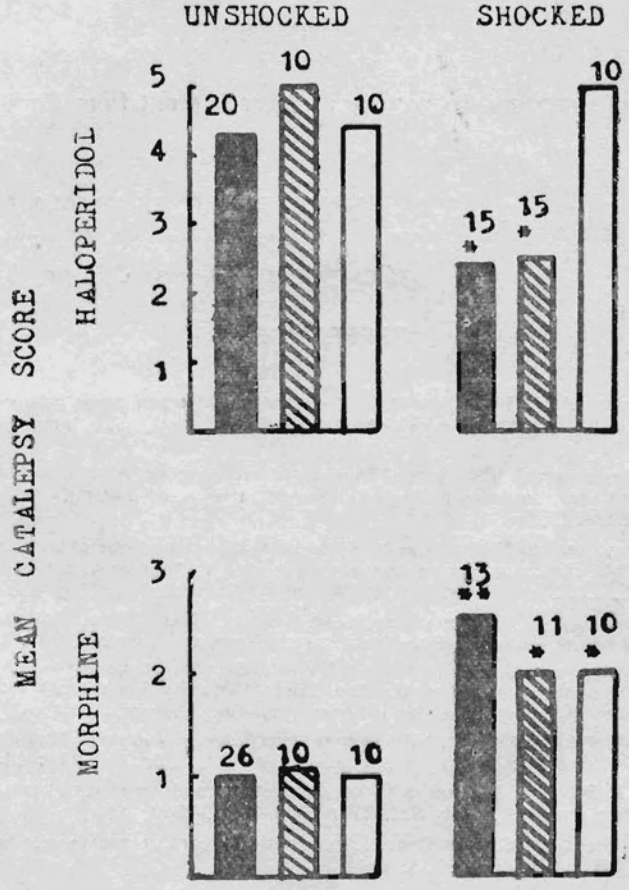

Fig. 1 : Mean scores indicating intensity of catalepsy induced by haloperidol and morphine in unshocked rats and rats given ECS-treatment for 10 days (see text for details). The animals were given no drug(■), or were given diazepam (2.5 *mg/kg*, sc, ▨) or carbamazepine (40 *mg/kg*, po, □)once each day for 10 days. In shocked groups, the drugs were given once a day, 1 hr after administration of ECS. Asterisks indicate the probability of difference between a shocked group and its control (inshocked) group (*$P<0.05$, **$P<0.01$, Mann-Whitney U test). Number of rats in a group is specified above the block.

This study adds to the information on the consequences of ECS-treatment and their alterations by certain drugs. Carbamazepine and diazepam appeared to resemble each other qualitatively in having no influence on enhanced morphine catalepsy following ECS, just as they resembled in reducing enhancing effect of ECS on certain central monoamine-mediated behavioural responses (2). In view of this and the finding in a radioligand binding study (8) that carbamazepine is also bound to benzodiazepine receptor sites in rat brain, it was not expected that only one of the two drugs (viz., carbamazepine) will effectively block the effect of ECS on haloperidol catalepsy. It is difficult to speculate upon why diazepam exerted to such effect.

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REFERENCES

1. Balsara, J.J., J.H. Jadhav, M.P. Mulev and A.G. Chandorkar. Effect of drugs influencing central 5-hydroxytryptaminergic mechanisms on morphine-induced catalepsy in the rat. *J. Pharm. Pharmac.*, **31** : 255–257, 1979
2. Bhavsar, V.H., V.R. Dhumal and V.V. Kelkar. The effect of some anti-epilepsy drugs on enhancement of monoamine-mediated behavioural responses following the administration of electroconvulsive shocks to rats. *Eur. J. Pharmac.*, **74** : 243–247, 1981.
3. Green, A.R. The behavioural and biochemical consequences of repeated electroconvulsive shock administration to rats and the possible clinical relevance of these changes. In "Enzymes and neurotransmitters in Mental Disease' by Usdin, E., T.L. Sourkes and M.B.H. Youdim. New York, Wiley, pp. 455–467, 1980.
4. Green, A.R., M.R. Bloomfield, C.K. Atterwill and D.W. Costain. Electroconvulsive shock reduces the cataleptogenic effect of both haloperidol and arecholine in rats. *Neuropharmacology*, **18** : 447–451, 1979.
5. Green, A.R., D.W. Costain and J.F.W. Deakin. Enhanced 5-hydroxytryptamine and dopamine mediated behavioural responses following convulsions-III. The effects of monoamine antagonists and synthesis inhibitors on the ability of electroconvulsive shock to enhance responses. *Neuropharmacology*, **19** : 907–914, 1980.
6. Herman, B.H., F. Leslie and A. Goldstein. Behavioural effects and *in vivo* degradation of intraventricularly administered dynorphin (1–13) and D-Ala2-dynorphin (1–11) in rats. *Life Sci.*, **27** : 883–892, 1980.
7. Holaday, J.W. and G.L. Belenky. Opiate like effects of electroconvulsive shock in rats : a differential effect of naloxone on nociceptive measures. *Life Sci.*, **27** : 1929–1938, 1980
8. Skeritt, J.H., G.A.R. Johnson and S. Chen Chow. Interactions of carbamazepine with benzodiazepine receptors. *J. Pharm. Pharmac.*, **35** : 464–465, 1983.

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