

LETTER TO THE EDITOR

DIFFERENTIAL EFFECT OF BUPROPION ON HALOPERIDOL AND MORPHINE CATALEPSY IN THE RAT

Sir,

( Received on July 11, 1990 )

The cataleptogenic effect of haloperidol is attributed to blockade of postsynaptic striatal D-2 dopamine (DA) receptors (1). High doses of morphine induce immobility and catalepsy in the rat by blocking DA receptors (2). Since bupropion, a newly introduced antidepressant drug, selectively inhibits DA uptake in rat brain *in vivo* (3) and the neuronal reuptake of DA into synaptosomal preparations of rat striatum (4) we have studied the effect of bupropion pretreatment on haloperidol and morphine induced catalepsy in the rat.

Albino rats of either sex, 150 to 200 g, with free access to a standard diet and tap water were used in groups of 10 for each treatment. Each animal was used once only. All observations were made at room temperature (22 to 24° C) between 10.00 and 16.00 hr in a noiseless diffusely illuminated room.

Catalepsy was scored according to Costall and Naylor (5). Animals were tested for the presence of catalepsy by placing both front limbs of the animal over a 10 cm high wooden block. If the animal maintained the imposed posture for atleast 10 sec it was said to be cataleptic and scored one point. For each further 10 sec it continued to maintain the cataleptic posture one point was given. Animals were tested for catalepsy 1 hr after haloperidol and 30 min after morphine treatment.

Bupropion HCL (Burroughs Wellcome) was dissolved in distilled water while haloperidol (Searle) and morphine sulphate (Bengal Immunity) injection solutions were diluted with distilled water. Doses refer to the forms mentioned. All drugs were injected *ip* in a volume of 0.1 ml/100 g body weight. Bupropion (or distilled water in control

groups) was injected 30 min before haloperidol or morphine.

The results were evaluated statistically by the Mann-Whitney U-Test for non-parametric data.

Haloperidol (1.5 mg/kg) and morphine (15 mg/kg) induced catalepsy in rats without causing loss of righting reflex or apparent change in muscle tone and motor coordination. Bupropion (25, 35 and 50 mg/kg) did not induce catalepsy in rats when the animals were tested upto 2 hr after injection. On the contrary, rats receiving bupropion (25, 35 and 50 mg/kg) exhibited an increase in locomotor activity and animals receiving 50 mg/kg dose also exhibited mild degree of stereotyped behaviour characterised by periodic sniffing. Pre-treatment with 25 mg/kg bupropion significantly ( $P < 0.001$ ) antagonised while pre-treatment with 35 mg/kg bupropion completely abolished the cataleptic effect of haloperidol (Table I). However, pre-treatment with 25 mg/kg bupropion had no significant effect on morphine induced catalepsy but pre-treatment with 35 and 50 mg/kg bupropion did significantly ( $P < 0.001$ ) potentiate the cataleptic effect of morphine (Table I).

Haloperidol induces catalepsy by blocking postsynaptic striatal D-2 DA receptors (1). Antagonism of haloperidol catalepsy by bupropion can be explained as follows. Normally, following the blockade of postsynaptic striatal DA receptors by neuroleptics there is a compensatory "feed-back" increase of nigro-striatal dopaminergic neuronal activity with resultant increase in DA release which counteracts to some extent the neuroleptic induced blockade of DA receptors (6). Bupropion, by blocking the neuronal reuptake of DA which is



released during the compensatory feed-back mechanism, increases the concentration of DA at postsynaptic striatal DA receptor sites with resultant antagonism of haloperidol catalepsy.

However, in the present study bupropion pretreatment potentiated morphine catalepsy indicating

TABLE I: Effect of bupropion (BUP) pretreatment on haloperidol (HAL) and morphine (MOR) induced catalepsy in rats.

Pretreatment and drug (dose, mg/kg)	Catalepsy Score Mean $\pm$ S.E.M., (n=10)
Vehicle (water) + HAL 1.5	3.8 $\pm$ 0.13
BUP 25 + HAL 1.5	0.5 $\pm$ 0.22*
BUP 35 + HAL 1.5	0.0
Vehicle (water) + MOR 15	0.8 $\pm$ 0.24
BUP 25 + MOR 15	1.6 $\pm$ 0.49
BUP 35 + MOR 15	3.8 $\pm$ 0.13*
BUP 50 + MOR 15	4.0 $\pm$ 0.00*

\*P<0.001 in comparison with respective control group (Mann-Whitney U-Test).

Numerals following the drugs indicate their doses (mg/kg).

thereby that mechanism other than blockade of DA receptors by morphine is involved in its cataleptogenic effect. Our finding concurs with the observation of Iwatsubo and Clouet (7) that morphine does not block DA receptors and with the report of Costall and Naylor (8) which states that different mechanisms and sites are involved in the induction of haloperidol and morphine catalepsy. Further, the reports of Costall and Naylor (5) and Balsara et al (9) indicate that the activation of the central 5-HT system has a facilitatory effect on the catalepsy induced by morphine. Recently it has been reported that DA facilitates the release of 5-HT from 5-HT nerve terminals either by stimulating the DA receptors located on 5-HT nerve terminals (10) or by entering the 5 HT neuron (11). We postulate that bupropion, by blocking the reuptake of DA into DA neurons, makes more DA available to interact with 5-HT neurons and thus enhances the activity of central 5-HT system with resultant potentiation of morphine catalepsy.

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