

## THE ROLE OF THE SEROTONERGIC SYSTEM IN THE "WET DOG" SHAKE BEHAVIOUR INDUCED BY SODIUM N-DIPROPYL ACETATE

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### SUMMARY

It is known that experimental animals used in pharmacological research behave in certain ways with the influence of various neurotransmitters in the central nervous system. In this research, we have studied the effect of buspiron on the wet dog shake behaviour, with respect to its relationship with the serotonergic system, after the administration of n-dipropyl acetate which is used in the treatment of epilepsy and 5-hydroxytryptophan which is a serotonin precursor.

### ÖZET

Santral sinir sistemindeki çeşitli nörotransmitterlerin etkilenmesiyle farmakolojik araştırmalarda kullanılan deney hayvanlarının belli bazı davranışlarda bulunduğu bilinmektedir. Serotoninin prekürsörü olan 5-hidroksitriptofan ve günümüzde epilepsi tedavisinde kullanılan n-dipropil asetat verilmesinden sonra görülen ıslak köpek sallanması davranışının serotonerjik sistemle ilişkisini gözönüne alarak yaptığımız bu çalışmada buspironun bu davranışa etkisi araştırılmıştır.

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**Key words:** "Wet dog" shake, n-dipropyl acetate, serotonin, buspiron.

## INTRODUCTION

Some of the pharmacological investigations made are directed at the observation of drugs which make certain behavioural changes in the laboratory animals by affecting the neurotransmitters in the central nervous system. These drugs belong to different pharmacological groups and effect the synthesis and breakdown of neurotransmitters in the brain or specific receptors, resulting in characteristic actions. The behavioural changes according to the type of mediator which takes part in the activated or inhibited system vary and thus the results in the activation of the serotonergic system occurs in rats as the shake of a wet dog and is called the "Wet Dog" shake (WDS) behaviour.

The shake caused by the drugs was first seen and named by Winkler during the withdrawal of opiates in rats (1). In 1977, Bedard and Pycock reported that WDS which is seen after 5-hydroxytryptophan (5-HTP) injection to the mice can be used as a model for measuring the brain's serotonin (5-HT) activity (2). On the other hand acute administration of sodium n-dipropylacetate (DPA) in rats causes WDS behaviour (3, 4). It is known that acute and chronic administration of DPA to rodents has been shown to elevate brain concentrations of 5-hydroxyindolacetic acid (5-HIAA) possibly by stimulating 5-HT turnover (5). It has been shown that the inhibition of 5-HT synthesis by p-chlorophenylalanine also blocked the WDS response to DPA and administration of L-tryptophan, which stimulates 5-HT synthesis and increases this response to DPA (6).

On the other hand it has been claimed that DPA-evoked behaviour is similar to the morphine abstinence syndrome, suggesting the possibility of a complex interaction between GABA (gamma-aminobutyric acid) ergic, 5-hydroxytryptaminergic and opiate systems in the production of WDS behaviour induced by DPA (7).

The purpose of the present study was to clarify further the mechanism of the WDS produced by DPA, and in particular the involvement of serotonergic system in WDS behaviour.

## MATERIAL and METHOD

### Experimental

Male wistar rats weighing 200-250 g were used throughout all experiments. Two hours before the injections each rat was placed individually in a cage in a quiet room and had free access to food and water.

All drugs were administered by the intraperitoneal route in volume doses of 0.2 ml/100 g body weight. WDS induced by DPA was observed continuously for 30 minutes after each injection immediately after placing the rat into an individual cage (35 cm long x 15 cm high x 25 cm wide). WDS was scored as the number of whole-body shakes occurring during this period. The effects of various drug pretreatments on WDS behaviour were examined in separate groups of rats. Each group was made up of 15 rats. All drugs were dissolved in 0.9 % NaCl saline and it was used as control. Rats were pretreated with buspirone, cyproheptadine and 5-HTP an hour before DPA was administered.

Drug pretreated groups were compared with control group by Student's t-test.

5-hydroxy-L-tryptophan and sodium n-dipropylacetate were obtained from Sigma. Cyproheptadine HCl and Buspiron HCl were gifted from İ. E. Kimya Evi T. A. Ş. and Nobel İlaç Sanayii, respectively.

**Table1:** The effect of buspirone HCl, cyproheptadine HCl and 5-hydroxy-L-tryptophan on WDS induced by DPA (350 mg/kg). All values are mean  $\pm$  SD.

Pretreatment	Dose (mg/kg)	No of WDS after DPA injections
Control	—	31 $\pm$ 5.1
Buspirone HCl	10	8 $\pm$ 2.3*
Cyproheptadine HCl	5	6 $\pm$ 3*
5-hydroxy-L-tryptophan	100	69 $\pm$ 2.2*

\* Significant difference ( $p < 0.01$ ) from control value.

## RESULT and DISCUSSION

Serotonin mediated behavioural models have proved valuable in the examination of the effects of drugs on 5-HT function (2, 8, 9, 10). One of these models is WDS behaviour caused by different drugs (1, 11, 12). It is known that acute administration of DPA in rats causes WDS behaviour and this behavioural syndrome is thought to be an expression of central 5-HT receptor activation (3). In our study we also found after 5-HTP administration the number of WDS behaviour induced by DPA increased (Table 1). On the other hand it has been shown that cyproheptadine efficiently blocked WDS evoked by carbachol (13). We studied the effect of cyproheptadine which is a serotonin 5-HT<sub>2</sub> receptor antagonist on the number of WDS induced by DPA. Our results point to cyproheptadine as a blocker of WDS induced by DPA (Table 1).

In our study we have examined the effect of buspirone which is an anxiolytic drug that affects the serotonergic system, on the WDS behaviour caused by DPA.

It is known that behavioural, electrophysiological and receptor binding experiments gradually led to the idea that buspirone owes much of its anxiolytic activity to its ability to attenuate central 5-hydroxytryptamine neurotransmission (14). It has been shown that 5-HT syndrome brought on by either 5-methoxy-N, N-dimethyltryptamine or 8-OH-DPAT is known to be inhibited by pre-administration of buspirone (15). Such data suggest that buspirone exerts an antagonistic action on 5-HT function or inhibition of 5-HT release in the intact animal.

In our study, it was seen that buspirone prevents the WDS behaviour in rats which is caused by DPA and our results indicate an involvement of 5-hydroxytryptaminergic system in the control of WDS behaviour induced by DPA (Table 1).

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