

Benzhexol Causes Conditioning Place Preference in Male Rats

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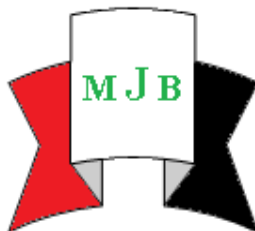
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Abstract

Background: Benzhexol hydrochloride (Trihexyphenidyl) is a potent anticholinergic agent. Abuse of benzhexol has been noted with increasing frequency in recent years

Aim of the study: to determine the conditioning place preference of benzhexol administration in the male rats.

Materials and methods: Sixteen male, adult, albino rats were used in this experiments. The animals were randomly divided into 2 groups, eight rats for each group. Each rat of group 1 was placed in the control compartment and once the rat enter the drug compartment, the animal received N.S. in equal volume to the benzhexol dose,, orally (p.o.), by gastric tube. Each rat of group 2 was placed in the control compartment and once the rat enter the drug compartment, the animal received benzhexol 0.2 mg/kg, p.o., by gastric tube. Previous two steps were repeated twice daily for 10 days. On 11th day, each rat in was placed in the control compartment for 10 minutes and all behaviors of the animals were recorded by video camera.

Results and conclusion: In group 2 (benzhexol 0.2 mg/kg), the time which spent in the drug chamber (white and brown color) significantly increased ($P<0.05$) as compared with the time which spent in the control chamber. This study reported that administration of 0.2 mg/kg of benzhexol, twice daily (pd), for 10 days caused conditioning place preference in the rats.

Keywords: Benzhexol, conditioned place preference test, rat

عقار البنز هكسول يسبب تفضيلاً شرطياً للمكان في ذكور الجرذان

الخلاصة

يعتبر البنز هكسول هايدروكلورايد (الارتين) دواءً فعالاً مضاداً للكولينرجك، و ان اساءة استعمال هذا الدواء زاد بشكل مضطرب في السنوات الاخيرة . هدف البحث هو لبيان تفضيل المكان الشرطي لعقار البنز هكسول في ذكور الجرذان باستعمال اختبار تفضيل المكان الشرطي. تم استعمال ستة عشر جرذاً ذكراً، قسمت الى مجموعتين بواقع ثمانية حيوانات في كل مجموعة وقد وضع كل جرذ من المجموعة الاولى في قسم السيطرة و في حال دخوله قسم الدواء يعطى الحيوان حجماً من النورمال سلاين مساوياً لجرعة البنز هكسول، مرتين يومياً عن طريق الفم بواسطة انبوبة المعدة. و قد تم وضع كل جرذ من المجموعة الثانية في قسم السيطرة و في حال دخوله قسم الدواء يعطى الحيوان ٠,٢ ملغم/كغم من البنز هكسول , مرتين يومياً عن طريق الفم بواسطة انبوبة المعدة. كررت الخطوات السابقتين مرتين يومياً لمدة عشرة ايام. في اليوم الحادي عشر من الدراسة ان الوقت الذي قضته حيوانات المجموعة الثانية في قسم الدواء قد ازداد زيادة ذو قيمة ($P<0.05$) نسبة الى الوقت الذي قضته الحيوانات في قسم السيطرة. اثبت هذا البحث ان اعطاء ٠,٢ ملغم/كغم من البنز هكسول، مرتين يومياً عن طريق الفم للجرذان لمدة عشرة ايام سبب تفضيلاً شرطياً للمكان.

Introduction

Conditioned place-preference paradigm is a behavioral paradigm which has been used extensively in the study of the neural mechanisms of addiction [1].

In experiments involving conditioned place-preference paradigm, rats repeatedly receive a drug in one compartment (the drug compartment) of a two-compartment box. Then during the test phase, the rat is placed in the box drug-free, and the proportion of time it spends in the drug compartment, as opposed to the equal-sized but distinctive control compartment, is measured. Rats usually prefer the drug compartment has been associated with the effects of the drugs to which humans become addicted [2].

Benzhexol hydrochloride (Trihexyphenidyl) is a potent anticholinergic agent [3]. It causes reversible blockade of cholinomimetic action at muscarinic receptors [4]. Benzhexol can be used for treatment of Parkinson's [5], extrapyramidal side effects, such as tardive dyskinesia, occurring during antipsychotic treatment [6,7,8], dystonia [9], tremor [10], excessive salivation [11], spasmodic torticollis [12].

Abuse of benzhexol has been noted with increasing frequency in recent years [13,14,15,16].

Aim of the study: to determine the conditioning place preference of benzhexol administration in the male rats.

Materials and methods

1- Animals

Sixteen male, adult, albino rats were used in this experiments. Their weights were 150-200 g. The rats were housed in the Animal House of the College of Medicine/Babylon University, and kept on 25°C and 12 hours light –dark cycle with water and food *ad libitum*. After two weeks of adaptation, the animals were randomly divided into 2 groups, eight rats in each group.

2-Drug

Benzhexol HCL (Parkizol tablet, 5mg, PHARMALINE, Lebanon) was dissolved in 50 ml of N.S., so the final product contained 0.1 mg of benzhexol in each ml.

3-Conditioned place-preference box

As described by John (2000), a box (60 cm x 20 cm x 40 cm) was made by the researcher and a plate (containing a small opening allowing the rat to transferred freely from one compartment to another) divided a box in to two equal compartments (Picture 1). One of the compartments was white and brown in color and the other was brown. The white and brown compartment was considered as a drug compartment (rats repeatedly received a drug in this compartment), while the brown compartment was considered as a control compartment. During the test, the rats were placed in the control compartment, and the proportion of the time which was spent in the drug compartment was measured (John, 2000).



Picture 1 Conditioned place-preference box

4- Procedure

- a- Each rat of group 1 was placed in the control compartment and once the rat enter the drug compartment, the animal received N.S. in equal volume to the benzhexol dose,, p.o., by gastric tube.
- b- Each rat of group 2 was placed in the control compartment and once the rat enter the drug compartment, the animal received benzhexol 0.2 mg/kg, p.o., by gastric tube.
- c- Previous two steps were repeated twice daily for 10 days.
- d- On 11th day, each rat was placed in the control compartment for 10 minutes and all behaviors of the animals were recorded by video camera.

Statistical analysis

The results were expressed as mean \pm standard error of the mean (SEM).

Statistical analysis was carried out by using one way ANOVA. Differences were considered statistically significant if the p value is lower than 0.05.

Statistical analysis was carried out by using 17th edition of SPSS[®] statistics for Windows[®]

Results

In control group, there is no significant difference ($P > 0.05$) between the time which spent in the drug chamber and the time which spent in the control chamber, while in group 2 (benzhexol 0.2 mg/kg), the time which spent in the drug chamber (white and brown color) significantly increased ($P < 0.05$) as compared with the time which spent in the control chamber (brown color) (**Picture 2 and Figure 1**)



Picture 2 Rat from group 2 in drug chamber (white and brown color) of the conditioned place preference test.

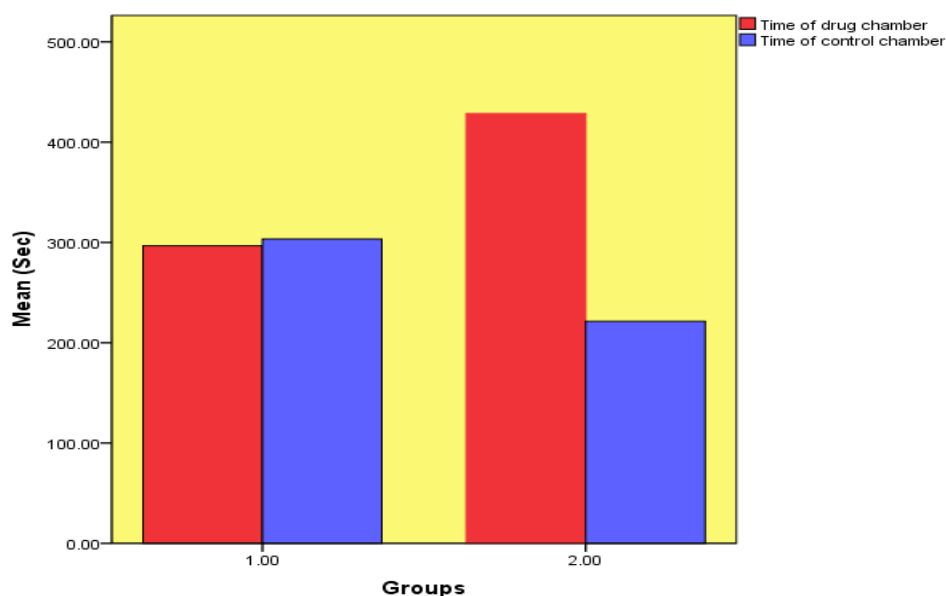


Figure 1 Mean of the times which spend in the drug chamber (red color) and control chamber (blue color) in the conditioned place-preference test in two groups; group 1 (control group) and group 2 (benzhexol 0.2 mg/kg).

Discussion

This study reported that administration of 0.2 mg/kg of benzhexol, p.d, for 10 days caused conditioning place preference in the rats. Up to our

knowledge, no previous data were found about the conditioning place preference of benzhexol. However, this finding agrees with other studies which reported that all addictive

drugs have conditioning place preference. Bardo *et al* (1984) reported that animals displayed condition place preference as a significant increase in duration spent within morphine-associated environment [17]. The results of Nomikos and Spyraiki study (1988) showed that place preference conditioning procedure to be a valid test for evaluating rewarding properties of cocaine [18]. Shoaib *et al* (1993) published a report of conditioned place preference produced by nicotine [19].

Conditioned place preference, has been used extensively to probe the psychological [20] and neurobiological [21] mechanisms underlying the rewarding properties of addictive drug.

Conclusion

Benzhexol has reward effect in male rats.

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