Benzhexol Causes Conditioning Place Preference in Male Rats

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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 experiment. 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 enters 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 enters 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

 uninstall the benzhexol هيدروكلورايد (الآرين) دواءً فعالاً مضاداً للكوليوكسين. وان استعمال هذا الدواء راز بشكل متكررين في السنوات الأخيرة. هدف البحث هو تبيان تفضيل مكان الشرطي للمعتاد البينزكسول في ذكور الجرذان باستعمال اختبار تفضيل المكان الشرطي. تم استعمال ستة عشر ذكوراً كسمت الجماعتين بواقع ثمانية حيوانات في كل جماعة وقد وضع كل جرذ من المجموعة الأولى في قوس السيطرة وفي حال دخوله قوس الدواء وضع على الحيوان حجماً من الميم ملاتين لجرعة البينزكسول، مرتين يومياً عن طريق الفم بواسطة نبية المعدة. وقد تم وضع كل جرذ من المجموعة الثانية في قوس السيطرة وفي حال دخوله قوس الدواء وضع على الحيوان 0.2 ملغ/كم من البينزكسول. مرتين يومياً عن طريق الفم بواسطة نبية المعدة. كررت الخطوات السباقتين مرتين يومياً لمدة عشرة أيام. في اليوم الحادي عشر من الدراسة ان الوقت الذي قضته الحيوانات المجموعة الثانية على قوس الدواء قد ازداد زيادة نمو قيمه (P<0.05) نسبة إلى الوقت الذي قضته الحيوانات في قوس السيطرة. هذا البحث ان أطعمة 0.2 ملغ/كم من البينزكسول، مرتين يومياً عن طريق الفم للجرذان لمدة عشرة أيام بسبب تفضيل 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).
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 ± 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)
Rat from group 2 in drug chamber (white and brown color) of the conditioned lace 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, pd, 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 Spyrraki 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.

**References**


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