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DIFFERENTIAL EFFECT OF CAFFEINE ON MEMORY AND LEARNING

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ABSTRACT

Caffeine and related xanthine compounds are psychostimulants that affect memory and learning. Caffeine is consumed by a large population of the world, so it is necessary to know its effects on brain. This study aims to determine the effects of caffeine on memory acquisition, memory consolidation, memory retention and learning. We gathered data where rats were used for this study and experiments on inhibitory avoidance task and habituation. Different doses of caffeine were used, 30 minutes before and after training and 30 minutes before test session. The research showed that caffeine improves memory consolidation but at low to moderate dozes. Caffeine affects memory in different ways on different dozes and it also depends on the kind of memory task.

1. INTRODUCTION

Caffeine belongs to methyl-xanthine group of compounds that have a psychostimulant effect on central nervous system CNS (Heidari *et al*., 2020) [1]. Studies show that caffeine and related xanthine products have differential effect on memory and learning (Angelucci *et al.*, 1999) [2]. Adenosine is abundant in the central nervous system (CNS). Adenosine is central excitatory and inhibitory neurotransmitter in the brain (Liu *et al.*, 2019) [3]. Adenosine is a neuromodulator in CNS with specific receptors. In the brain, adenosine and adenosine receptors regulate the discharge of neurotransmitters and are important in the regulation of sleep, cognition, memory, and learning (Sebastião and Ribeiro, 2009) [4]. Caffeine binds to adenosine receptors, which inhibit the binding of adenosine to its receptor. This blockage of adenosine receptors minimizes the release of neurotransmitters. When receptors attach to adenosine, neural activity diminishes, and we feel sleepy.

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Caffeine blocks adenosine receptors by binding to them (Institute of Medicine (US) Committee on Military Nutrition Research 2001) [5]. Caffeine is present in tea, coffee and a lot of beverages. It is one of the compound with a lot of consumption all over the world. Two billion cups are consumed everyday of coffee alone (Washington Post, 2019). A lot of people, around the world are consuming caffeine daily in the form of coffee, tea etc., so it is necessary to study its effect on brain function.

There is a controversy in the improving or impairing effects of caffeine on memory and habitual learning. A study was conducted to determine the improving or impairing effects of caffeine on brain functioning. For this purpose, rats were administered with different doses of caffeine and undergone inhibitory avoidance test and habituation test.

2. MATERIALS AND METHODS

The animals used in this research are rats. These animals were kept in the environment where the temperature was maintained (22-24℃). The food and water were available *ad libitum*. The experiments were conducted between 7:00 AM and 12:00 PM. A

set of 12 cage mates were maintained in cages. Caffeine was dissolved in saline (0.9% NaCl) and was administered intraperitoneal in a volume of 0.1 ml/10 g body weight.

Each group consisting of 12 rats was administered with different doses of caffeine and returned to its cage to observe the differential effect of caffeine. The 24 groups of rats received different concentrations of caffeine i.e., 1, 3, 10, 30 and 100 mg/kg. These mice had to perform inhibitory avoidance task with a training interval of 48 hours. The schedule of drug administration was 1) 30 minutes before training; 2) immediately after training; 3) 30 minutes before the test; 4) 30 minutes before the training and 30 minutes before the test. The inhibitory avoidance task apparatus consisted of a box with two chambers. The box was divided into an illuminated chamber and a dark chamber of the same size by a wall with a door. During training session, the animal was placed in the illuminated chamber facing the door. When the door was opened, the animal entered into the door. The time taken by animal to enter the door was calculated. The animal that took more than 30 seconds to enter into the dark chamber was eliminated and replaced with another animal. When the animal entered the dark chamber, it received a 0.15mA electric shock and then the animal was returned to its cage. The test session was similar to training session with the only difference that the animal did not receive any electric shock. The time taken by the animal to enter the dark chamber was calculated.

Before each of the 5-habituation session, 2 groups of animals received 30 mg/kg of caffeine. Another 5 groups of mice received 1, 3, 10, 30, 100 mg/kg immediately after each session of habituation to a new environment. In habituation box, three infrared lights were pointing to the photocells for 5 minutes. The animals were allowed to freely explore the habituation box. The number of times the animal crossed the lines was computed. A decrease in these scores was taken as a measure of retention (Fiani *et al.*, 1986).

3. RESULTS

Inhibitory Avoidance

In the training, groups of all the animals took relatively similar time to enter the dark chamber. Control animals learned not to go into the dark chamber because the time they take to enter into the dark chamber in the test was greater than that of entering into the dark chamber in the training. Caffeine at doses higher than 10 mg/kg impaired memory acquisition. Post-training caffeine at the doses of 1 to 30 mg/kg improved memory consolidation.

The administration of 100 mg/kg caffeine had no effect on retention. Caffeine, when administered 3 or 10 mg/kg 30 min before the test improved memory retrieval.

There was no effect of caffeine at the doses of 1, 30 or 100 mg/kg in the test session scores. A phenomenon of dependency on the drug state did not cause the impairing effect of pre-training caffeine. The animals which received 3–100 caffeine, 30 min before the training and 30 min before the test session showed low retention scores as compared to the control group.

Habituation

There was a difference in the baseline scores of the animals, so it was difficult to calculate the differences in the lower locomotor activity. This was the indication that caffeine altered habituation. It was evident that 30 mg/kg pre-training caffeine administration did not affect habituation. On the first training day, pre-training caffeine had no effect on rearing scores. It was concluded that pre-training 30 mg/kg caffeine administration impaired habituation. The effect of post-training administration of caffeine on habituation shows that caffeine could affect both performance and memory retention. Caffeine administration after training shows that only memory consolidation was affected by treatment.

4. DISCUSSION

In this study, we studied different views mentioned in contemporary literature. There was a confusion, whether caffeine impairs or improves memory consolidation or learning behavior. We examined the behavior of rats when they were administered with different doses of caffeine by examining them in inhibitory avoidance task and habituation task. We tried to answer the following question 1) What is the effect of different doses of caffeine on memory consolidation and habitual learning?

The results described above suggest that caffeine has differential effects on different concentrations. The administration of drug before the training session can affect performance, attention, memory acquisition. Caffeine can improve the exploratory behavior in an open area. It is observed that caffeine has little effect on memory acquisition. Pre-training of caffeine

impairs the habituation. Memory acquisition was impaired but memory retention was improved by the use of caffeine.

A lot of research shows that caffeine when administered before training impairs learning. It is in contrast to a general belief that caffeine improves memory and learning. Impairing effect of caffeine is stronger than memory consolidation because after training session, the caffeine would still be present in the blood. However; administration of caffeine after the training session improves memory consolidation. Caffeine administration after habituation did not improve retention. We can generalize that caffeine improves memory consolidation but at a very low levels and it depends on the type of memory task.

5. CONCLUSION

The conclusions which can be drawn from this study are 1) Higher doses of caffeine before training impairs memory retention. 2) Caffeine improves memory consolidation but at low doses. This improvement cannot be generalized for all type of behavior. 3) Caffeine at moderate doses improves memory retrieval before test.

6. CONFLICT OF INTEREST

Author has declared that there is no conflict of interests regarding the publication of this article.

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