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Effect of acute and chronic hypertension on short- and long-term spatial and avoidance memory in male rats

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Abstract

It has been demonstrated that hypertension can lead to coronary heart disease, heart failure, stroke, and memory loss. In this study we investigated the effect of acute and chronic hypertension on the avoidance and spatial learning and memory in rats. The forty male rats were divided into acute hypertensive, chronic hypertensive and control for each group rats. Hypertension was induced by Deoxy Corticosterone Acetate (DOCA)-salt method. DOCA was injected 30 mg/kg of body weight subcutaneously, twice a week. These rats received NaCl 1% instead of tap water for drinking throughout the experiment. The control group received normal saline injection with usual drinking water. Spatial learning and memory was investigated by Morris water maze test and passive avoidance learning by Shuttle box test in the rats after hypertension induction. Results showed that acute hypertension impaired short-term memory in passive avoidance learning. However, acute and chronic hypertension did not affect spatial learning and memory. These data suggest that simple uncomplicated hypertension does not remarkably alter cognition.

Keywords: Hypertension; Passive avoidance learning; Spatial memory; Rat

1. Introduction

Hypertension occurs when the blood is under increased pressure, pushing against the walls of blood vessels. Blood pressure between 120 to 140/80 to 90 is "pre-hypertension" and over 140/90 is definite hypertension. Hypertension can lead to coronary heart disease, heart failure, stroke, kidney failure, and other problems such as memory loss [1].

Hypertension can damage to blood vessels by causing a build-up inside the blood vessels and making them narrow. The brain must have a certain amount of blood flow to work normally. If the amount of blood flow is less than it should be, the brain cannot work efficiently. This can lead to memory loss and other symptoms [2]. While in the early part of the 20th century clinicians believed that essential hypertension was necessary for normal physiological function; more recent studies have clearly indicated the deleterious nature of chronic elevation of arterial pressure on many organ systems. Nearly 30 years ago, data from Wilke and Eisdorfer suggested that hypertension may lead to memory impairments [3] and many subsequent reports have supported this relationship in humans [4–8]. Several additional studies suggest that high blood pressure contributes to cognitive deficits in aging individuals [9,10], but other research indicated that cognitive function gradually declines with age in humans, irrespective of arterial pressure [11,12] and that this age-related impairment extends to spatial learning and memory tasks [13,14]. Previous study also supported the hypothesis that high blood pressure (especially existent over an extended period of time) would be responsible for cognitive deteriora-

Abbreviations: DOCA, Deoxy Corticosterone Acetate; SBP, systolic blood pressure; SHR, spontaneously hypertensive rats; ACE, angiotensin converting enzyme.

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tion in the elderly. Those with the highest blood pressure were found to have a more marked cognitive decline, especially in the velocity of memory recall and psychomotor coordination [15]. Together, demonstrated that chronic, severe hypertension did not impair spatial learning and memory in rats [16]. Thus, while clinical studies continue to suggest a relationship between hypertension and learning and memory impairments, the independent contribution of hypertension to memory dysfunction is unclear. The aim of the present study was to clarify further the effects of acute and chronic hypertension on short- and long-term spatial and avoidance memory in male hypertensive rats.

2. Materials and methods

2.1. Experimental animals

Forty male wistar rats (weight 200–250 g) were housed one in each cage and kept under controlled conditions (temperature 20–23 °C), relative humidity 40–70% and light/darkness cycle 12/12 h (lights on at 8:00 a.m.). Food and water were available ad libitum throughout the experiment.

2.2. Experimental design

After recovery, the animals were randomly divided into acute hypertensive, chronic hypertensive and control for each group rats. Hypertension was induced by Deoxy Corticosterone Acetate DOCA-salt treatment as previously described [17]. DOCA (Iran Hormone Co, Iran) was injected 30 mg/kg of body weight subcutaneously, twice a week, and tap water for drinking was replaced by 1% NaCl throughout the treatment period. In control groups, normal saline (N/S) was injected with the same volume.

The groups were as follow:

Group 1 acute hypertension ($n = 10$): DOCA-salt injection for 6 weeks.
Group 2 chronic hypertension ($n = 10$): DOCA-salt injection for 12 weeks.
Group 3 acute control ($n = 10$): N/S injection for 6 weeks.
Group 4 chronic control ($n = 10$): N/S injection for 12 weeks.

2.3. Blood pressure measurement

At the end of behavioral testing the animals were anesthetized with urethane (1.4 g/kg, ip), and supplementary doses (0.7 g/kg) were given when required. The left femoral artery was cannulated with polyethylene catheter (PE-50) filled with heparinized saline and the arterial tube was connected to a pressure transducer (Harvard). The arterial pressure was continuously recorded by both a Harvard polygraph and a computer program written in this laboratory. Comparison of blood pressure measurement in groups 1 and 2 showed that DOCA-salt hypertension was induced successfully.

2.4. Behavior

2.4.1. Morris water maze test

Animals were tested in a spatial version of Morris water maze test as described previously [18,19]. The Morris water maze consisted of a circular water tank (120 cm diameter, 50 cm height) that was partially filled with water (25 °C). The training was started by acclimating the rat to the task environment with 2 days of free-swimming in the pool with no platform. Each session lasted for 2 min. The pool was divided virtually into four equal zones, labeled N–S–E–W. A platform (10 cm diameter) was placed in one of the four maze zones (the target zone) and submerged 1.5 cm below the water surface. The platform remained in the same zone during the entire experiment (Fig. 1). The rats were required to find the platform using only distal spatial cues available in the testing room. The cues were maintained constant throughout the testing. The rats received four consecutive daily training trials in the following 5 days, with each trial having a ceiling time of 60 s and a trial interval of approximately 30 s. The rat had to swim until it climbed onto the platform submerged underneath the water. After climbing onto the platform, the animal remained there for 30 s before the commencement of the next trial. The escape platform was kept in the same position relative to the distal cues. If the rat failed to reach the escape platform within the maximally allowed time of 60 s, it was gently placed on the platform and allowed to remain there for the same amount of time. The time to reach the platform (latency in seconds) was measured.

2.4.2. Probe trial

A probe trial was performed (after 1 week for short term and 1 month for long term) where in the extent of memory consolidation was assessed. The time spent in the target zone

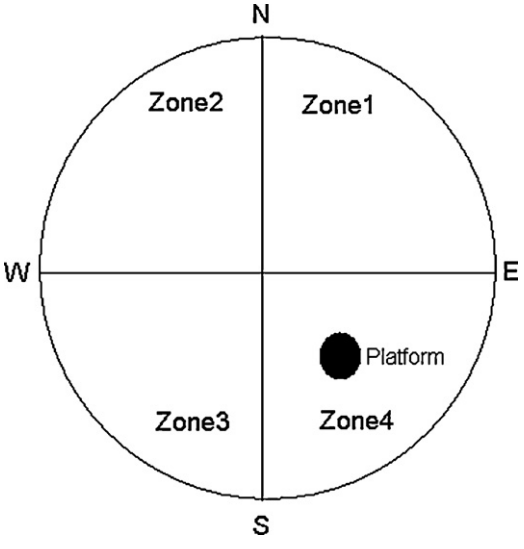

Fig. 1. Schematic diagram of tank and site of the platform.