

Research report

Spontaneously hypertensive, Wistar-Kyoto and Sprague-Dawley rats differ in performance on a win-shift task in the water radial arm maze

Koreen M. Clements^{a,*}, Patricia E. Wainwright^b^a Department of Psychology, University of Waterloo, Waterloo, Ont., Canada N2L 3G1^b Department of Health Studies & Gerontology, University of Waterloo, Waterloo, Ont., Canada N2L 3G1

Received 13 July 2005; received in revised form 9 September 2005; accepted 19 September 2005

Available online 15 November 2005

Abstract

The spontaneously hypertensive rat (SHR) is a commonly used animal model of attention deficit hyperactivity disorder. Previous literature is inconclusive with respect to the exact nature of memory impairments in this strain. The objective of this study was to assess spatial memory as measured by performance of male SHR, Wistar-Kyoto (WKY) and Sprague-Dawley (SD) rats on a win-shift version of the water radial arm maze. On this task, all strains made more errors on Trial 4 when the mnemonic demand was highest, and showed a similar response when the delay was increased from 60 s to 2 h on Week 3. Both SHR and WKY rats made more reference memory errors than SD, however, SHR showed minimal improvement over weeks. The increase in errors may be due to a greater inclination of SHR and WKY to use a chaining strategy of entering consecutive arms than SD. Furthermore, the number of incomplete arm entries into reference memory arms decreased over weeks in WKY and SD, but increased in SHR, suggesting increased impulsivity of SHR at the later stages of testing. Although based on number of errors, the data indicate that SHR may have memory deficits, the data relating to arm entries suggest that the minimal improvement in SHR over weeks may have been due to greater impulsivity in the later weeks, rather than defective memory. Thus, these findings are consistent with SHR having impairments with selection of appropriate behavioural responses in a goal-directed task.

© 2005 Elsevier B.V. All rights reserved.

Keywords: Attention deficit hyperactivity disorder (ADHD); Spatial memory; Spontaneously hypertensive rats (SHR); Sprague-Dawley rats; Water radial arm maze (wRAM); Win-shift task; Wistar-Kyoto rats (WKY)

1. Introduction

The spontaneously hypertensive rat (SHR) is a commonly used animal model of attention deficit hyperactivity disorder (ADHD). ADHD is a behavioural disorder that affects 4–12% of grade school children and is more prevalent in males than females with a ratio of 3:1 [41]. The symptoms, which include impulsivity, hyperactivity and an inability to sustain attention, are thought to arise from deficits in executive functioning, including working memory, attentional control, and decision-making [2]. Neurodevelopmental theories of ADHD suggest that there is reduced activity of dopamine systems in the cortical regions, leading to cognitive deficits, and over activity in the subcortical regions, leading to behavioural hyperactivity [33].

The spontaneously hypertensive rat is considered an appropriate model of ADHD because it displays the key attributes, such as hyperactivity, impulsiveness, and difficulties in sustaining attention (face validity), corresponds to the theoretical rationale, such as abnormalities in the dopaminergic system (construct validity), and is able to predict new aspects of behavioural, genetic, and neurobiological characteristics of the condition [34]. Although cognitive impairments are not a definitive characteristic of ADHD, many individuals with ADHD have lower IQs, reading impairments and learning difficulties [13,35]. There is also evidence to suggest that individuals with ADHD may have verbal [17,24,9] and visuo-spatial [24,39] working memory deficits. Thus, SHR has the potential to make a useful contribution by describing the pattern of memory deficits that may apply to ADHD. This paper describes the first of a series of studies in which we addressed this question. All these studies were conducted using different versions of the water radial arm maze in order to assess strain differences in spatial learning, procedural learning, and conditioned emotional

* Corresponding author. Tel.: +1 519 888 4567x5060; fax: +1 519 746 2510.
E-mail address: kmfrisa@uwaterloo.ca (K.M. Clements).

responses. In this paper, we describe the outcome with respect to the spatial learning abilities of SHR in comparison to Wistar-Kyoto (WKY) and Sprague-Dawley (SD) rats.

Previous work examining spatial memory in SHR has used either the Morris water maze or the land radial arm maze. In the place-learning version of the Morris water maze, an animal must use spatial information in order to locate a stationary hidden platform. As the position of the platform in relation to the extra-maze cues stays constant over trials, this is an example of what is referred to in animal studies as reference memory [11]. Some studies indicate that SHR were impaired compared to controls [14,15,23,5,6]; in contrast, other studies report that SHR performed better than controls [40,38,13]. However, it is important to note that these studies varied in terms of the control group used, making it difficult to draw conclusions. This is because the interpretation of SHR performance has been shown to be dependent on the control strain used. For example, in a study that included both SD and WKY controls, SHR were worse than SD, but better than WKY [7,8]. Similarly, in the delayed matching-to-place (DMP) version of the Morris water maze SHR were worse than SD in terms of their ability to find the platform, but better than WKY [43]. In the DMP task, the platform is located in a different position for each testing session; therefore, in order to solve this task, an animal must use both long-term information about the spatial relationship between extra-maze cues (reference memory) and short-term information about the exact platform location that is relevant only to the specific testing session. This type of short-term information is an example of what is considered working memory in animal studies [10] (also referred to as episodic short-term memory [11]). Previously in our laboratory, we also found that SHR performed better than WKY on the DMP task; however, as the WKY did not appear to use a short-term memory strategy to solve the task it is difficult to draw conclusions as to how SHR would have compared with a strain showing normal performance [4].

Similarly inconsistent findings are seen with respect to the land radial arm maze, where food is used as the reward. Successful performance on this maze requires the use of a spatial win-shift strategy, where an animal must learn during a testing session to shift away from the arm choices that were rewarded previously. In the standard version of the radial arm maze, where all arms are baited, the task examines spatial working memory. SHR made more errors on this task than WKY and Wistar [18]. In addition, when compared to Wistar, SHR were also found to make more errors after short (5 s) and long (1 h) delays [27]. In contrast, another study found that SHR made fewer errors than WKY [25]. The win-shift task can also be used to measure reference memory by baiting only a constant sub-set of the arms and, under these conditions, SHR made fewer total and fewer reference memory errors than SD [42]. It should be noted that all these findings refer to studies conducted in young (3-month-old) rats, and so cannot be related to the effects of chronic hypertension.

Inbred WKY rats are the most frequently used control strain in studies of SHR, because both the SHR and WKY inbred strains were derived originally from the same outbred albino

Wistar-Kyoto stock [3]. However, recent literature suggests that the WKY may not be the best control group for several reasons: (1) their behavioural profile differs from standard control strains [30,8,12], (2) they may not be as genetically similar to the SHR as is generally believed [22], and (3) they may be better employed as a potential animal model of depression [16,31,37]. Therefore, in the present study, in addition to WKY, the outbred albino SD strain was used to represent the “normal” laboratory rat.

In the present study, we used a water version of the radial arm maze, which eliminates some of the disadvantages of the dry land version, such as food deprivation and odour trails [19]. This task measured both working and reference memory, with each testing session comprising four trials, where on each trial the animal used spatial extra-maze cues to locate one of four hidden platforms in an eight-arm radial arm maze submerged in a circular tank of water. At the end of each trial the located platform was removed for the duration of the testing session, such that memory demands increased over trials. Once the animals were trained, the mnemonic demands of the task were increased further by lengthening the delay between Trials 2 and 3 from 60 s to 2 h. As it is difficult to reconcile the inconsistencies in the literature cited above to support a directional hypothesis with respect to WKY, the working hypothesis was that SHR would perform differently from the WKY control, and show impairments relative to the SD control.

2. Materials and methods

2.1. Animals

This study was approved by the Animal Care Committee at the University of Waterloo in compliance with the Animals for Research Act of Ontario and the Guide for the Care and Use of Experimental Animals from the Canadian Council on Animal Care. Sample size calculations indicated 16 animals in each group were needed to support an effect size of 1 SD ($\alpha = .05$, $\beta = .80$). Therefore, 4-week-old male Spontaneously Hypertensive ($n = 16$), Wistar-Kyoto ($n = 16$), and Sprague-Dawley ($n = 16$) rats obtained from Charles River Laboratory, Quebec, were used in these studies. Rats of the same strain were group-housed (four to five per cage) and cages contained plastic tubes to enrich the environment. Water and laboratory chow (5001, PMI Nutrition International, St. Louis, MO) were available ad libitum. Animals were kept under a reverse 12-h light:12-h dark schedule so that behavioural testing could be done during the dark cycle when rats are normally active. The study was conducted in two cohorts, with all strains represented equally in each cohort, and behavioural testing began when rats were 6 weeks old. Thus, the animals in this study can be considered juvenile, which is consistent with their use as a model of ADHD, which is recognized as a developmental condition. Experimenters were blind to strain during behavioural testing and scoring of the data.

2.2. Apparatus

The water radial maze consisted of an eight-arm maze (55 cm centre diameter, 35 cm arm length, 15 cm arm width, 35 cm height) submerged in a circular white plastic tank (1.52 m diameter, .50 m height) that was filled with water to a depth of 20 cm. The temperatures of both the water and the room were maintained at 23 ± 1 °C. Soluble, non-toxic, white, and black Temptra paint was stirred into the water in order to obscure the location of the movable escape platforms (14 cm $\times$ 14 cm) that were positioned no more than 2 cm below the surface of the water. A variety of black and white geometric shapes were located throughout on the walls of the testing room.

Download English Version:

<https://daneshyari.com/en/article/4316247>

Download Persian Version:

<https://daneshyari.com/article/4316247>

[Daneshyari.com](https://daneshyari.com)