Physiology & Behavior 162 (2016) 52–60

Contents lists available at ScienceDirect

Physiology & Behavior

journal homepage: www.elsevier.com/locate/phb

Sex-specific effects of daily exposure to sucrose on spatial memory performance in male and female rats, and implications for estrous cycle stage

Kirsten N. Abbott [a], Margaret J. Morris [b], R. Fred Westbrook [a], Amy C. Reichelt [a],*

[a] School of Psychology, UNSW Australia, Sydney 2052, Australia
[b] School of Medical Sciences, UNSW Australia, Sydney 2052, Australia

HIGHLIGHTS

- Examined the impact of sucrose consumption on recognition memory tasks.
- Sucrose exposed male rats were impaired at place and object-in-place recognition.
- Sucrose exposed female rats were not impaired at place recognition during proestrus.
- Role for estrogen in facilitating hippocampal dependent spatial memory.

ARTICLE INFO

Article history:
Received 30 November 2015
Received in revised form 22 January 2016
Accepted 25 January 2016
Available online 29 January 2016

Keywords:
Spatial memory
Sucrose
Hippocampus
Estrogen
Sex
Synaptic plasticity

ABSTRACT

Excessive consumption of sugar sweetened drinks is proposed to produce functional changes in the hippocampus, leading to perturbations in learning and memory. In this study we examined the impact of 2 h daily access to 10% sucrose (or no sucrose in controls) on recognition memory tasks in young male and female rats. In Experiment 1 we tested rats on memory tasks reliant on the hippocampus (place recognition), perirhinal cortex (object recognition), and a combination of hippocampus, prefrontal cortex and perirhinal cortex (object-in-place memory). Exposure to sucrose for 2 h a day for 14 days prior to behavioral testing did not affect object recognition, but impaired spatial memory to an extent in both male and female rats. Male rats exposed to sucrose were impaired at both place recognition and object-in-place recognition, however female rats showed no impairment in object-in-place performance. Plasticity within the hippocampus is known to increase during the proestrus phase of the estrous cycle and is related to higher levels of circulating estrogens. In Experiment 2 we tested place recognition and object-in-place memory in 10% sucrose exposed or non-exposed control female rats both during the metestrus (low estrogen) and proestrus (high estrogen) phases of their cycle on place recognition and object-in-place memory. Both sucrose exposed and control female rats were able to perform place object-in-place recognition correctly during metestrus and proestrus, however sucrose exposed rats were only able to perform place recognition correctly during proestrus. This indicates that when hippocampal function is compromised, endogenous estrogens may boost memory performance in females, and that males may be at more risk of high sugar diet induced cognitive deficits.

1. Introduction

High sugar diets are a major contributing factor to the increased rates of obesity worldwide and are associated with the increase of metabolic diseases, cardiovascular diseases and type 2 diabetes [1–3]. Sugar-sweetened beverages (SSBs) account for 80% of the increase in added sugar consumption from 1962–2000 [4]. Of particular concern is the fact that sugar intake is highest in adolescents and young adults than any other age group [5, 6]. Thus we sought to determine the behavioral effects of SSB consumption in young rats by interrogating effects on memory processes.

Emerging research has demonstrated that high energy diets are capable of compromising cognitive function in humans, as well as exacerbating cognitive decline and dementia [7, 8]. The hippocampus, a region critical for spatial learning and memory, is particularly vulnerable to the effects of high energy diets [9]. Deficits in cognitive flexibility and hippocampal-dependent memory have been found in both healthy middle-aged [10] and young adults [11] with self-reported higher intake of refined sugar than those with less intake, independent of age and body mass index (BMI).

---

* Corresponding author.
E-mail address: a.reichelt@unsw.edu.au (A.C. Reichelt).

http://dx.doi.org/10.1016/j.physbeh.2016.01.036
0031-9384/

Studies have examined the effects of high sugar diets in rats on spatial memory in the water maze [12–14], Barnes maze [15] and place recognition tasks [16], suggesting excessive dietary sugars negatively impacts hippocampal-dependent memory consolidation and retrieval. Exposure to high sugar diets has been shown to reduce hippocampal dendritic spine density, reduce long-term potentiation [12], reduce hippocampal neurogenesis [17] and increase levels of pro-inflammatory markers [9, 18]. These studies allowed continuous access to the high-sugar diet conditions, however recent research has demonstrated that 2 h daily access to 10% sucrose solution for 4 weeks evoked an enduring impairment in recognition memory for objects in a spatial arrangement measured by the object-in-place task in male rats [19].

The object-in-place task has elements of object recognition and object location tasks used to assess rodent object memory [20–24]. In this task rats explored the location of four novel unique objects in an open field during the sample phase. After a delay interval, a test phase was administered with the locations of two objects reversed. Increased investigation of the moved objects indicated memory for these objects and their original locations. Spontaneous exploration memory tasks in male and female rats have been used to establish sex effects on recognition memory [25]. In spatial memory tasks, male rodents have been shown to demonstrate performance that is superior to female conspecifics [26–28]. However, the performance of female rodents on object recognition and object location tasks often is enhanced by elevated levels of ovarian steroids, in particular estrogens including estradiol, which increase when ovulation occurs during the proestrus period of the estrous cycle [29]. Simulation of proestrus by injection of estradiol to ovariectomized female rats has been shown to enhance performance on object and place recognition memory [30]. In the object-in-place task, both male and female rats were able to discriminate moved from unmoved objects after a brief 5 min delay [25]. However, gonadally intact males, but not diestrus (low estrogen) females, were able to discriminate object locations after a 30 min delay. Furthermore, ovariectomized female rats treated with estradiol and progesterone showed memory for object configurations following a 60 min delay while ovariectomized vehicle-treated females and gonadally intact males did not. These results indicate that female rats can outperform males on the object-in-place task, particularly when circulating levels of estrogens are elevated and when recognition memory is challenged by an extended delay.

In the current studies we utilized memory tasks that examine the spontaneous exploratory behavior of rodents to test memory. As sex differences have been observed in spontaneous exploration memory tasks, Experiment 1 sought to establish whether sex influenced memory performance following sucrose exposure. Male and female rats were tested on object and place recognition, which are known to be sensitive to hippocampal function (place recognition) [31, 32] and perirhinal cortex function (object recognition) [33, 34], as well as object-in-place recognition. In Experiment 2 we sought to dissect the impact of estrous phase by examining spatial memory performance in female rats during metestrus (low estrogen) and proestrus (high estrogen). Thus, Experiment 2 aimed to establish whether endogenous ovarian hormones influence performance in tasks dependent on hippocampal plasticity – object-in-place and place recognition memory – in sucrose exposed and control female rats.

2. Methods

2.1. Experiment 1

2.1.1. Subjects

Male ($N = 24$) and female ($N = 24$) albino Sprague Dawley rats (supplied by Animal Resources Center, Western Australia) arrived in the laboratory at 3 weeks of age (weight range males 50–58 g, females 45–50 g). They were housed in plastic cages (60 cm length × 26 cm high × 40 cm wide) with 4 rats per cage in a colony room that was on a 12 h light-dark cycle (lights on at 7:00 am), maintained at a temperature of 21 ± 2 °C and a humidity of $55 \pm 5\%$. Rats were acclimated to the laboratory for 7 days during which they were handled each day. Behavioral testing occurred in the light phase between 11.00 am and 4.00 pm. The experimental procedures were approved by the University of New South Wales Animal Ethics Committee in accordance with the Animal Code of Practice for the Care and Use of Animals for Scientific Purposes.

2.2. Behavioral procedures

Fig. 1A shows the timeline of the behavioral experiments. Three cages of male and three cages of female rats were randomly allocated to the sucrose and control conditions. Each day from day 1–day 28 (postnatal days (P) 28–56), rats in the sucrose condition received 2 h access (between 8.00 am and 10.00 am) to a 10% sucrose solution (w/vol; CSR® white sugar; Victoria, Australia) in their home cages. The sucrose solution provided a caloric density (1.7 kJ/ml) similar to that of commonly available sugar-sweetened beverages. Consumption was recorded by weighing the bottles before and after the 2 h sucrose access period for each of the three cages of males and the three cages of females. All rats had ad lib access to chow and water at all times.

Rats were tested between days 14–28 of sucrose access (P42–P56). Each test took place between 11.00 am and 4.00 pm. Each rat was tested in the object, place, and object-in-place recognition tasks. All rats were tested on the object and place recognition tasks (counter-balanced for order) and then on the object-in-place task. To minimize interference effects that may arise from conducting multiple recognition tests we varied the sample objects to ensure they are perceptually different in terms of material, color, shape and size (see Section 2.2.1) as overlapping features can further tax recognition memory [35]. Furthermore, the familiar holding cage during the delay period may further prevent interference arising between the sample and test phase.

2.2.1. Object and place recognition

The apparatus consisted of an open-field arena (50 cm × 50 cm × 60 cm) constructed from black PVC plastic. A video-camera positioned directly above the arena recorded test behavior to a DVD. The room was dimly lit (25 Lux) by an overhead light. The objects used were commercial products (e.g., glass beer bottles, ceramic coffee mugs, plastic water bottles, tin cans, glass jars) that differed in height (7.5–15 cm) and width (4.5–8 cm). Rats were familiarized with the arena for 10 min per day on 2 consecutive days, and testing occurred on the following day. Half of the rats in the sucrose and control conditions were first tested on the object recognition task and the place recognition task on the following day, and the remaining rats in each condition were tested on the place recognition task first and the object recognition task on the following day. Each task consisted of a familiarization and test phase. The familiarization phase in both tasks involved placing each rat into the arena which contained two identical objects. The objects were 15 cm apart and located in the center of the arena. The rat was then removed after 5 min and placed into a holding cage for 5 min. During this time, the arena and the objects were cleaned with 70% ethanol. The rat was then returned to the arena for the test phase. In the object test, two objects occupied the same locations as before; one was an identical copy of the objects that had been present in the familiarization phase but the other was a new object but the other was a new object (Fig. 1C). If rats remembered the identity of the original objects, they spent more time exploring the new than the old object [20]. In the place test, two identical copies of the objects that had been presented were again present; one of the objects occupied one of the original locations in the center of the arena but the other object was now located in one of the four corners of the arena (counter-balanced across rats) (Fig. 1D). If rats remembered the original location of the objects, they spent more time exploring the object in the new location than the object that remains in the same location [32]. Each test lasted for