



## Research report

# High-sucrose diets in male rats disrupt aspects of decision making tasks, motivation and spatial memory, but not impulsivity measured by operant delay-discounting



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## HIGHLIGHTS

- Young male rats consumed 10% sucrose solution for 28 days.
- Group differences were observed in place recognition and forced choice alternation.
- Sucrose consumption alters spatial and working memory.
- No group differences were observed in instrumental delay-discounting.
- Sucrose consumption does not alter this aspect of impulsivity.

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## ABSTRACT

Excessive consumption of sugar sweetened drinks is proposed to produce functional changes in the hippocampus and prefrontal cortex, leading to perturbations in behavioural control. Impairments in behavioural control have been observed in obese people on tasks that involve making choices, including delay-discounting, indicative of increased impulsivity. In this study we examined the impact of 2 h daily access to 10% sucrose (or no sucrose in controls) in young male rats on behavioural tasks reliant on hippocampal function including delay-discounting, T-maze forced choice alternation and place recognition memory, as well as progressive ratio to measure motivation. We observed deficits in place recognition memory and T-maze forced choice alternation, indicative of hippocampal deficits in rats with a history of sucrose consumption. Moreover, rats with a history of sucrose consumption were less motivated to lever press for rewards on a progressive ratio schedule. However, rats with a history of sucrose consumption performed equally to control animals during the delay-discounting task, suggesting that they discounted for reward size over a delay in a manner comparable to control animals. These findings indicate that high-sucrose diets impact on spatial and working memory processes, but do not induce impulsive-like choice behaviours in rats, suggesting that unhealthy diet choices may not influence this aspect of decision-making behaviour.

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## 1. Introduction

Overconsumption of diets high in refined sugar is not only linked to the increasing rate of obesity worldwide, but has been linked to cognitive decline, particularly impairments in memory [1–3]. Studies in both human and rodent models have provided evidence of specific hippocampal-dependent learning and mem-

ory impairments with Western-style diet (high refined sugar and saturated fat) consumption [3]. Deficits in cognitive flexibility and hippocampal-dependent memory have been found in both healthy middle-aged [4] and young adults [5] with self-reported higher intake of refined sugar than those with less dietary sugar intake, independent of age and body mass index (BMI). Recent research in rats from Beilharz et al. [6] suggest that excessive refined sugar intake alone may have a greater negative influence on hippocampal function than excessive intake of sugar and saturated fat combined, particularly during the early stages of cognitive decline. In partic-

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ular, studies with rodents have demonstrated that spatial memory is disrupted by consumption of high-sucrose diets [7–10].

The persistence in consumption of these diets in spite of negative physiological changes is proposed to be related to the highly rewarding properties of high sugar diets, as consumption leads to activation of the mesocorticolimbic dopamine reward system and alteration in dopamine receptor levels in brain regions essential for reward processing and behavioural control [11]. However, consumption of high sugar foods also alters behaviour such as goal-directed action [7,12], motivation [13,14] and aspects of decision making [10]. These behavioural changes may predicate the formation of maladaptive or impulse-driven eating behaviours leading to the development of obesity.

Impulsivity is a multi-dimensional construct describing behavioural tendencies to act prematurely, engage in risk-taking and sensation-seeking, and to make suboptimal choices or actions [15]. Impulsive choices can be defined by an organism's preference for a small, immediate reward over a larger, delayed reward. The behavioural process of delay-discounting is thought to underlie impulsive choice (i.e., the devaluation of a reward as the delay to its receipt increases). Delay-discounting is a measure of the degree by which an individual is driven by immediate gratification vs. the prospect of larger, but delayed, rewards.

The hippocampus has been associated with choices that involve waiting, which may relate directly to the representation of time, as evidence suggests that the hippocampus is specialised to represent temporal aspects of events [16–18]. Hippocampal damage has also been demonstrated to impact upon decision-making behaviours, in particular deciding between immediate and delayed rewards. Patients with hippocampal damage make disadvantageous choices that are random or poorly suited for developing strategies that benefit them in the long term [19–21]. Similarly, experiments in rats with hippocampal lesions reveal analogous deficits, indicative of an unwillingness to make choices that require waiting, even for high-valued rewards [22–27]. Previous studies with hippocampal lesion rats have been conducted where a choice was imposed between a maze arm that was reinforced on a continuous reinforcement schedule and one that was reinforced on a partial reinforcement schedule [28]. Hippocampal lesion and sham-lesion controls animals equally preferred the continuously reinforced arm. However, when a 10 s delay was introduced in the continuously reinforced arm, the hippocampal lesioned animals switched preference to the arm with partial, but still immediate reward; indicating that hippocampal lesions impaired tolerance to delayed rewards, despite a decreased probability of gaining reinforcement. Another feature of delay-discounting is its sensitivity to reward magnitude, i.e. the bigger the reward, the longer the animal is willing to wait. Previous findings have demonstrated that hippocampus lesions decrease the value of the delayed reward, suggesting an important role of the hippocampus in value-associated decision making [24,25].

Relative reinforcing value, delay of gratification and delay-discounting paradigms have been used to study the impact of obesity-inducing diets on behaviour. A progressive ratio task to measure the breakpoint (a measure of a rat's willingness to perform a number of responses for a reward) was conducted to establish whether motivation to respond for food rewards differed across groups. The "breakpoint" is the maximal number of responses an animal is prepared to make to procure reinforcement, and is used as a measure of the incentive value of the reward [29,30]. This task has previously been shown to be sensitive to a history of sucrose consumption in young rats [13,14]. Palatable food reinforcement availability and difficulties in delaying gratification are risk factors for weight gain in young people, and both are related to individual differences in overweight/obesity [31]. Human studies have further identified that obese participants demonstrate

risky patterns of decision-making in the Iowa Gambling Task [32] and exhibited more impulsive patterns of choice for monetary outcomes than non-obese participants on delay-discounting tasks [33,34].

Tasks that require behavioural restraint, failures of which indicate impulsivity, are impacted by high-sucrose diets. Excessive consumption of high sugar soft drinks has been associated with mental distress, hyperactivity and conduct problems that may be related to impulsive behaviours were highest in adolescents who self-reported high levels of soft drink consumption (>800 ml/day; [35]). A recent study of adolescents used a Go/No Go task to measure response control and sustained attention in male and female participants who consumed large quantities of soft drinks. The results demonstrated greater inhibitory problems in males, but not females [36].

Mangabeira et al. [37] previously demonstrated the effects of 30 days of sucrose consumption followed by a 7-day period of abstinence in rats, which altered performance of a differential reinforcement of low rate (DRL) schedule. In this procedure a minimum interval of time (20 s) was required between lever presses to procure water as reinforcement, and the difficulty an animal has in withholding a response across an increasing delay in reinforcement is considered an index of impulsivity. Only animals that were subjected to sugar abstinence presented impaired DRL performance [37], indicative of an impulsive phenotype. This impairment in DRL performance has also been observed in rats with hippocampal lesions [38], suggesting that sucrose consumption impacts on hippocampal mediated choice behaviour and the ability to control responding.

Thus, with evidence demonstrating that high-sucrose diets impact negatively on hippocampally-mediated cognitive control mechanisms, we sought to examine the effect of a high-sucrose diet preparation in young rats on a delay-discounting task requiring choices between large and small rewards. The rats with a history of sucrose consumption would be expected to shift to the low, but immediate reward lever at shorter delays than control rats, generating a steeper discounting curve, indicative of intolerance to delays. To further study the impact of sucrose consumption on choice behaviour we utilised a progressive ratio task to modulate reinforcement availability, and T-maze forced choice alternation to examine working memory for the location of a reward, as it has been proposed that deficits in the executive control system of working memory may explain some of the cognitive and behavioural problems exhibited by impulsive people [39,40]. Disruption of performance of these tasks could afford a rationale by which an unhealthy diet may influence the development of maladaptive behaviours, such as the observed impairment in delayed gratification seen in obesity [31], providing a behavioural mechanism that underpins overconsumption.

## 2. Methods

### 2.1. Subjects

Male Sprague-Dawley rats (N = 48) were used across the experiments (Experiment 1 & 2, N = 24; Experiment 3, N = 24). Rats arrived in the laboratory at 3 weeks of age, diet administration began aged 4 weeks. Rats were housed in groups of 4 in plastic cages (26 × 40 × 60 cm) on a temperature of 21 ± 2 °C on a 12 h light/dark cycle (lights on at 7 a.m.). Rats were weighed twice a week on Tuesday and Friday and were given ad libitum access to water and chow. All procedures were approved by the UNSW Animal Ethics Committee (Experiments 1 and 2) and RMIT Animal Ethics Committee (Experiment 3).

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