

# Neurobehavioral Effects of High-Sugar Diet Assessed Using IntelliCage: Impairments in Learning, Memory, Cognitive Flexibility and Addiction-like Behavior in Mice

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## Abstract

Excessive consumption of dietary sugar has been linked to metabolic and neurocognitive dysfunction, yet the behavioral consequences remain insufficiently characterized. Using the IntelliCage automated behavioral system, we investigated the long-term impact of a high-sugar diet (HSD) on learning, memory, cognitive flexibility, activity, and addiction-like behaviors in mice. Adult swiss albino mice were divided into control (standard chow) and HSD groups for 6 weeks. Behavioral tasks included place learning, reversal learning, activity monitoring, and sucrose preference. Mice on HSD exhibited deficits in acquisition and retention of memory tasks, impaired reversal learning indicative of reduced cognitive flexibility, altered locomotor activity, and enhanced sugar preference resembling addiction-like behavior. These findings suggest that chronic HSD consumption impairs cognitive performance in mice, with implications for understanding diet-related neurocognitive disorders in humans.

**Keywords:** High-sugar diet; IntelliCage; Memory; Cognitive flexibility; Addiction-like behavior; Mice

## 1. Introduction

The global increase in sugar consumption has raised concerns about its potential impact on health, not only in terms of obesity and metabolic syndrome but also regarding cognitive and behavioral outcomes [1,2]. Epidemiological studies suggest links between excessive sugar intake and cognitive decline, particularly in hippocampus-dependent memory [3]. Animal models have shown that high-sugar diets can impair learning, memory, and synaptic plasticity [4–6].

Traditional behavioral assays for rodents often involve human interference, which may introduce bias and stress. The IntelliCage system provides an automated, high-throughput, and ethologically relevant platform for behavioral assessment in group-housed mice [7]. This system allows continuous monitoring of activity, learning, and preference behaviors under minimally invasive conditions.

The present study aimed to evaluate the effects of chronic high-sugar diet consumption on neurobehavioral functions in mice, focusing on memory, activity, cognitive flexibility, and addiction-like behaviors using IntelliCage paradigms.

## 2. Materials and Methods

### 2.1. Animals and Housing

Adult male swiss albino mice (n=4, 8 weeks old) were housed in groups under standard 12:12 h light-dark cycles. All experimental procedures were approved by the Institutional Animal Ethics Committee.

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## 2.2. Diets

Control group (Group-1) (n=2): standard rodent chow and water ad libitum. High-sugar diet (HSD) group (Group-2) (n=2): chow supplemented with 25% sucrose solution as drinking water. The dietary regimen lasted 6 weeks.

## 2.3. IntelliCage System

The IntelliCage (TSE Systems, Germany) consists of four operant conditioning corners equipped with RFID detectors, doors, and lick sensors. Mice were identified via RFID microchips.

## 2.4. Behavioral Protocols

- Adaptation Phase: all corners accessible, free exploration.
- Place Learning Task: mice learned to associate one corner with water access.
- Reversal Learning (Cognitive Flexibility): correct corner shifted after acquisition.
- Activity Monitoring: spontaneous visits and nose-pokes recorded.
- Sucrose Preference Test (Addiction-like behavior): preference for sucrose vs water monitored.

## 2.5. Data Analysis

Behavioral parameters (learning curves, error rates, corner visits, lick counts) were extracted using IntelliCage software. Group comparisons were performed using t-tests, with significance set at  $p = 0.05$  (Fig. 1C).

## 3. Results

### 3.1. General Activity

HSD mice displayed decreased nosepokes and corner visits and reduced exploratory variability, suggesting lesser activity with restricted patterns (Fig. 1A, 1B, 1C).

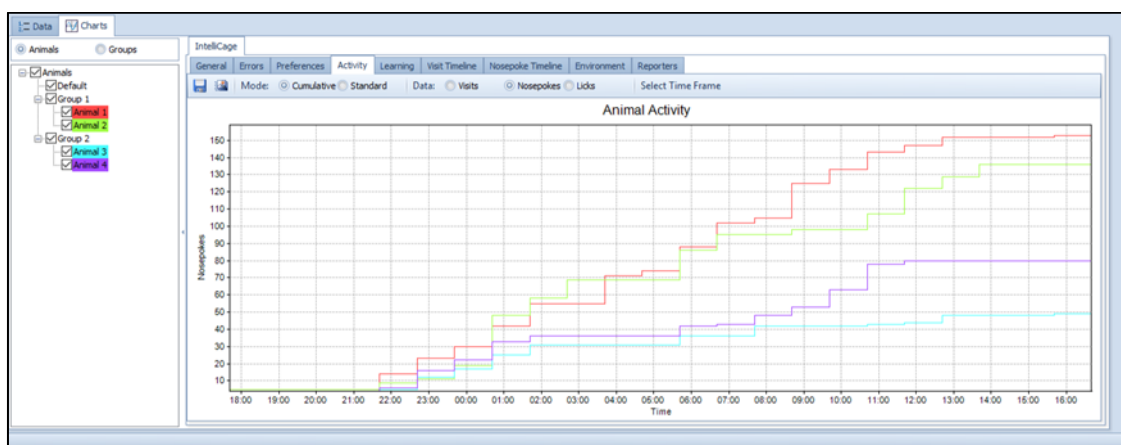


Figure 1A Graph representing the number of nosepokes in control(Group-1) vs. high-sugar diet (HSD) mice(Group-2)

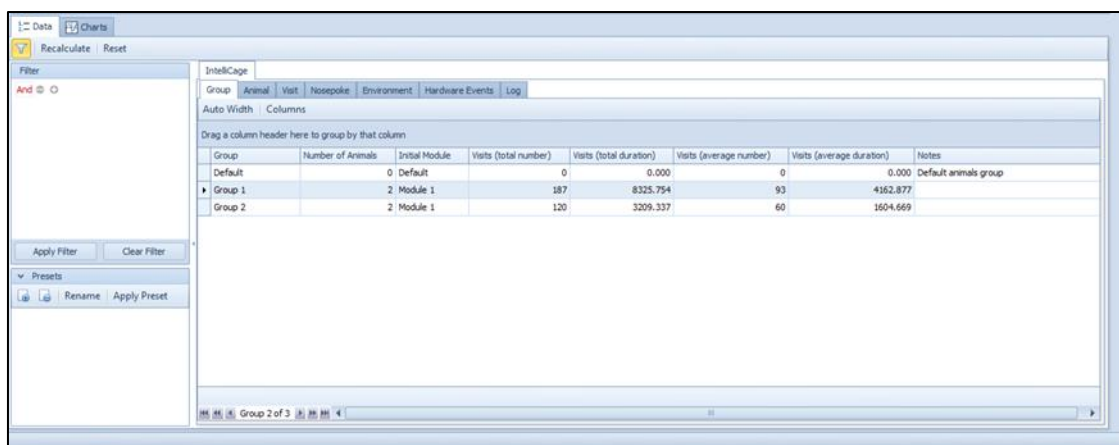


Figure 1B Table showing the number of corner visits in control(Group-1) vs. high-sugar diet (HSD) mice(Group-2)

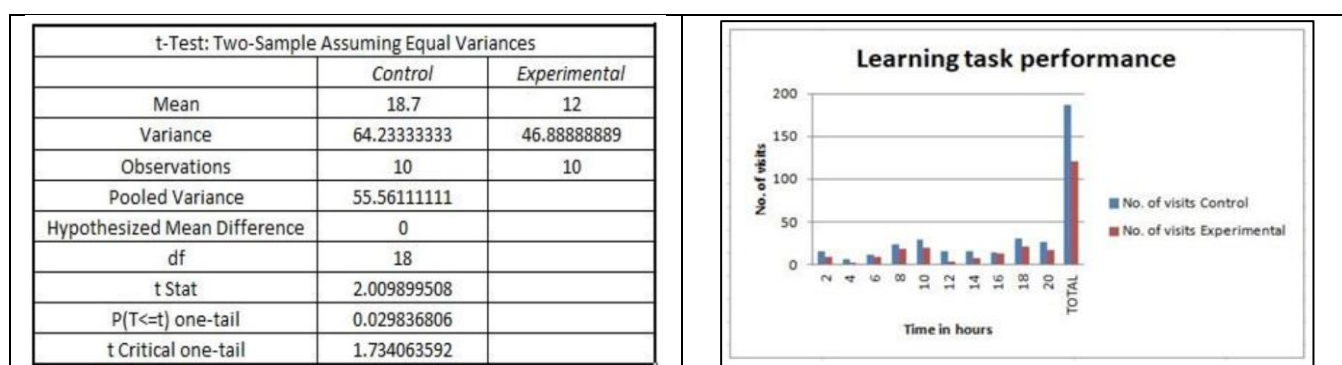


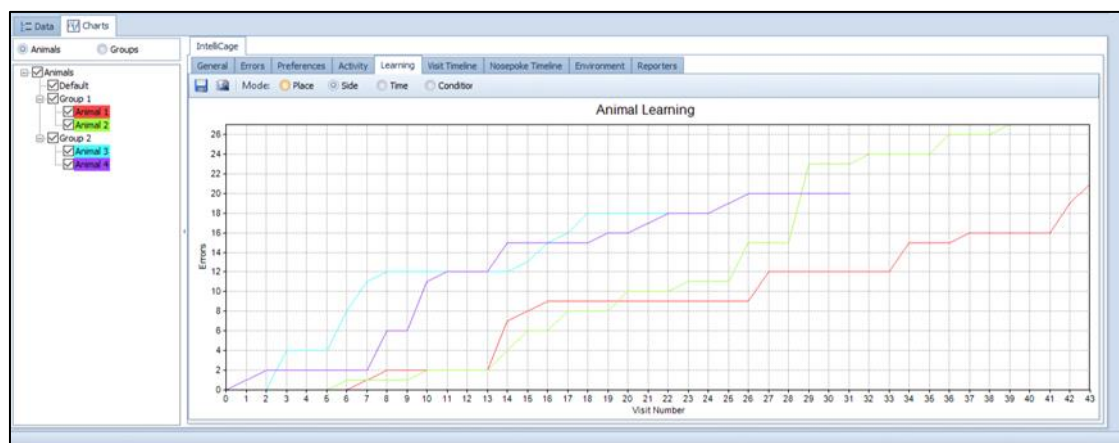
Figure 1C Statistical analysis (t-Test)

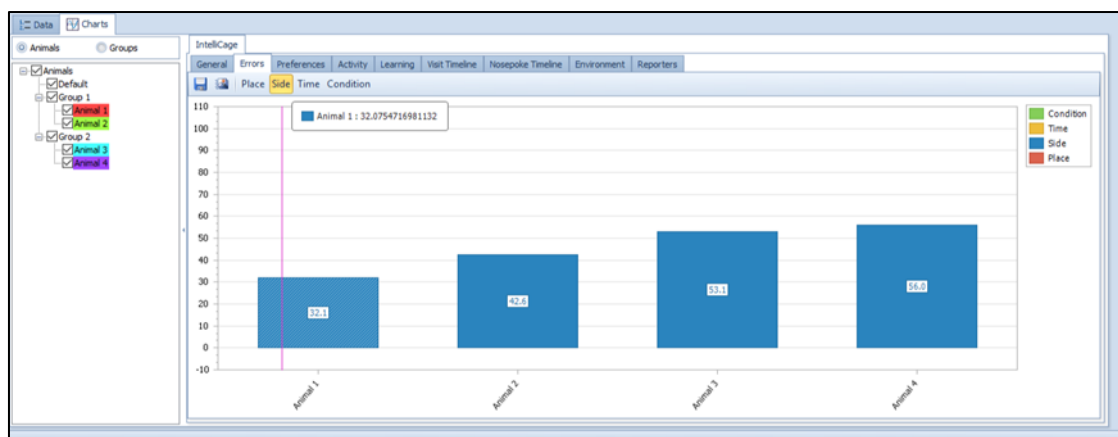
**Figure 1** General Activity Patterns

### 3.2. Learning and Memory

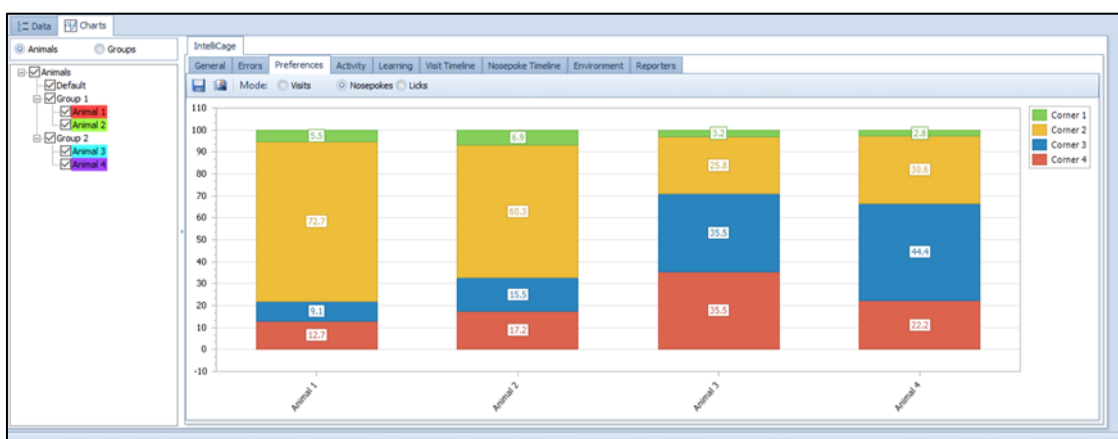
During place learning, control mice quickly acquired the correct corner (corner-2), while HSD mice required significantly more trials and made more errors for acquiring the correct corner (corner-3) (Fig. 2A, 2B, 2C). Retention tests confirmed impaired memory consolidation in HSD mice.

Figure 2 Learning and Cognitive Flexibility

**Figure 2A** Learning and error curves of control(Group-1) and HSD(Group-2) mice during place learning



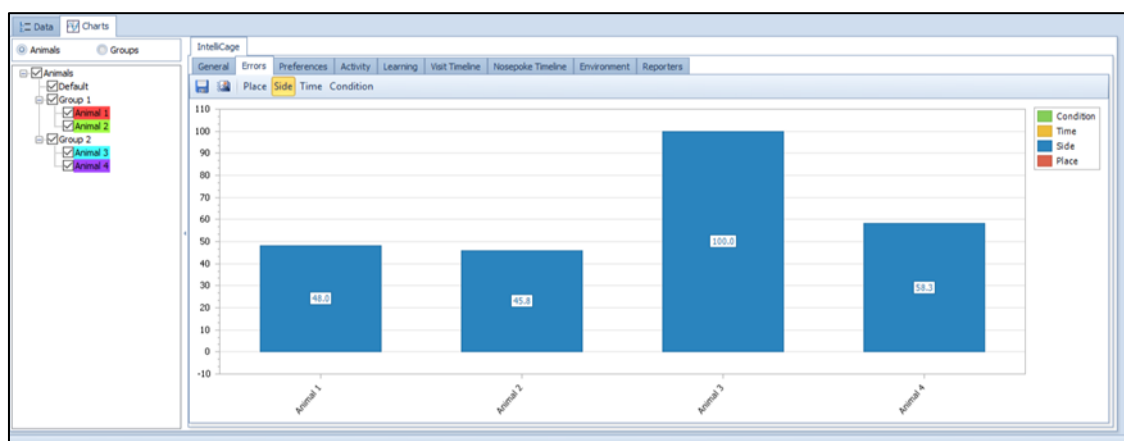
**Figure 2B** Error rates of control(Group-1) and HSD(Group-2) mice during place learning



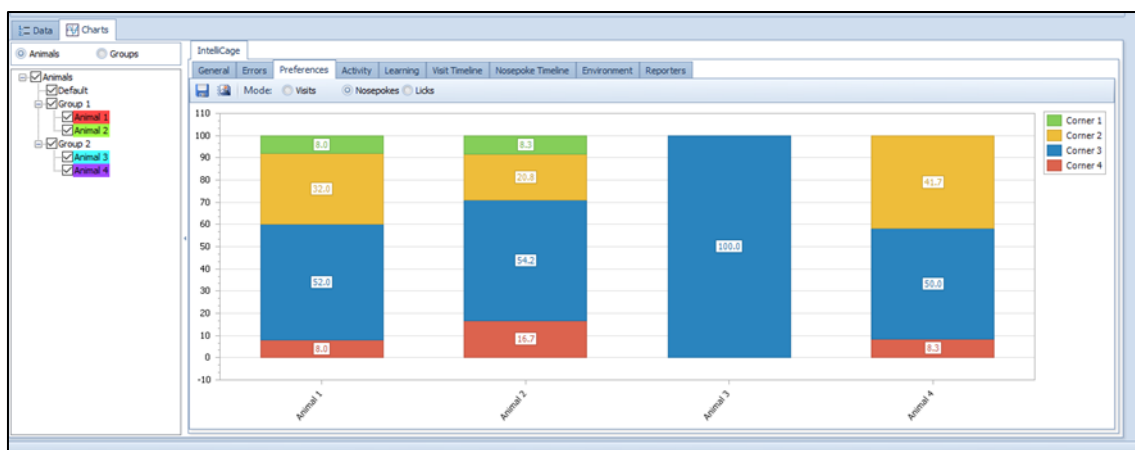
**Figure 2C** Correct corner preference of control(Group-1, corner-2) and HSD(Group-2, corner-3) mice during place learning

### 3.3. Cognitive Flexibility

In reversal learning, control mice adapted to new conditions within a day, whereas HSD mice exhibited prolonged perseveration and significantly delayed adaptation (Fig. 2D, 2E).



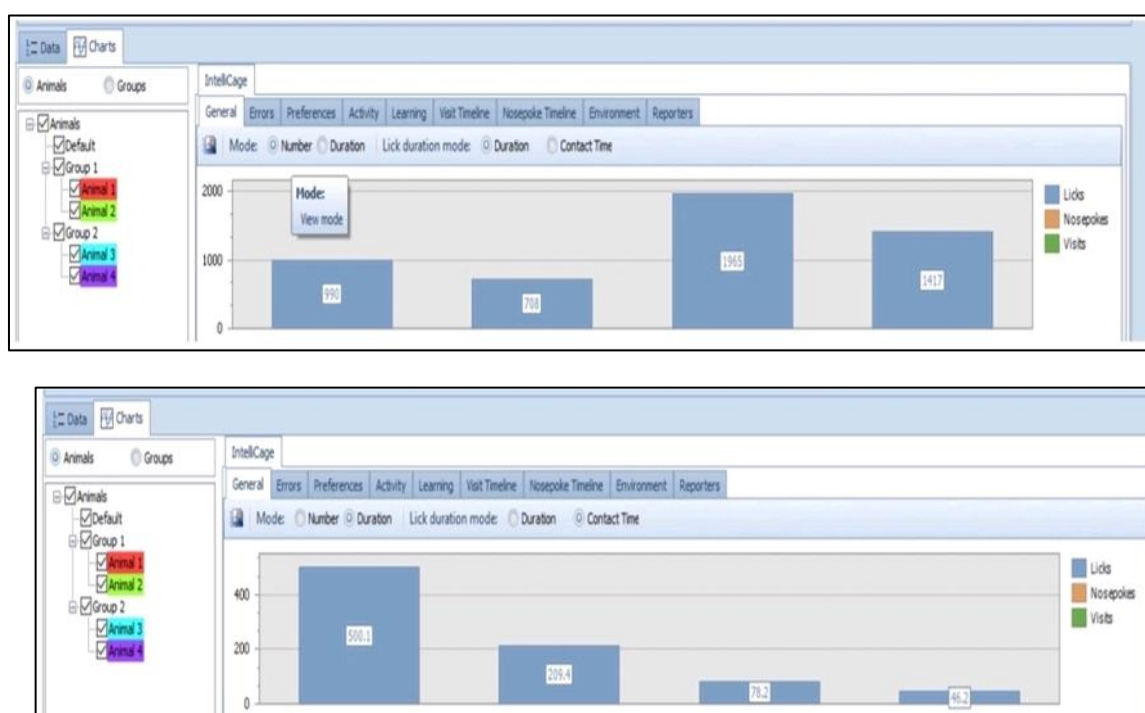
**Figure 2D** Error rates of control(Group-1) and HSD(Group-2) mice during reversal learning.



**Figure 2E** Correct corner preference of control(Group-1, corner-3) and HSD(Group-2, corner-2) mice during reversal learning

### 3.4. Addiction-like Behavior

Sucrose preference was significantly higher in HSD mice, with compulsive corner checking as suggested by their behaviour towards normal water as sucrose was unavailable (Fig. 3).



**Figure 3** Number of licks and duration of contact time of control(Group-1) and HSD(Group-2) mice

### Figure 3 Addiction-like Behavior

**Table 1** Summary of Behavioral Outcomes

Behavioral Domain	Measure	Control Group	HSD Group
General Activity	Corner visits, Nosepokes	More	Fewer
Learning & Memory	Correct corner preference, Errors	More correct corner preference, Fewer errors	Less correct corner preference, More errors

Cognitive Flexibility	Reversal learning adaptation	Within a day	Delayed
Addiction-like Behavior	Lick number, Duration of contact time	Fewer lick number, More contact time	Higher lick number, Less contact time

#### 4. Discussion

Our findings demonstrate that chronic high-sugar diet impairs learning, memory, and cognitive flexibility in mice while enhancing addiction-like preference behaviors. These results align with previous rodent studies showing diet-induced hippocampal dysfunction and dopamine signaling alterations [8–10].

The IntelliCage system allowed continuous, automated assessment, reducing experimenter bias and stress-related artifacts. Importantly, the observed behavioral impairments mirror early cognitive symptoms in humans with excessive sugar consumption and metabolic dysfunction [11,12].

Mechanistically, sugar-induced insulin resistance, hippocampal synaptic plasticity reduction, and altered dopamine transmission may underlie these effects [13,14]. Future studies should integrate neurophysiological and molecular analyses, as well as test potential interventions such as closed-loop neuromodulation, to mitigate sugar-induced cognitive decline.

Limitations: This study used only male mice, and effects in females may differ. Additionally, molecular correlates were not examined.

#### 5. Conclusion

Chronic high-sugar diet leads to reduced activity, impaired memory, reduced cognitive flexibility, and addiction-like behavior in mice. These results highlight the cognitive risks of modern dietary patterns and support further translational research.

#### Compliance with ethical standards

##### *Disclosure of conflict of interest*

No conflict of interest with any research group.

#### References

- [1] World Health Organization. Guideline: Sugars intake for adults and children. WHO, 2015.
- [2] Lustig RH et al. The toxic truth about sugar. *Nature*. 2012;482:27–29.
- [3] Kanoski SE, Davidson TL. Western diet consumption and cognitive impairment: links to hippocampal dysfunction and obesity. *Physiol Behav*. 2011;103:59–68.
- [4] Beilharz JE et al. Consumption of a Western-style diet impairs hippocampal-dependent memory in rats. *Brain Behav Immun*. 2014;38:165–176.
- [5] Reichelt AC. Adolescent high-fat, high-sugar diet results in altered memory and reward function. *Front Behav Neurosci*. 2016;10:203.
- [6] Jurdak N et al. Chronic sucrose consumption increases behavioral reactivity and impairs spatial memory. *Physiol Behav*. 2008;95:556–562.
- [7] Kiryk A et al. Cognitive abilities of mice assessed by the IntelliCage: automated behavioral screening of large cohorts. *Front Behav Neurosci*. 2020;14:593952.
- [8] Noble EE et al. Western diet impairs hippocampal function and memory in rodents. *Neurosci Biobehav Rev*. 2019;103:177–190.
- [9] Rada P et al. Sugar-induced neural adaptations in reward pathways. *Brain Res*. 2005;1068:93–102.

- [10] Johnson PM, Kenny PJ. Dopamine D2 receptors in addiction-like consumption of palatable food. *Nat Neurosci.* 2010;13:635–641.
- [11] Yeomans MR. Effects of sugar consumption on cognitive function in humans. *Nutrients.* 2017;9:964.
- [12] Beilharz JE, Maniam J, Morris MJ. Diet-induced cognitive deficits: the role of fat and sugar. *Nutrients.* 2015;7:6719–6738.
- [13] Stranahan AM, Mattson MP. Metabolic stress and synaptic plasticity in neurodegenerative disease. *Nat Rev Neurosci.* 2012;13:103–115.
- [14] Kullmann S et al. Insulin resistance and impaired brain glucose metabolism in obesity. *Nat Rev Endocrinol.* 2016;12:161–171.