Maternal Consumption of a Western-type Diet During Gestation and Lactation Increases Depression-Related Behavior and Novelty Reactivity but not Body Weight in Rat Offspring

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Introduction

- Adolescents and young adults are at the highest risk for major depression. In fact, according to the CDC, roughly 43 % of high school students reported a depressive episode in 2021 alone.
- Death by suicide, an outcome of untreated depression, is the leading cause of death in children aged 10-14 and the 3rd leading cause of death in ages 15-24.
- The Western dietary pattern contains large amounts of processed foods, fried foods, refined carbohydrates, sugar-sweetened beverages, salt, red and processed meats. As a result, over 70% of Americans consume excess oils, fats, and sugars including pregnant women.
- The detrimental effects of the Western diet on *physical* health are well-established. Recently, the Western diet has been shown to adversely affect mental health.
- Specifically, the *children* of women with Western dietary patterns during pregnancy were shown to exhibit almost twice the rate of depression compared to children of mothers with healthy dietary patterns.
- Western dietary patterns have also been associated with cognitive deficits.
- The objective of this study was to determine if maternal consumption of a Western-type diet during versus after neurodevelopment increases behaviors related to depression, anxiety, and cognition in a rat model.

Key Findings

- Consumption of a high fat/sucrose (HFS), Western diet by mothers *during* neurodevelopment *increased*:
  -Depression-related behavior, particularly in male offspring
  -Novelty reactivity, a behavior associated with addiction.
- In contrast, consumption of the HFS diet by the offspring themselves *after* neurodevelopment *did not affect* any behaviors measured.
- The HFS diet did not affect body weight.

Methods

- Animals adapted to the facility for at least one week. Female rats (dams) were placed with sires (males) for 1 week to ensure mating. The facility diet was consumed during mating.
- Following separation from the sires, dams were placed on either a low-fat, control diet (CON; AIN93G) or a high-fat diet containing sucrose (HFS diet). Dietary composition is shown in Table 1.
- Dams consumed these diets through gestation (3 weeks) and lactation (3 weeks).
- The offspring (pups) were weaned at 3 weeks of age onto the control or HFS diets and consumed these diets until behavioral testing at 10 weeks of age (adolescent). There were 10 males and 10 females/group.
- Behavioral testing consisted of the forced swim (FST), shuttle box escape, open field, O-maze, and holeboard test. Figure 1 shows the timeline of behavioral testing. Figure 2, the devices. Table 2 indicates the behavioral outcomes for each test and how they relate to mood, novelty reactivity, and cognition.
- All diets were consumed *ad libitum* with the exception of the evening prior to holeboard testing, when rats were fasted to ensure motivation to consume the holeboard bait.
- All rats were group housed under standard conditions in the Comparative Research Facility at Texas State University according to the Guide for the Care and Use of Laboratory Animals, 8th Edition. All procedures were approved by the IACUC, protocol #7616.

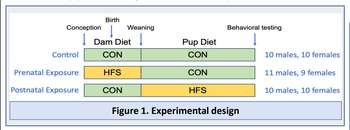

Figure 1. Experimental design

Table 1. Diets

	Control Diet (CON; AIN93G)		High-Fat/Sucrose Diet (HFS)	
Macronutrients	*g%*	*kcal%*	*g%*	*kcal%*
Protein	20	20	24	20
Carbohydrate	64	64	41	35
Fat	7	16	24	45
Total		100		100
kcal/g	4.0		4.8	
Caloric Ingredients	*g*	*kcal*	*g*	*kcal*
Casein	200	800	200	800
L-Cystine	3	12	3	12
Corn Starch	397.5	1590	64.2	257
Maltodextrin 10	132	528	100	400
Sucrose	100	400	172	691
Soybean oil	70	630	25	225
Lard	0	0	175	1575

Table 2 Behavioral Tests

Day	Test	Outcome	Significance
1	Forced Swim	Time immobile	Increased immobility = depression
2	Shuttle Box Escape	Number of escapes, latency to escape	Increased escapes and decreased latency = better ability to learn under stress (coping)
3	Open Field	Time moving in novel environment	The slope of the line between d1 and d1 reflects novelty reactivity, a behavior associated with thrill seeking and addiction
4	Open Field	Time moving in familiar environment	
5	Elevated O-maze	Time in open arms	Anxious rats prefer the dark, closed arms. Less anxiety = more time in open arms.
6	Holeboard	Visits and repeated visits to holes baited with vanilla cookies	*Working memory ratio* = initial entries divided by total entries + re-entries = how well a rat remembers within one day Reference memory ratio = entries into baited holes divided by total entries = how well a rat remembers day to day
7	Holeboard		
8	Holeboard		
9	Holeboard		
10	Holeboard		
11	Holeboard		
12	Holeboard		

Figure 2. Behavioral testing equipment. The Comparative Research Facility's Behavioral Suite houses (A) one rat-sized forced swim chamber, (B) two shuttle box escape chambers in environmental isolation units, (C) two open field chambers, (D) one elevated O-maze, and (E) two holeboard inserts for the open field chambers

Results

❖ Sex and prenatal, but not postnatal, exposure to a Western-type diet increases depression-related behavior

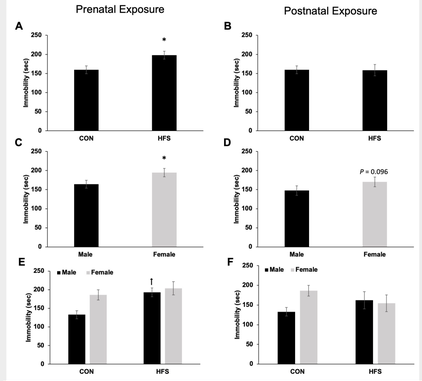

Figure 2. Effect of consumption of high fat sucrose (HFS), Western-type diet by dams during or offspring after neurodevelopment on offspring depression-related behavior in the forced swim test. Rats were placed in an inescapable cylinder of water for 15 min on day one and 5 min on day 2. Immobility on day 2 was scored using video recordings. Offspring are grouped by dam diet, control (CON) or HFS in (A), offspring diet in (B), sex in (C) and (D) and subdivided further in (E) and (F). Data shown are mean ± SEM of n = 20 per dietary group (A, B), n = 19 females and n = 21 males (C), n = 20 females and 20 males in (D), and in (E, F) n = 10 per group with the exception of prenatal HFS females where n = 9 and prenatal HFS males where n = 11. *Significantly different from CON diet (P < 0.05). ‡Significantly different from CON within sex.

❖ Neither sex nor exposure to a Western-type diet affected behavioral coping

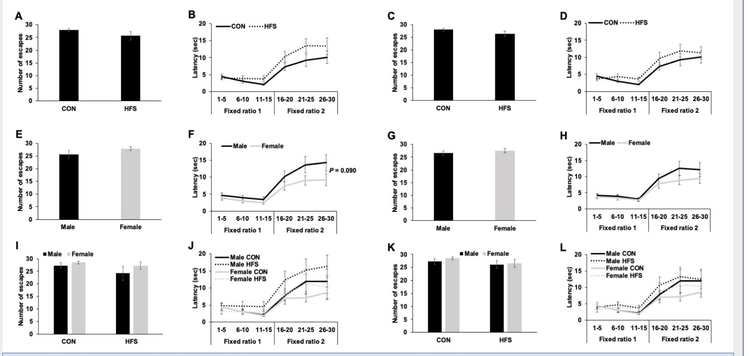

Figure 3. Effect of consumption of high fat sucrose (HFS), Western-type diet by dams during or offspring after neurodevelopment on behavioral coping, or the ability to learn under stress in the shuttle box escape test. Rats were placed in the shuttle box device and experienced 30 randomized footshocks requiring one (fixed-ratio 1) or two (fixed-ratio 2) crossings to terminate the shock. With respect to the impact diet on number of escapes and escape latency offspring are grouped by dam diet, control (CON) or HFS in (A), offspring diet in (B), sex in (C) and (D) and subdivided further in (E) and (F). Data shown are mean ± SEM of n = 20 per dietary group (A, B), n = 19 females and n = 21 males (C), n = 20 females and 20 males in (D), and in (E, F) n = 10 per group with the exception of prenatal HFS females where n = 9 and prenatal HFS males where n = 11.

❖ Prenatal, but not postnatal, exposure to a Western-type diet increases novelty reactivity

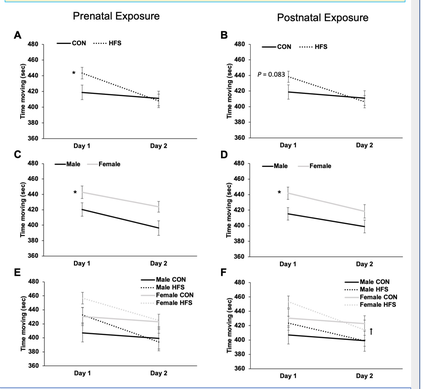

Figure 4. Effect of consumption of high fat sucrose (HFS), Western-type diet by dams during or offspring after neurodevelopment on offspring novelty reactivity in the open field test. Rats were placed in open field for 10 minutes on two consecutive days. Offspring are grouped by dam diet, control (CON) or HFS in (A), offspring diet in (B), sex in (C) and (D) and subdivided further in (E) and (F). Data shown are mean ± SEM of n = 20 per dietary group (A, B), n = 19 females and n = 21 males (C), n = 20 females and 20 males in (D), and in (E, F) n = 10 per group with the exception of prenatal HFS females where n = 9 and prenatal HFS males where n = 11. *Significantly different from CON diet (P < 0.05). ‡Significantly different from CON within sex.

❖ Sex, but not exposure to a Western-type diet affects anxiety-related behavior

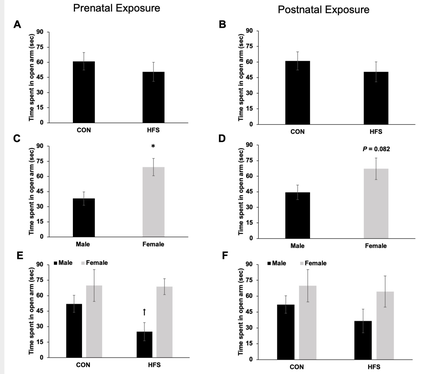

Figure 5. Effect of consumption of high fat sucrose (HFS), Western-type diet by dams during or offspring after neurodevelopment on offspring anxiety-related behavior in O-maze test. Rats were placed on elevated O-maze platform containing two open arms and to close arms. Offspring are grouped by dam diet, control (CON) or HFS in (A), offspring diet in (B), sex in (C) and (D) and subdivided further in (E) and (F). Data shown are mean ± SEM of n = 20 per dietary group (A, B), n = 19 females and n = 21 males (C), n = 20 females and 20 males in (D), and in (E, F) n = 10 per group with the exception of prenatal HFS females where n = 9 and prenatal HFS males where n = 11

❖ Sex, but not exposure to a Western-type diet, impacts learning and memory

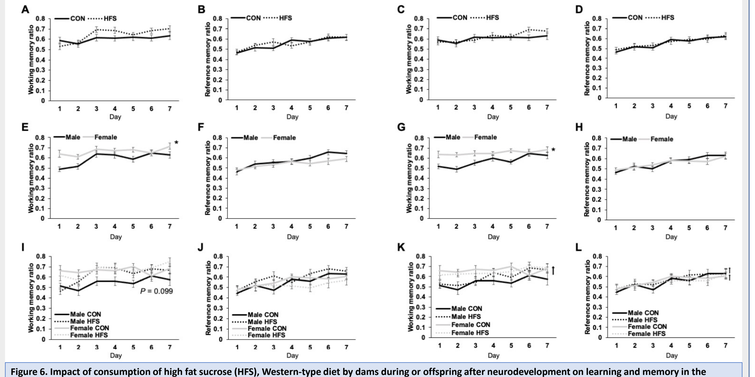

Figure 6. Impact of consumption of high fat sucrose (HFS), Western-type diet by dams during or offspring after neurodevelopment on learning and memory in the holeboard test. Rats were placed in the holeboard which contained 4 baited holes, containing cookies, and 16 total holes. Rats were tested over 7 days, with 5 trials each day. Offspring are grouped by dam diet, control (CON) or HFS in (A), offspring diet in (B), sex in (C) and (D) and subdivided further in (E) and (F). Data shown are mean ± SEM of n = 20 per dietary group (A, B), n = 19 females and n = 21 males (C), n = 20 females and 20 males in (D), and in (E, F) n = 10 per group with the exception of prenatal HFS females where n = 9 and prenatal HFS males where n = 11. *Significantly different from CON diet (P < 0.05). ‡Significantly different from CON within sex.

❖ Sex but not exposure to a Western-type diet affects body weight

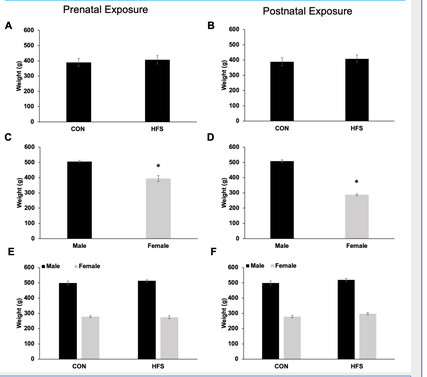

Figure 7. Effect of consumption of high fat sucrose (HFS), Western-type diet by dams during or offspring after neurodevelopment on offspring body weight. Offspring are grouped by dam diet, control (CON) or HFS in (A), offspring diet in (B), sex in (C) and (D) and subdivided further in (E) and (F). Data shown are mean ± SEM of n = 20 per dietary group (A, B), n = 19 females and n = 21 males (C), n = 20 females and 20 males in (D), and in (E, F) n = 10 per group with the exception of prenatal HFS females where n = 9 and prenatal HFS males where n = 11. *Significantly different from CON diet (P < 0.05).

Summary

- Consumption of Western-type diet by dams during pup neurodevelopment adversely impacted behaviors related to depression and novelty reactivity in adolescent pups.
- Consumption of Western-type diet by pups after weaning did not affect any behaviors measured.
- The effects on depression-related behavior were more pronounced in adolescent male rats.
- Sex affected behaviors related to depression, novelty reactivity, anxiety, and learning.
- Male rats were larger than female rats, as expected, but diet did not affect weight.

Conclusion

Mirroring observations in humans, consumption of a Western-type diet by rat mothers during pup brain development adversely impacted offspring behavior in adolescence, even in the absence of offspring obesity.

Future research will explore how maternal diet affects these behaviors throughout the lifespan and if diet, probiotic, or drug interventions can prevent or treat these deficits.

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