Examining How Prenatal Alcohol Exposure Interacts with Cafeteria Diet to Affect Metabolic Health and Gut Microbiome in Rats

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Hello, and thank you for coming to listen to me explaining my poster, examining how prenatal alcohol exposure interacts with cafeteria diet to affect metabolic health and gut microbiome in rats.

To start on slide number two, a little bit of background. Prenatal alcohol exposure is a global issue, affecting at least 9% of the population, and is associated with cognitive challenges and adverse metabolic outcomes.

Research has shown an increased risk of developing metabolic syndrome following PAE, which is characterized by insulin resistance, obesity, and glucose dysregulation, in addition to altered body composition, often manifested as excess abdominal fat.

PAE has also been associated with selective eating and altered self-regulation of hunger and satiety. And these behaviors matter because modern diets are increasingly high in fat and sugar, and these diets may lead to or worsen the long-term metabolic effects seen in individuals with prenatal alcohol exposure.

Therefore, I ask the question: How does PAE interact with postnatal diet to shape metabolic health?

You go to slide number three with my methods.

Here to address this question, I use our lab's PAE animal model using the liquid ethanol diet, with alcohol exposure happening throughout gestation.

After weaning, PAE and control animals were offered palleted control diet or cafeteria diet. And cafeteria diet is an animal model used to study obesity where animals are fed junk food like chips, chocolate, salami, and pretzels, with the expectation that cafeteria diet would exacerbate the already existing PAE metabolic effects.

To assess these effects, we assessed body weight, daily food intake or energy consumption, insulin resistance, which is a precursor to type 2 diabetes, energy expenditures that tells us how much oxygen is being consumed, which is an indicative of how much energy is being burnt, body composition, and fecal microbiome samples that happened before and after dietary exposure.

So going to slide number four with the results, page number four. Normally, we expect animals that eat more food to gain more weight, but what I found is more complex after monitoring their body weight and daily food intake.

So, looking at figures in slide number four, we see in the top middle figure that in males, PAE and control animals fed cafeteria diet ate the same amount of food. But when you look at that figure on its left, so for the body weight, compared to rats on the standard diet, PAE rats fed cafeteria diet started to show higher body weight much earlier than controls. And you can see that with the green shade on that figure.

But females told the opposite story, where alcohol-exposed rats maintained similar body weight as controls despite consuming more food, as seen in the bottom middle figure.

The orange shade on the body weight of females is an indicative of an increased body weight for those on the cafeteria diet. In addition, cafeteria diet did show an increase in fat percent compared to lean, and that is from the figures on the far right of slide number four.

Going further into slide number five, cafeteria diet also induced insulin resistance in both prenatal treatment conditions based on diet solely. Looking at the relative oxygen consumption, so again, how much energy is being burnt through respiration, through consuming oxygen. We see a decrease in oxygen consumption in male, as seen in the figure there. So despite that, there's no treatment condition. So that's not really explaining to us how males on the cafeteria diets are weighing more despite eating the same amount of food.

In the females, we don't see any effect of diet or treatment, but we do see in both sexes that in the dark, which is as expected, the rodents are more active during the dark than in the light cycle, so you see an increase in oxygen consumption during that dark cycle.

Now, looking at the results from microbiome analysis, the reason we assess microbiome analysis is to investigate the effects of the gut-brain axis. So our lab and our collaborators did show that PAE induces dysregulation in the composition of the bacteria in your guts and any dysregulation of the bacteria in your guts can lead to effects on the brain through, again, the gut-brain axis by increased inflammation, and that has been shown in various studies.

Inflammation can therefore lead to dysregulations in cognition or even metabolic health. So we wanted to test or see in this study if there are any dysregulation in gut microbiome.

So at the bottom of slide five, we're still at slide five, it tells us that for males, PAE disrupted the richness of microbiome. That's seen as the differences in Shannon index at the bottom left, while cafeteria only had an effect on control animals, seen as the increase in Shannon index. And that is in adulthood after the cafeteria exposure and the diet exposure.

For males, we see similar results when comparing the differences in composition across the groups, so that's the beta diversity. We see that the solid circles in the male graph for beta diversity, those are significantly different between each other, specifically control of PAE on the standard diet.

In females, though, cafeteria animals had different compositions compared to standard animals, seen in the beta diversity here. So the solid circles combined and the open circles combined are significantly different between each other.

We don't see effects on the richness and evenness of the microbiome within females at adulthood, and that's under the alpha diversity figure for females.

So moving on to slide number six or page number six. Overall, the results tell us that PAE is reshaping metabolism differently in males and females when challenged with an unhealthy diet. We see that PAE induced differential gut microbiome shifts of adult males across diets, whereas these shifts were diet driven in females.

We also saw that cafeteria diet impaired metabolic health in both PAE and control animals, seen as induced insulin resistance and increased body fat percent.

My ongoing studies are investigating potential central and peripheral mechanisms that may help explain this differential

response of males and females to cafeteria diet and how PAE reprograms metabolic health.

Thank you for listening.