Childhood Obesity

Maternal Health and Diet’s Effect on Offspring Metabolic Function

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Key Players

- **Elinor Sullivan, Ph.D.**
  - University of Portland and OHSU
  - Brain & Behavior

- **Antonio Frias, M.D., Ph.D.**
  - Director High Risk Pregnancy Clinic, OHSU
  - Placenta
• Rates of obesity in pregnant women are rapidly increasing (Lu et al. 2001).

• Currently, at least a third of all pregnant women in the US are obese (King 2006).

• Goal: Use a Nonhuman primate model to examine the impact of maternal obesity on offspring’s risk of developing obesity and energy balance regulation.
Maternal Health and Diet’s Effect on Offspring Metabolic Function

- The monkey model
- Complications
- Consequences
- Interventions

ONPRC
The monkey model

Maternal Diet

CTR (15% Calories from Fat)

HFD/WSD (36% of Calories from Fat)

McCurdy et al. 2009
Like human women, nonhuman primate mothers range in sensitivity to the high fat diet.
Complications

- Placental Function
- Inflammation
- Metabolic Systems
- Brain Development
Hyperinsulinemia and hyperglycemia (GDM) cause complications in placental function.

What are the potential impacts of HFD consumption?
- Inflammation
- Vascular dysfunction
Impact of maternal diet on placental health

Frias et al, Endocrinology, 2010
DCE-MRI to identify regional placental blood flow differences by cotyledon
Dietary Lipids

Postprandial sat. FFA

N3

N6/N3 ratio

Placenta

Postprandial sat. FFA

N3-FFA

N6/N3 ratio

MATERNAL

Insulin resistant obesity

Fetal

Cytokines

Oxidative damage

Insulin resistance

Metabolic mal-programming

Pregnancy complications

Placenta secretes cytokines into the fetus

TLR4 (?)
It all starts with the placenta

**MATERNAL HEALTH**
- Maternal Obesity
- Maternal weight
- Pregnancy Wt gain
- Gestational Diabetes
- Preterm delivery
- Preeclampsia

**MATERNAL DIET**
- Under-nutrition
- Malnutrition
- Protein Restriction
- Vitamin Deficiency
- Essential Fatty Acid Defic.
- Over-nutrition/ diets high fats
Abnormal development of metabolic systems

- Increased liver TGs
- Hepatic Insulin Resistance
- Muscle insulin resistance
- Decreased pancreatic alpha cell mass
- Cardiac hypertrophy
Juvenile Offspring

Maternal Diet

CTR 13% FAT

HFD 35% FAT

Postnatal Diet

CTR 13% FAT

HFD 35% FAT

Weaning
(8 months old)

CTR/CTR

HFD/CTR
Complications in brain development

- Inflammation in the brain
- Persistent neurochemical imbalances.
- Abnormalities in connectivity with cortical regions
- Abnormal behavior?
Consequences

- Metabolic Complications
  - Feeding Behavior
- Stress & Anxiety
  - Sex Differences
- Social Behavior
- Cognitive function
HFD offspring have abnormalities in metabolic adaptive responses

- Normal body weight and adiposity when maintained on a standard chow
- Increased Weight gain when challenged on a HFD
- Increased Food intake
- Changes in food preferences for high fat and high sugar diets
HFD offspring have abnormalities in metabolic adaptive responses

- HFD Offspring have an increase metabolic rate during the active period.
- HFD offspring have abnormal metabolism during the night (inactive period).
Sex Differences in offspring behavior

Sullivan et al. 2010  J. Neuroscience 2010; 30 3826-3830
Abnormalities in social behavior

**Shrieks**

- Frequency vs. Introduction
- Bars show higher frequency for HFD compared to CTR.
- Significant difference indicated by asterisk (*)

**Successful contacts during introduction**

- Percent of Time vs. Initiate and Receive
- Bars for HFD show higher percentage compared to CTR.
- Significant differences indicated by asterisks (*)

**Time Spent alone**

- Percent of Time Spent Alone vs. CTR and HFD
- HFD has a higher percentage compared to CTR.
- Significant difference indicated by asterisk (*)

**Social Play**

- Percent of Time Engaged in Social Play vs. CTR and HFD
- HFD has a higher percentage compared to CTR.
- Significant difference indicated by asterisk (*)
Consequences & Causes

- Diet
- Obesity
- Insulin resistance
- Maternal Behavior
Consequences & Causes

- Diet
- Obesity
- Insulin resistance
- Maternal Behavior

![Maternal Body Fat Percentage](image)
- CTR vs HFD
- % Body Fat

![Fetal Liver Triglycerides](image)
- Control vs O-HFD R vs O-HFD S
- Triglycerides (mg/g)

![Anxiety Behaviors](image)
- Number of Occurrences
- Normal CTR vs Obese CTR vs Normal HFD vs Obese HFD
Maternal Diet and Health are important

MATERNAL HEALTH
Maternal Obesity
Maternal weight
Pregnancy Wt gain
Gestational Diabetes
Preterm delivery
Preeclampsia

MATERNAL DIET
Under-nutrition
Malnutrition
Protein Restriction
Vitamin Deficiency
Essential Fatty Acid Defic.
Over-nutrition/ diets high fats

We cannot always do anything about the current health, but diet changes are achievable.
Interventions: When and what is safe

Pre-pregnancy

- Weight loss prior to pregnancy – OPTIMAL
- Diet and exercise
- Pharmacotherapy
- Surgery

During pregnancy

- Weight loss during pregnancy – to be avoided
- Diet and exercise
- Pharmacotherapy
- Surgery
Bariatric Surgery

• Grayson et al., Science Translational Medicine 2014
  – Rat study: Weight loss induced by RYGB and VS prior to becoming pregnant.
  – Offspring showed increased glucose tolerance and adiposity

• Several Groups (Galazis, N et al, Eur J Ob Gyn 2014; Wilis, K et al. Best Pract Res Clin Ob Gyn, 2015)
  – Bariatric surgery on women – induced weight loss
  – Children born after surgery showed much greater outcomes that siblings born before the surgery.
  – However, some studies have shown increased incidence of SGA and preterm births.
Roberts, Pound et al., FASEB 2014
Maternal Resveratrol treatment: Placenta

Roberts, Pound et al., FASEB 2014
Maternal Resveratrol treatment: fetus

Roberts, Pound et al., FASEB 2014
Interventions: When and what is safe

Pre-pregnancy
- Weight loss prior to pregnancy – OPTIMAL
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  - Surgery

During pregnancy
- Weight loss during pregnancy – to be avoided
  - Diet and exercise
  - Pharmacotherapy
  - Surgery

Offspring
- Weight loss during pregnancy – is it too late?
  - Diet and exercise
  - Pharmacotherapy
  - Surgery
Postnatal diet intervention

Anxiety Behaviors in Females

Stereotypic Pacing in Males

Exercise?
Maternal HFD Consumption Has an Enduring Impact on the Developing Offspring

Sullivan and Grove 2010
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