# Pre-pregnancy obesity, gestational weight gain and child Attention Deficit Hyperactivity Disorder symptoms

Bernard F. Fuemmeler, PhD, MPH
Associate Professor
Community & Family Medicine

DukeMedicine

# Overview

- Summarize extant research on pre-pregnancy obesity and child neurodevelopment
- Present data from Newborn Epigenetics Study (NEST)

# Maternal Nutrition

- Maternal nutrition affects the prenatal environment and offspring physiology and biology
  - Dutch famine study has shown increased risk of diabetes, cardiovascular disease, stress and breast cancer associated with low birth weight
  - Low birth weight is also a risk factor for neurobehavioral problems
- A more common perturbation of maternal nutrition is over-nutrition
  - Excess bodyweight increases risk of perinatal complications
  - May also “program” a cascade of adverse metabolic and neurodevelopmental problems

# Obesity and pregnancy

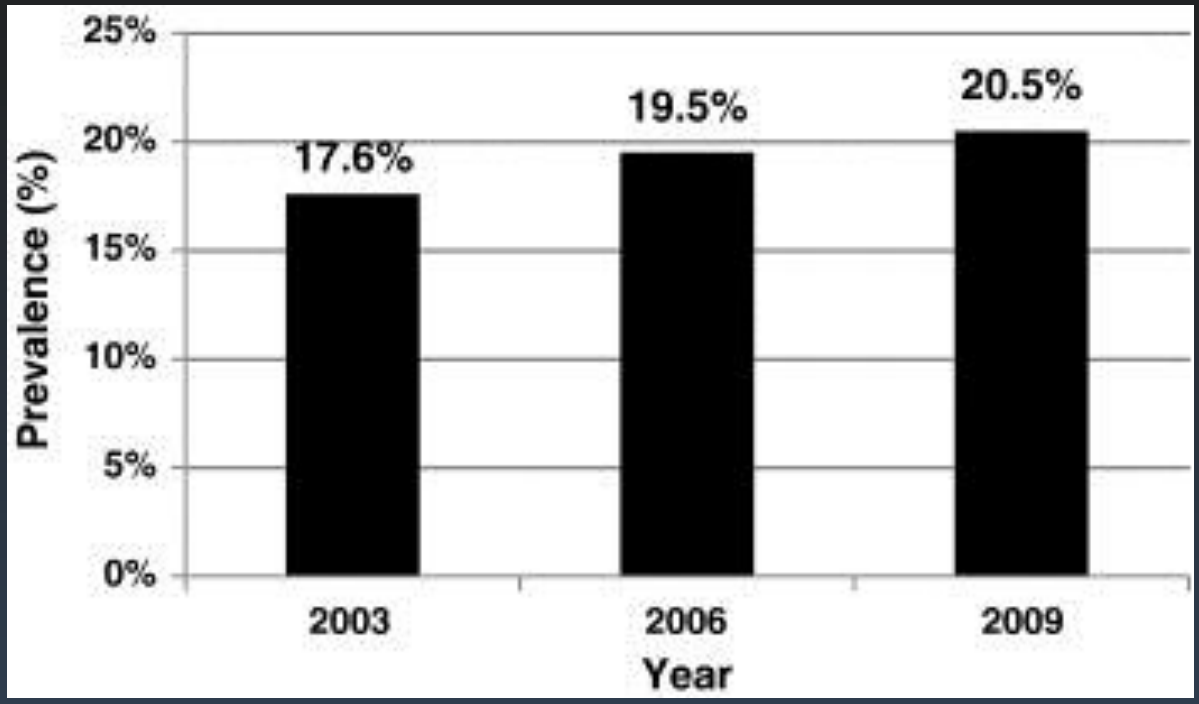


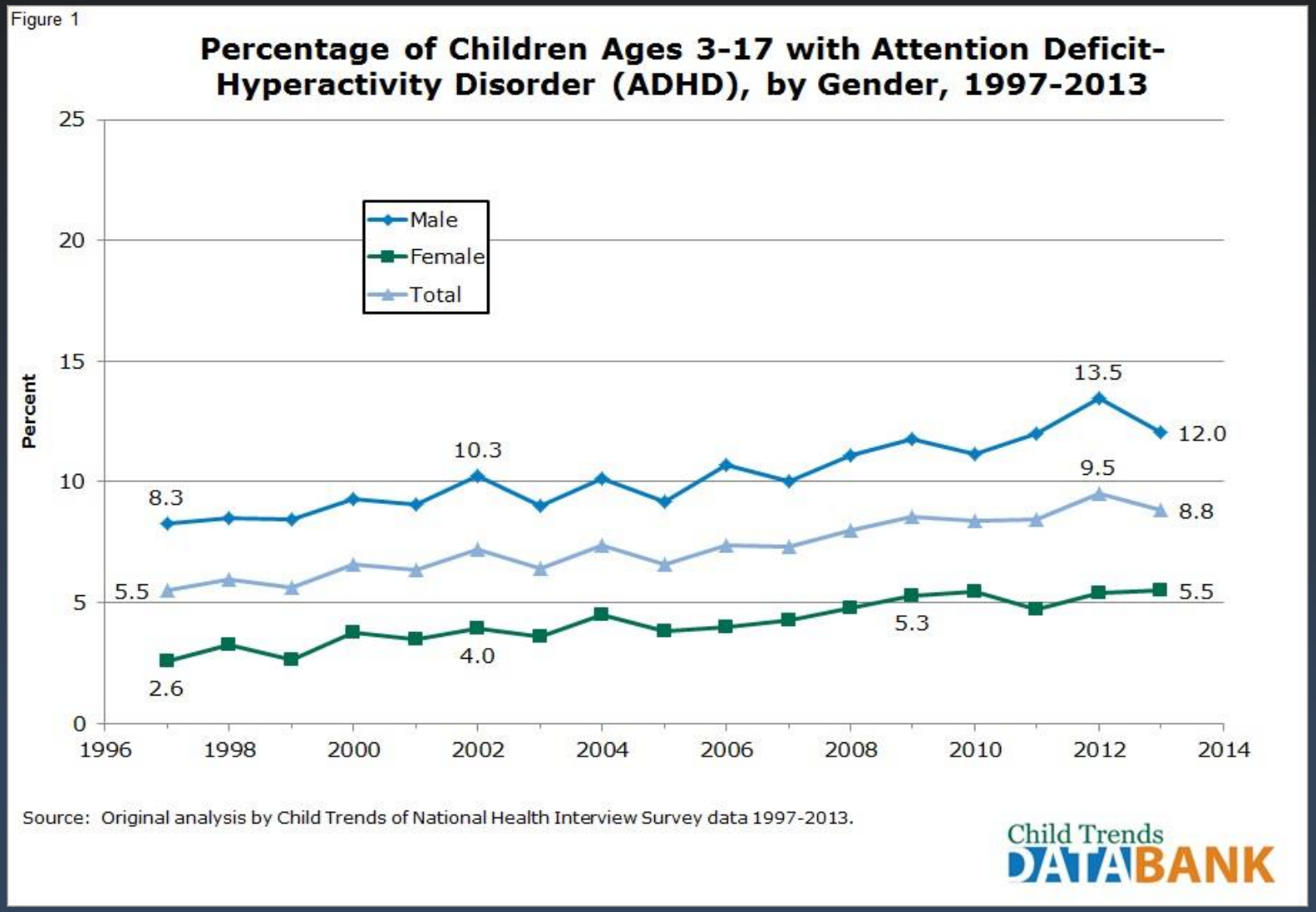

Fig. 1. Pre-pregnancy obesity (BMI ≥ 30 kg/m2) prevalence among 20 US States, 2003, 2006, and 2009. P-trend < 0.001. Prevalence estimate is standardized to the sample's 2003 race–ethnicity and age distribution. Standard errors are: 2003—0.4, 2006—0.4, 2009—0...

S.C. Fisher, S.Y. Kim, A.J. Sharma, R. Rochat, B. Morrow

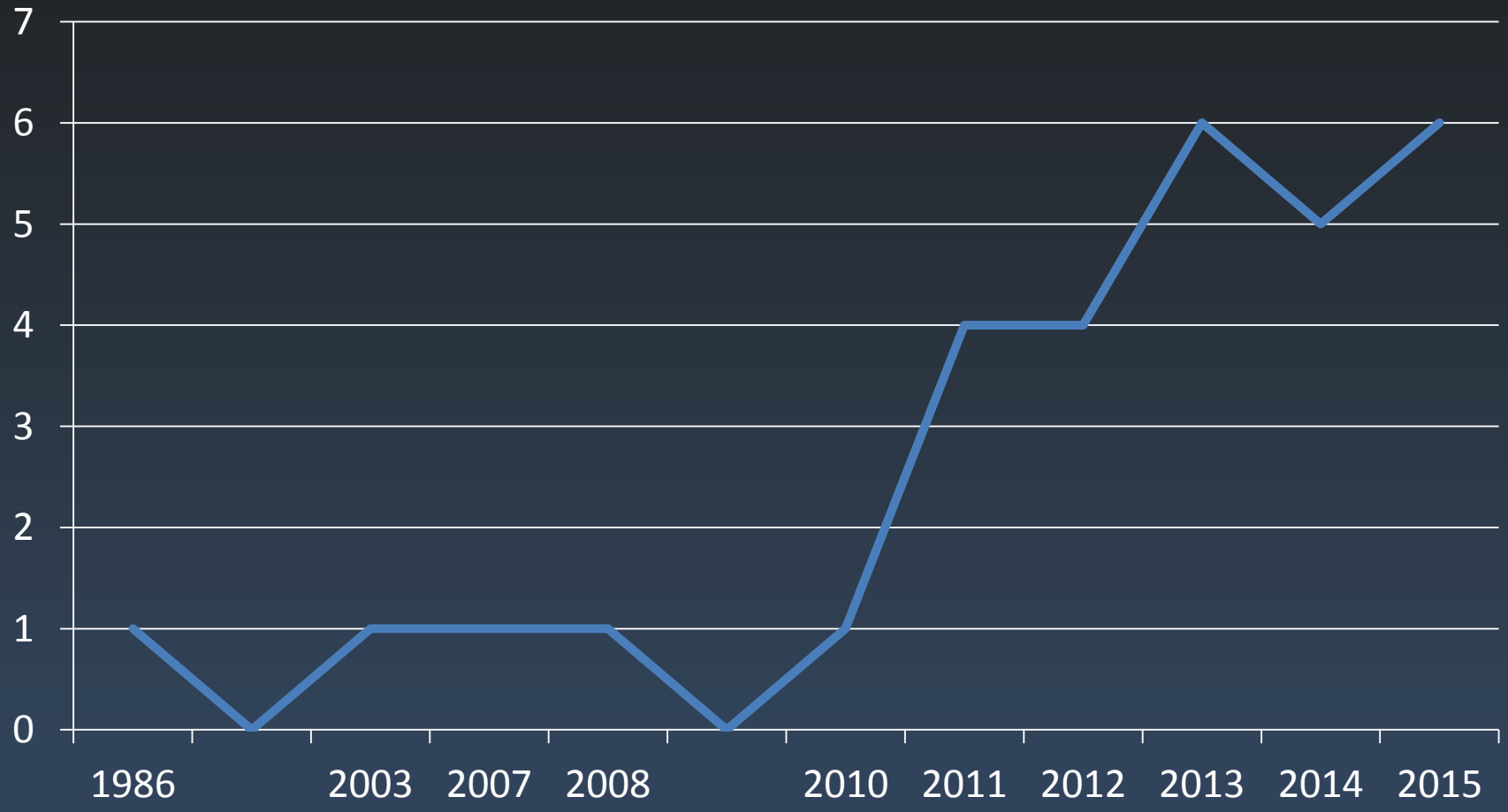
**Is obesity still increasing among pregnant women? Pre-pregnancy obesity trends in 20 states, 2003–2009**

Preventive Medicine, Volume 56, Issue 6, 2013, 372–378

# Increasing rates of neurodevelopmental disorders



# Number of Publications on Pre-pregnancy Obesity and Neurodevelopment (30 publications since 1986)



# The role of maternal obesity in the risk of neuropsychiatric disorders

*Heidi M. Rivera*[1], *Kelly J. Christiansen*[2] *and Elinor L. Sullivan*[1,2]*

[1] *Division of Diabetes, Obesity, and Metabolism, Oregon National Primate Research Center, Beaverton, OR, USA,*
[2] *Department of Biology, University of Portland, Portland, OR, USA*

**TABLE 1 | Summary of human research demonstrating that maternal obesity increases the risk for mental health disorders.**

| Child outcome | Maternal factor | References | Study design |
|---|---|---|---|
| ↑ ADHD symptomology/Risk | ↑ Pre-pregnancy BMI | Rodriguez et al., 2008 | Cohort |
| | | Rodriguez, 2010 | Cohort |
| | | Chen et al., 2014 | Cohort |
| | | Buss et al., 2012 | Cohort |
| | ↑ GWG | Rodriguez et al., 2008 | Cohort |
| | Gestational diabetes & SES | Nomura et al., 2012 | Cohort |
| | | Schmitt and Romanos, 2012 | Survey; Cohort |
| | ↓ Dietary intake of omega-3 fatty acids | Field, 2014 | Case-control |
| ↑ ASD risk/Severity of symptoms | ↑ Pre-pregnancy BMI | Krakowiak et al., 2012 | Case-control |
| | | Reynolds et al., 2014 | Cohort |
| | | Moss and Chugani, 2014 | Cohort |
| | | Dodds et al., 2011 | Cohort |
| | | Bilder et al., 2013 | Case-control; Cohort |
| | ↑ GWG | Dodds et al., 2011 | Cohort |
| | | Bilder et al., 2013 | Case-control; Cohort |
| | Diabetes, hypertension, or pre-eclampsia | Krakowiak et al., 2012 | Case-control |
| | | Dodds et al., 2011 | Cohort |
| | | Lyall et al., 2012 | Cohort |
| | | Wallace et al., 2008 | Cohort |
| ↑ Anxiety/depression risk | ↑ Pre-pregnancy BMI | Rodriguez, 2010 | Cohort |
| | | Van Lieshout et al., 2013 | Cohort |
| | | Colman et al., 2012 | Cohort |
| ↑ Schizophrenia risk | ↑ Pre-pregnancy BMI | Jones et al., 1998 | Cohort |
| | | Schaefer et al., 2000 | Cohort |
| | ↑ GWG | Kawai et al., 2004 | Case-control |
| | Pre-eclampsia/hypertension and diuretic treatment | Dalman et al., 1999 | Cohort |
| | | Eide et al., 2013 | Cohort |
| | | Sorensen et al., 2003 | Cohort |
| ↑ Food addiction | ↑ BMI 5 months post-delivery | Rising and Lifshitz, 2005 | Cohort |
| | ↑ Intake of sweets during pregnancy | Brekke et al., 2007 | Cohort |
| ↑ Anorexia nervosa/ Bulimia nervosa risk | ↑ BMI 6 months post-delivery Disordered eating | Stice et al., 1999 | Cohort |
| | ↑ Intake of sweets during pregnancy | Lamerz et al., 2005 | Survey |
| ↑ Risk of cognitive impairments | ↑ Pre-pregnancy BMI | Hinkle et al., 2012 | Cohort |
| | | Tanda et al., 2013 | Survey; Cohort |
| | | Neggers et al., 2003 | Survey |
| | | Heikura et al., 2008 | Cohort |
| | | Brion et al., 2011 | Cohort |
| | | Craig et al., 2013 | Case-control |

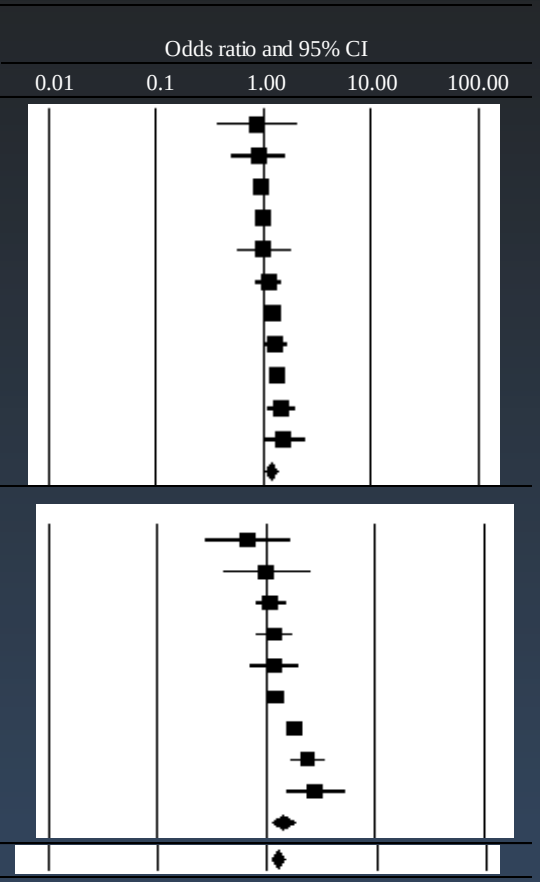
*Abbreviations: ADHD, attention deficit hyperactivity disorder; ASD, autism spectrum disorder; BMI, body mass index; GWG, gestational weight gain; SES, socioeconomic status.*

# Meta-Analysis (preliminary results)

Table 1

*Children of mothers with above-average BMI exhibit more adverse neurocognitive outcomes*

| Study Name / Cohort | Outcomes within study | Odds ratio | Lower limit | Upper limit |
|---|---|---|---|---|
| Moss (2014), Early Childhood Longitudinal | 1 | 0.87 | 0.36 | 2.09 |
| Heikura (2008), 1966 Northern Finland Birth | 1 | 0.90 | 0.50 | 1.61 |
| Brion (2011), Avon Longitudinal | Combined | 0.95 | 0.90 | 1.01 |
| Brion (2011), Generation R | Combined | 1.00 | 0.91 | 1.10 |
| Heikura (2008),1986 Northern Finland Birth | Combined | 1.01 | 0.56 | 1.83 |
| Jo (2015), Infant Feeding Practices | Combined | 1.11 | 0.85 | 1.46 |
| Gardner (2015), Stockholm Youth | 1 | 1.24 | 1.14 | 1.35 |
| Suren (2014), Norwegian Mother and Child | 1 | 1.29 | 0.99 | 1.69 |
| Rodriguez (2010), Swedish Pregnancy | Combined | 1.36 | 1.22 | 1.51 |
| Rodriguez (2008), Nordic Network on ADHD, Finland | 1 | 1.47 | 1.10 | 1.96 |
| Rodriguez (2008), Nordic Network on ADHD, Denmark | 1 | 1.55 | 0.98 | 2.44 |
| **Overweight v. Normal Weight, Random Effects model** | | **1.16** | **1.03** | **1.32** |
| Moss (2014), Early Childhood Longitudinal | 1 | 0.67 | 0.27 | 1.68 |
| Heikura (2008),1966 Northern Finland Birth | 1 | 1.00 | 0.40 | 2.50 |
| Jo (2015), Infant Feeding Practices* | Combined | 1.09 | 0.80 | 1.49 |
| Suren (2014), Norwegian Mother and Child | 1 | 1.17 | 0.81 | 1.69 |
| Antoniou (2014), Twins and Multiple Births Association Heritability | 1 | 1.18 | 0.70 | 1.99 |
| Rodriguez (2010) Swedish Pregnancy | Combined | 1.21 | 1.02 | 1.44 |
| Gardner (2015), Stockholm Youth | 1 | 1.80 | 1.59 | 2.04 |
| Jo (2015), Infant Feeding Practices** | Combined | 2.39 | 1.63 | 3.50 |
| Heikura (2008),1986 Northern Finland Birth | Combined | 2.79 | 1.49 | 5.23 |
| **Obese v. Normal Weight, Random Effects model** | | **1.42** | **1.13** | **1.79** |
| **Overweight and Obese v. Normal weight, Random Effects model** | | **1.26** | **1.11** | **1.43** |



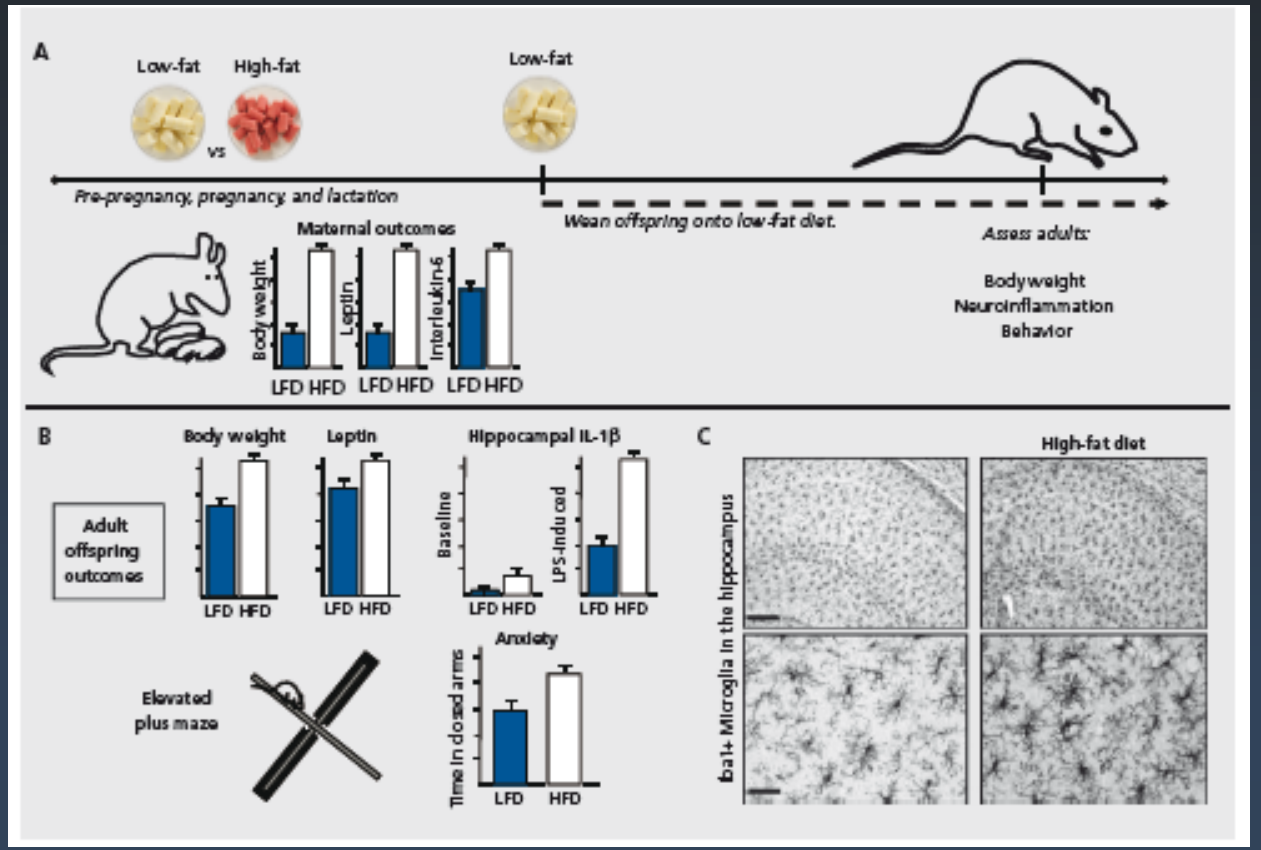

*Obese I classification, **Obese II/III classification

*Note* . The test for heterogeneity was significant for each of the three comparisons ($p < .001$), indicating that the variability of odds ratios was greater than that which would be expected due to sampling error alone. All three comparisons used *adjusted* odds ratios that generally controlled for maternal-related variables (e.g., age, education), child-related variables (e.g., gender, birth weight) and/or heritable characteristics (e.g. parental ADHD symptoms, parental IQ). Measured outcomes represented any neurocognitive indicator reported for the study (e.g., diagnosis of autism, IQ, behavioral and emotional symptoms).

# Maternal nutrition and offspring neurodevelopment

- Preclinical studies show that prenatal exposure to maternal obesity, weight gain and high fat diet alter body weight, brain development and offspring behavior.

- Pups born of heavier dams have elevated pro-inflammatory cytokine expression
- Pups are more likely to display behaviors indicative of emotional dysregulation and learning/memory deficits




Bilbo SD, Tsang V. Enduring consequences of maternal obesity for brain inflammation and behavior of offspring. FASEB J 2010;24:2104-2115.

THE JOURNAL OF
CHILD PSYCHOLOGY AND PSYCHIATRY

*Journal of Child Psychology and Psychiatry* 51:2 (2010), pp 134–143 doi:10.1111/j.1469-7610.2009.02133.x

# Maternal pre-pregnancy obesity and risk for inattention and negative emotionality in children

**Alina Rodriguez**[1,2,3]

[1]Department of Psychology, Uppsala University, Sweden; [2]Dept of Epidemiology and Public Health, Lifecourse Epidemiology, Imperial College, London, UK; [3]MRC Social Genetic Developmental Psychiatry Centre, Institute of Psychiatry, King's College, London, UK

- Swedish population-based cohort (n=1714)
- Pre-pregnancy obesity was found to be associated with teacher ratings of inattention and emotional regulation difficulties at age 5 years

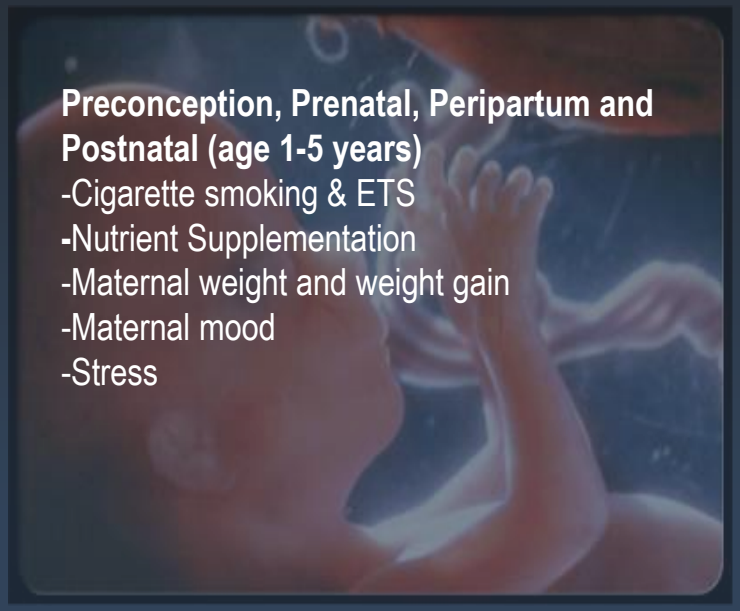
# Purpose of Our Study

Determine the extent to which pre-pregnancy BMI, obesity and gestational weight gain are associated with ADHD symptoms and related behaviors at age 3 years.

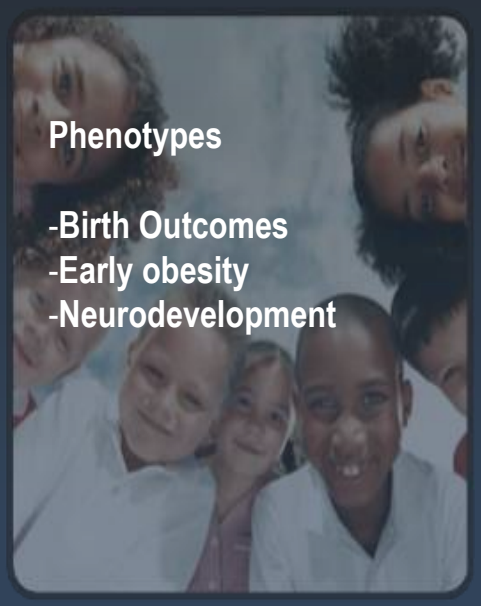
Study sample: Newborn Epigenetic Study (NEST)

# The Newborn Epigenetics STudy (NEST)

NEST seeks to improve our understanding of how environmental exposures during pregnancy and in the first few years of life influence the epigenome, birth weight, neurodevelopment, and early childhood growth.




**EPIGENETIC ALTERATIONS**



# The Newborn Epigenetics STudy (NEST)

- > 2000 women were enrolled at or near first trimester between 2006-2011
- Data/samples include
  - ✓ Prenatal maternal blood
  - ✓ Chord blood
  - ✓ Prenatal and postnatal survey data on exposures (reported toxin, nutrition & health behaviors) through child's 3rd year of life.
  - ✓ Extensive medical records data
  - ✓ ONGOING on a subset: neurodevelopmental phenotyping around self-regulation, child weight, physical activity, diet and postnatal blood and saliva samples from children

# NEST Self Regulation Study

- Mothers (n=400) completed a survey that included a set of standardized behavioral measures of self-regulation, child eating behaviors, and parenting
- Children were between the ages of 2-5 years of age (mean = 3 years)
- Measures:
  - Behavioral Assessment System for Children (BASC)
  - Behavior Rating Inventory of Executive Function (BRIEF)

# Sample Characteristics

- 48% AA; 44% White
- 52% with college degree
- 21% overweight; 32% obese
- 60% gained more than the recommended amount
- Primarily term infants
- Increasing ADHD symptoms among women who with higher pre-pregnancy BMI

Table 1. Sample characteristics overall and mean BASC ADHD and BRIEF GEC scores by sample characteristic

| | n | (%) | BASC ADHD | | BRIEF GEC | |
|---|---|---|---|---|---|---|
| | | | Mean | (SD) | Mean | (SD) |
| Overall | 340.0 | (100) | 8.08 | (3.6) | 92.88 | (20.6) |
| Mother age at delivery, years | | | | | | |
| 18-24 | 81 | (24) | 8.71 | (3.9) | 97.32 | (20.6) |
| 25-29 | 74 | (22) | 8.29 | (4.1) | 91.5 | (22.0) |
| 30-34 | 135 | (40) | 7.67 | (3.1) | 91.13 | (20.0) |
| 35 + | 50 | (15) | 7.82 | (3.2) | 92.42 | (19.4) |
| Maternal education level | | | | | | |
| Less than high school | 92 | (27) | 8.85 | (3.7) | 99.62 | (21.7) |
| High school and some college | 72 | (21) | 8.87 | (4.4) | 96.53 | (20.8) |
| College graduate | 176 | (52) | 7.36 | (3.0) [a] | 87.86 | (18.5) [a] |
| Race | | | | | | |
| White | 151 | (44) | 7.94 | (3.2) | 89.54 | (17.8) |
| Hispanic | 8 | (2) | 9.43 | (1.6) | 98.88 | (15.8) |
| Black | 164 | (48) | 8.23 | (4.0) | 95.37 | (22.6) |
| Other | 17 | (5) | 7.28 | (2.4) | 95.65 | (21.3) |
| Parity | | | | | | |
| Primiparous | 125 | (37) | 7.91 | (3.3) | 92.39 | (18.7) |
| 1 - 3 | 119 | (35) | 8.51 | (3.9) | 93.56 | (22.0) |
| ≥4 | 96 | (28) | 7.77 | (3.5) | 92.66 | (21.3) |
| Maternal ADHD Symptoms | | | | | | |
| Negative screen | 301 | (89) | 7.86 | (3.5) | 91.86 | (20.4) |
| Positive screen | 39 | (11) | 9.68 | (4.1) [b] | 100.69 | (20.2) [b] |
| Maternal smoking | | | | | | |
| Never smoke | 225 | (66) | 7.68 | (3.5) | 90.51 | (19.6) |
| Quit during pregnancy | 88 | (26) | 8.73 | (3.6) | 96.43 | (21.2) |
| Smoking during pregnancy | 27 | (8) | 9.22 | (4.0) [b] | 101 | (23.1) [b] |
| Prepregnancy BMI | | | | | | |
| Underweight | 22 | (6) | 6.70 | (3.1) | 80.59 | (14.2) |
| Normal weight | 138 | (41) | 7.76 | (3.3) | 91.66 | (19.3) |
| Overweight | 71 | (21) | 7.89 | (3.6) | 94.11 | (20.7) |
| Obese class I | 40 | (12) | 7.78 | (2.7) | 90.65 | (15.4) |
| Obese class II and III | 69 | (20) | 9.46 | (4.3) [b] | 99.25 | (24.9) [b] |
| Weight gain during pregnancy, IOM category | | | | | | |
| Less than recommended | 57 | (17) | 9.13 | (3.9) | 94.23 | (20.3) |
| Recommended | 78 | (23) | 7.05 | (3.0) | 88.47 | (18.4) |
| More than recommended | 205 | (60) | 8.19 | (3.6) [b] | 94.18 | (21.3) |
| Gestational age, weeks | | | | | | |
| 34 - 36 | 34 | (10) | 8.61 | (3.3) | 92.74 | (17.8) |
| 37 - 40 | 303 | (89) | 8.03 | (3.6) | 93 | (20.9) |
| ≥ 41 | 3 | (1) | 7.17 | (1.8) | 82.33 | (21.5) |
| Birthweight (g) | | | | | | |
| <2500 | 27 | (8) | 8.13 | (3.1) | 94.26 | (19.2) |
| 2500 - 4200 | 298 | (88) | 8.17 | (3.6) | 93.27 | (20.9) |
| ≥ 4200 | 15 | (4) | 6.27 | (2.5) | 82.53 | (12.4) |
| Child gender | | | | | | |
| Male | 180 | (53) | 8.31 | (3.7) | 92.52 | (21.2) |
| Female | 160 | (47) | 7.82 | (3.4) | 93.28 | (19.8) |

[a] $p < .001$ and b $p < .01$ for comparison from ANOVA.

# Association between pre-pregnancy BMI and BASC ADHD and BRIEF Scales

| | Continous BMI | | | | Categorical BMI | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Unadjusted | | Adjusted | | Underweight | | Normal (referent) | | Overweight | | Obese class I | | Obese class II | |
| | B | 95% CI | B | 95% CI | B | 95% CI | | | B | 95% CI | B | 95% CI | B | 95% CI |
| ***BASC ADHD Symptoms*** | | | | | | | | | | | | | | |
| BASC HY+AP | **0.16** | **(0.07, 0.25)** | **0.18** | **(0.08, 0.29)** | -2.71 | (-5.92, 0.49) | -- | -- | -0.13 | (-2.22, 1.95) | -0.17 | (-2.19, 1.84) | **3.60** | **(0.93, 6.17)** |
| BASC HY | **0.08** | **0.02, 0.14)** | **0.09** | **(0.02, 0.17)** | -1.21 | (-3.64, 1.22) | -- | -- | -0.10 | (-1.54, 1.35) | -0.13 | (-1.48, 1.21) | 1.73 | (-0.20, 3.67) |
| BASC AP | **0.08** | **(0.04, 0.12)** | **0.09** | **(0.05, 0.13)** | **-1.47** | **(-2.91, -0.03)** | -- | -- | 0.00 | (-0.88, 0.89) | 0.03 | (-1.02, 1.08) | **1.83** | (0.80, 2.86) |
| ***BRIEF*** | | | | | | | | | | | | | | |
| Global Executive Composite | **0.40** | **(0.15, 0.65)** | **0.46** | **(0.18, 0.74)** | **-12.20** | **(-19.6, -4.72)** | -- | -- | 1.93 | (-3.85,7.72) | -1.21 | (-7.45, 5.04) | **8.53** | **(1.14, 15.92)** |
| Inhibition | **0.10** | **(0.03, 0.17)** | **0.13** | **(0.05, 0.21)** | **-3.00** | **(-5.38,-0.62)** | -- | -- | 0.57 | (-1.15, 2.30) | -0.60 | (-2.33, 1.12) | **2.25** | **(0.31, 4.19)** |
| Shift Functions | **0.07** | **(0.02, 0.11)** | **0.07** | **(0.02, 0.12)** | **-1.72** | **(-2.95, -0.48)** | -- | -- | 0.21 | (-0.72, 1.15) | -0.51 | (-1.70, 0.68) | 1.06 | (-0.20, 2.32) |
| Emotional Control | 0.04 | (-0.01, 0.08) | 0.03 | (-0.02, 0.09) | -1.24 | (-2.94, 0.46) | -- | -- | -0.33 | (-1.40, 0.74) | -0.87 | (-2.03, 0.29) | 0.68 | (-0.71, 2.06) |
| Working Memory | **0.13** | **(0.06, 0.20)** | **0.15** | **(0.07, 0.23)** | **-3.07** | **(-5.24, -0.91)** | -- | -- | 1.20 | (-0.55, 2.95) | 0.55 | (-1.38, 2.48) | **3.38** | **(1.18, 5.57)** |
| Plan Organize | **0.07** | **(0.02, 0.11)** | **0.08** | **(0.03, 0.13)** | **-2.65** | **(-3.95, -1.35)** | -- | -- | 0.30 | (-0.72, 1.32) | 0.22 | (-1.01, 1.46) | 1.21 | (-0.04, 2.45) |

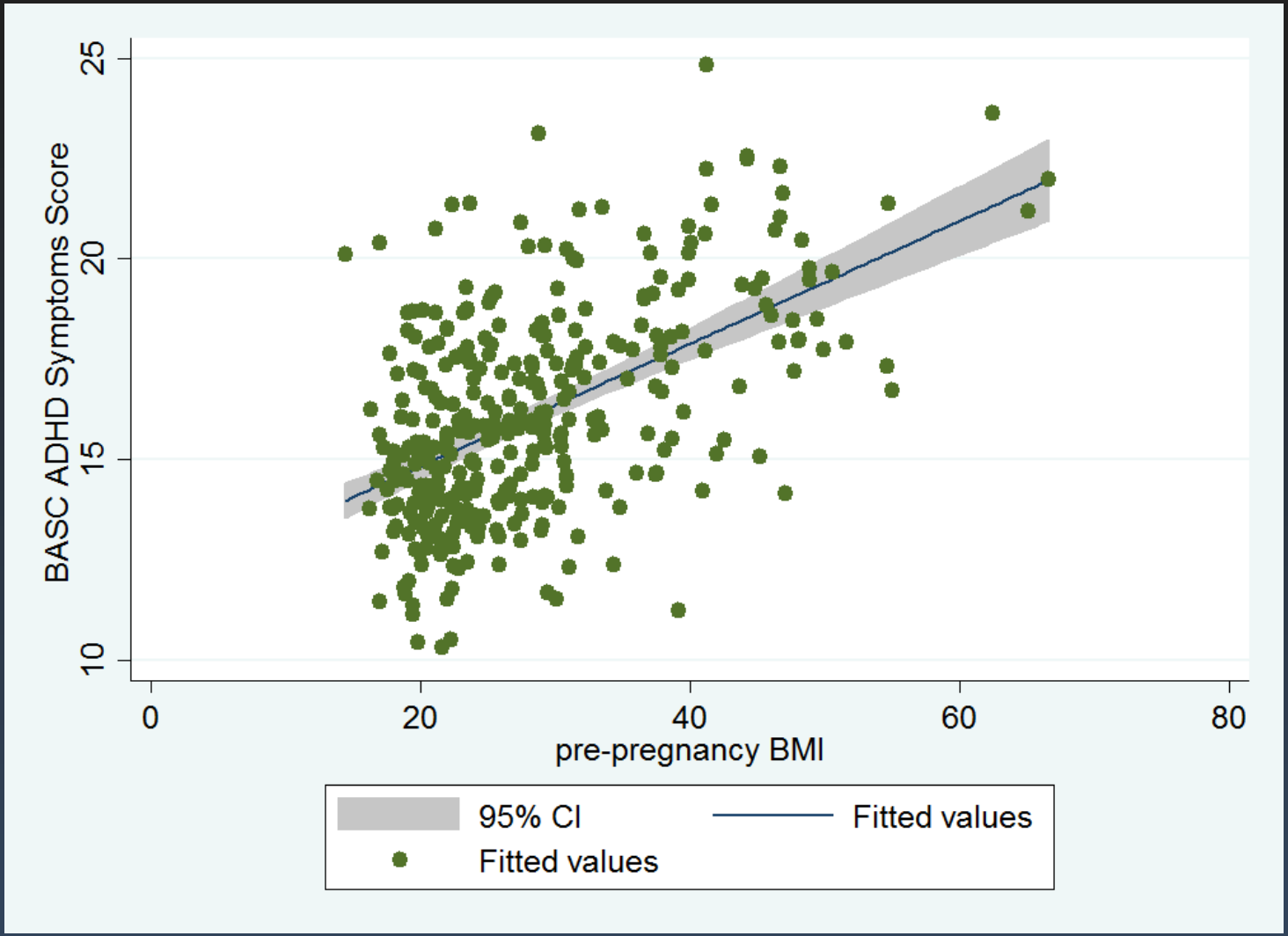
β=standardized beta; All models adjusted for parity, birthweight, child's age, gender, mom's age, race, education, gestational weeks, smoking and mothers ADHD

[a] model mutually adjusted for gestational weigh gain in addition to other covariates

[b] model mutually adjusted for prepregnancy BMI in addtion to other covariates .

All models adjusted for parity, birthweight, child's age, gender, mom's age, race, education, gestational weeks, smoking and mothers ADHD

Standardized Beta for BASC HYAP = .24; Standardized Beta for GEC = .20




Regression line adjusted for gestational weight gain parity, birth weight, child's age, gender, mom's age, race, education, gestational weeks, smoking and mothers ADHD

# Association between gestational weight gain and BASC ADHD and BRIEF Scales

| | Continous GWG | | | | Categorical GWG (IOM) | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | Unadjusted | | Adjusted | | Less than adequate | | Adequate (referent) | | More than adequate | |
| | B | 95% CI | B | 95% CI | B | 95% CI | | | B | 95% CI |
| ***BASC ADHD Symptoms*** | | | | | | | | | | |
| BASC HY+AP | -0.01 | (-0.11, 0.09) | 0.03 | (-0.08, 0.13) | 3.43 | (0.93, 5.93) | -- | -- | **1.71** | **(0.11, 3.32)** |
| BASC HY | -0.02 | (-0.08, 0.05) | 0.00 | (-0.08, 0.07) | **2.29** | **(0.54, 4.03)** | -- | -- | 0.94 | (-0.18, 2.07) |
| BASC AP | | | 0.03 | (-0.02, 0.08) | 1.07 | (-0.02, 2.15) | -- | -- | **0.74** | **(0.08, 1.40)** |
| ***BRIEF*** | | | | | | | | | | |
| Global Executive Composite | 0.00 | (-0.04, 0.05) | **0.28** | **(0.02, 0.53)** | 2.10 | (-4.70, 8.89) | -- | -- | 4.23 | (-0.74, 9.19) |
| Inhibition | 0.06 | (-0.02, 0.14) | 0.07 | (-0.01, 0.15) | 1.37 | (-0.58, 3.31) | -- | -- | **1.48** | **(0.06, 2.91)** |
| Shift Functions | 0.01 | (-0.03, 0.05) | 0.04 | (-0.01, 0.08) | 0.23 | (-0.92, 1.38) | -- | -- | 0.56 | (-0.30, 1.42) |
| Emotional Control | 0.03 | (-0.02, 0.08) | 0.04 | (-0.02, 0.09) | 0.65 | (-0.72, 2.02) | -- | -- | 0.61 | (-0.32, 1.55) |
| Working Memory | 0.04 | (-0.04, 0.11) | **0.07** | **(0.00, 0.15)** | 0.22 | (-1.78, 2.22) | -- | -- | 0.80 | (-0.68, 2.28) |
| Plan Organize | **0.04** | **(-0.00, 0.09)** | **0.06** | **(0.02, 0.11)** | -0.53 | (-1.77, 0.71) | -- | -- | 0.62 | (-0.31, 1.54) |

All models adjusted for parity, birthweight, child's age, gender, mom's age, race, education, gestational weeks, smoking and

[a] model mutually adjusted for gestational weigh gain in addition to other covariates

[b] model mutually adjusted for prepregnancy BMI in addtion to other covariates .

Standardized Beta for BASC GEC = 0.12

# Conclusion

- Data support an association between prepregnancy BMI, gestational weight gain and ADHD-related symptoms at 3 years of age
- Both hyperactive and inattention symptoms were related to pre-pregnancy BMI
- Emotional regulation was not related to pre-pregnancy BMI
- Analysis control for mother's ADHD symptoms
- We replicated these analyses using propensity score matching, restricting analyses to children born 37+ weeks gestation or to women without gestational diabetes and results remained similar

# Future Directions

**THRIVING**

**T**ranslating **H**ealth **RI**sks to understand **V**ariability
**I**n **N**eurodevelopment **G**rowth

# THRIVING

**Objectives**

1. Examine the extent to which maternal obesity related to individuals differences in appetite and executive functions and the degree to which these relate to risk for child obesity

2. Examine the extent to which proinflammatory cytokines mediated associations

# **THRIVING** Model

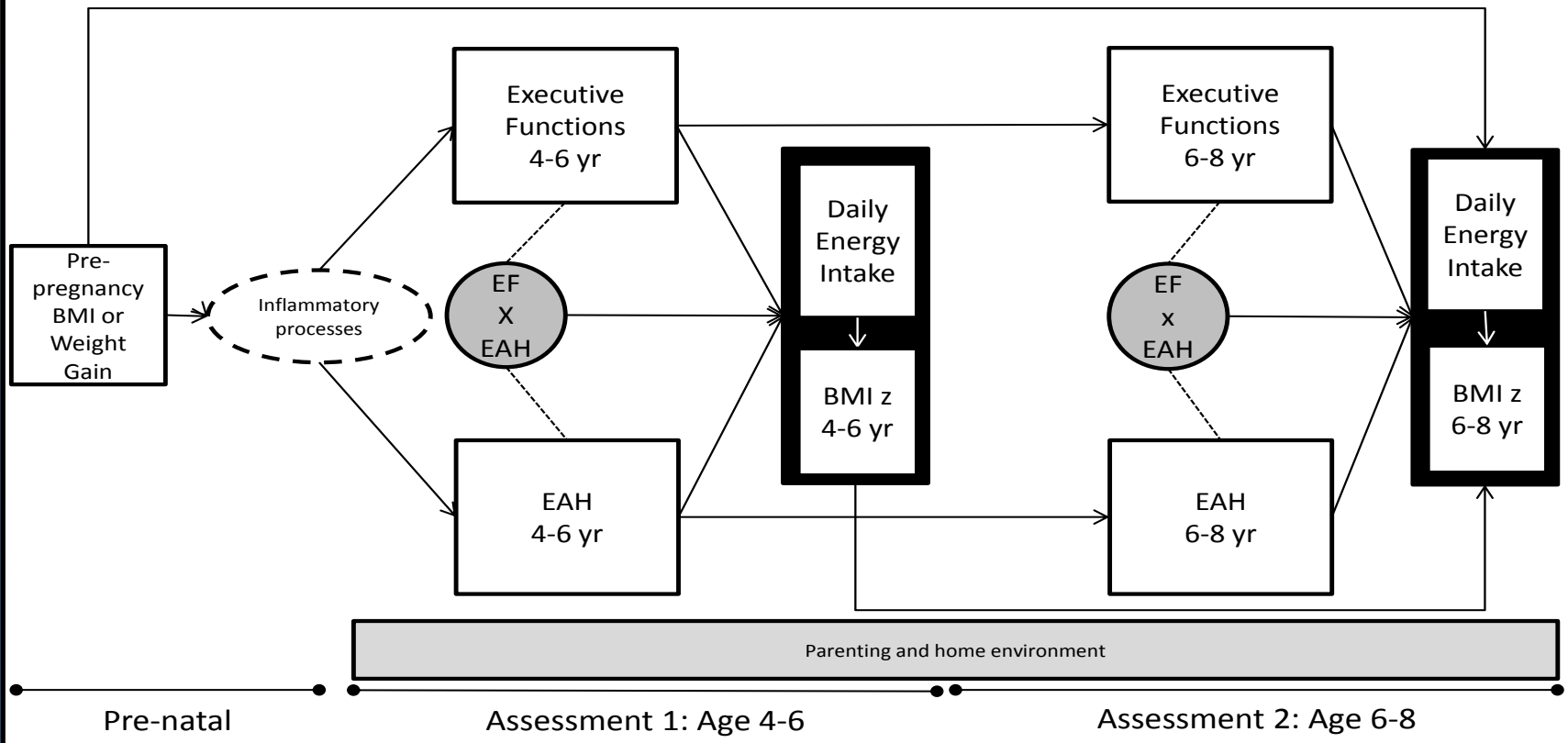



**Figure 3. Model guiding proposed work**

Note: Circle indicates interaction between executive functions (EF) and Eating in the Absence of Hunger (EAH). Final model predicting change in BMI from 4-6 and 6-8 (or obesity at age 6-8) will control for maternal characteristics (race/ethnicity, SES, intelligence score, parenting behaviors, stress/depressive symptoms), pregnancy/birth characteristics (obstetric risk conditions, parity, birthweight, gestational weeks), and child characteristics (BMI z at 3-5 years, age at assessment, gender). Prenatal exposure to maternal BMI and cytokines levels will be examined as predisposing factors to variation in EAH, executive functions and obesity. Parenting and home environment factors will be evaluated as moderators.

# THRIVING Measures

- Parent and teacher measures of self-regulation
- NIH toolbox to measure inhibitory control/attention, executive function, working memory, and language
- Children's gambling task to measure "hot executive" functioning
- Eating in the absence of hunger task

# Collaborators and Funding

- Scott Kollins, PhD
- Victor Wang, PhD
- Cathrine Hoyo, PhD
- Sara Neelon, PhD
- Staci Bilbo, PhD
- Nancy Zucker, PhD
- Ed Iversen, PhD

THRIVING: NICHD - 1R01HD084487
NEST – Self Regulation: NIA - 1R21AG041048