You are What Your Mother Ate: The Impact of Food and Stress on Biobehavioral Development

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www.eatingresearch.com
Talk Map

- The eating disorder spectrum.
- What does epidemiology teach about causes.
- A neuro developmental model of anorexia nervosa.
- Developmental antecedents
- Developmental plasticity & fitness
- **Trans generational patterns. Dr Nadia Micali**
- Clinical implications and treatments
RAN  BPAN  BN  npBN  BED  Obesity

Control appetite  Disinhibition appetite

Weight control strategies

Body Dissatisfaction

A dimensional Approach to Diagnosis
What do we know from epidemiology?
Time Trends in the Incidence of AN and BN in Primary Care in the UK

Turnbull et al., 1996; Currin et al., 2004
Cases presenting to primary care in UK (Micali et al 2012)

EDNOS BED most common diagnosis
• > 2 X ↑ prevalence of binge eating, purging (self-induced vomiting and/or laxative or diuretic misuse) and strict dieting or fasting for weight or shape control among both genders.

• The most common diagnosis in 2005 was either binge eating disorder or other “eating disorders not otherwise specified” (EDNOS; n=119, 4.2%).
Epidemiology facts

• Onset age 15-19 years
• Women > Men
• The prevalence of anorexia nervosa stable.
• Binge eating disorders, increasing and most common.
• Risk binge eating: ↑ Urban, Western.
Epidemiology suggests differences between Anorexia Nervosa and Bulimia Nervosa and Binge Eating Disorder.
Eating disorders as neurodevelopmental problems with biopsychosocial aetiology
CAVEATS

Case register studies linking early events and later hospital treatment mainly focus on AN. AN long history therefore we know about developmental factors.
We know less about early events for BN and BED.
We do know about early events for obesity.
A neurodevelopmental model of Anorexia Nervosa  (Connan et al 2003)
A Neurodevelopmental Model for Anorexia Nervosa

Genetic → Neonatal → Childhood → Adolescence →

Genes

Stress Hormone & Serotonin System

↑Oestrogen

↑Body Fat

↓Flexibility

Interpersonal Style

Disempowerment

Need to Negotiate Autonomy

Placation & Perfectionism

Avoidant Coping

‘Need for Control’

Catabolic Spiral

Brain Changes

Starvation

Chronic Stress

Body Image Issues

Genetic

Neonatal

Childhood

Adolescence

Biological

Social

Cultural Experience

Attachment Experience

Psychological

Cognition

Affect Regulation

Coping
Impact of Chronic Stress on Appetite & Weight

HYPERACTIVE DYSREGULATED HPA Axis

↑CRH

Anorexigenic Pathway

↓ Appetite & Weight

Orexigenic Pathway

Catabolic Spiral

Starvation

Adapted from Schwartz et al., 1995
Eating Disorders - Neurodevelopment factors – mechanisms building the evidence
Eating disorder BioPsychoSocial Model

Environment

Perinatal Adversity (in-womb)
- Stress
- Nutrition
- Anoxia (low oxygen to foetus)

Family & Peer Factors
- Fat talk (diet, idealisation thinness)
- Parental weight eating concern
- Teasing, criticism; “shapism”

Life events
- Loss
- Trauma
- Transitions

Genes

Genes x Environment

Infancy

↑ HPA axis
Metabolic response to ↑↓ nutrition

Childhood

5HTAA s allele x Parenting (Kawraultz et al 2011)
BDNF, DA

Puberty

Sensitivity genes 5HTAA s allele.

Culture: Easy access to palatable food, loss of social eating, idealisation thinness.

The Biological Matrix

Red lettering = hypothesis only
What do we know about genes, the early environment and the developmental template?
Genetic Factors

• Heritability 58-88% (*Bulik et al., 2000*)
• OCPD temperamental traits (*Lilenfeld et al., 1998*)
• Several putative genes in appetite or 5HT system (*Gorwood 2002*)
• Linkage to chromosome 1 for RAN (*Grice et al 2002, Devlin 2002*)
• Genome Wide Association (GWAS). No SNPs reached genome-wide significance but OPRD1 confirm, HTR1D ? (*Wang et al 2011*)
• Copy Number Variants (CNV) No evidence> HC. Rare 13q12 deletion (1.5Mb) (SCAS) n=2 & CNTN6/CNTN4 n=few. (*Wang et al 2011*).
Less is known about genes for BED & EDNOS

• However a lot more is known about obesity genes (many genes with small effects related to metabolism/appetite. 
  *Speliotes EK et al 2010*)
Pregnancy and perinatal
Pregnancy Stress

Pre pregnancy: life events/anxiety
Worrying during their pregnancy (10/40 AN vs. 2/40 HC p=0.028).
Shoebridge et al., 2000.
Worry AN vs Healthy sibling p=0.01
Taborelli et al submitted
Stress event pregnancy
64% AN vs 48%
Favero in preparation.
### Perinatal complications  ED risk

<table>
<thead>
<tr>
<th>Authors</th>
<th>sample</th>
<th>% OC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cnattingius et al. (1999)</td>
<td>781 AN case register</td>
<td>◆very preterm birth ◆cephalhematoma</td>
</tr>
<tr>
<td>Foley et al. (2001)</td>
<td>7 AN twins</td>
<td>◆pregnancy complications ◆preterm birth</td>
</tr>
<tr>
<td></td>
<td>42 BN twins</td>
<td></td>
</tr>
<tr>
<td>Lindberg &amp; Hjern (2003)</td>
<td>1122 AN case register</td>
<td>◆delivery complications</td>
</tr>
<tr>
<td>Favaro et al. (2006)</td>
<td>114 AN</td>
<td>◆pregnancy, hypoxic ◆dysmaturity</td>
</tr>
<tr>
<td></td>
<td>73 BN</td>
<td></td>
</tr>
</tbody>
</table>
Fetal Development and Birth Factors

Anorexia Nervosa

- **Small for date.**
- **Obstetric complications**

Systematic review no sig effects (NS prematurity [pooled OR 1.17, 95%CI: 0.91, 1.52]). (Krug et al in preparation)

Less is known about BED & EDNOS
Szyf, Meaney et al 2008

Early life → Genome → ADAPTATION → Stress

epigenome

PROGRAMMING OF STRESS CIRCUITS

Neuroendocrine Phenotype

External factors e.g. trauma

Internal factors e.g. sex, aging

Vulnerability/Maladaptation

susceptibility to disease/response to therapy
The epigenetic switch

Gene switched on
- Unmethylated CpG
- Histones acetylated
- Open chromatine

Gene switched off
- Methylated CpG
- Histone deacetylated
- Condensed chromatine
Effects of stress throughout the lifespan on the brain, behaviour and cognition (*Lupien et al Nature 2009*)

<table>
<thead>
<tr>
<th>Effect on HPA axis</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prenatal stress</td>
<td>Programming effects: ↑ Glucocorticoids</td>
</tr>
<tr>
<td></td>
<td>Differentiation effects: ↑ Glucocorticoids (maternal separation)</td>
</tr>
<tr>
<td></td>
<td>↓ Glucocorticoids (severe trauma)</td>
</tr>
<tr>
<td>Postnatal stress</td>
<td>Potentiation/incubation effects: ↑↑ Glucocorticoids</td>
</tr>
<tr>
<td></td>
<td>Maintenance/manifestation effects: ↑ Glucocorticoids (depression)</td>
</tr>
<tr>
<td>Stress in adolescence</td>
<td>Maintenance/manifestation effects: ↑ Glucocorticoids (cognitive decline)</td>
</tr>
<tr>
<td>Stress in adulthood</td>
<td>Maintenance/manifestation effects: ↓ Glucocorticoids (PTSD)</td>
</tr>
<tr>
<td>Stress in aging</td>
<td>Maintenance/manifestation effects: ↓ Glucocorticoids (PTSD)</td>
</tr>
</tbody>
</table>

- Rapid Growth
- Aging decline
Summary – perinatal stress risk

- Perinatal events ischemia-hypoxia, stress cause neurodevelopmental damage.
- ↑ Risk ExG neuroplasticity@ genes (BDNF, COMT, IGF2 polymorphisms etc).
- Epigenetic factors may be involved.
- Oversensitivity HPA axis – risk chronic stress.
Malnutrition in the womb

- Studies of children born to pregnant mothers who survived the “Dutch Hunger Winter” of World War II
- Also Chinese famine of 1959–1961 (St Clair et al., 2005; Xu et al., 2009)
- Risk Psychiatric problems and metabolic problems
Baby responds to undernutrition, placental dysfunction and other adverse influences by changing the growth trajectory.

A small body and a modified metabolism help to cope with a shortage of food.

High levels of nutrition later may trigger: hypertension, cardiovascular disease, glucose intolerance, kidney function (reduced number of nephrons), obesity.
Over nutrition in womb
Excess gestational weight gain

• **Mother:** ↑gestational diabetes, ↑ pre-eclampsia. *(Guelinckx et al 2008, Ohlson C et al 2008)* & ↑obesity risk *(Mamun AA et al 2010)*

• **Child:** ↑macrosomia, ↑stillbirth, offspring obesity (infancy, childhood and adulthood) *(Crozier SR et al 2010; Schack-Nielsen L, et al 2010).*

• Review: Heerwagen et al 2010
What about eating patterns during development in people with eating disorders?
Childhood Feeding AN

**Retrospective**
Case control study early feeding & GI problems
2X ↑ (Rastam et al 1992)
Dieting domain (Fairburn et al 1999, Karwautz et al 2001)

**Prospective**
Picky eating AN (Marchi & Cohen 1990)
Eating conflict, unpleasant Meals AN (Kotler 2001).
Childhood food weight shape BN,BED

**Retrospective**
Dieting domain (Fairburn et al 1997,1998, Streigel Moore et al )

**Prospective**
• Pica BN (Marchi & Cohen 1990)
• Teasing & critical comments about weight & shape & eating.
• “Fat Talk” (dieting, idealisation of Thinness) (Jacobi 2004, Stice 2002)
Risk Factors: Eating Patterns

Available online at www.sciencedirect.com

Research Report

Individual and family eating patterns during childhood and early adolescence: An analysis of associated eating disorder factors

Fernando Fernández-Aranda\textsuperscript{a,b,*}, Isabel Krug\textsuperscript{a,b}, Roser Granero\textsuperscript{c}, Jose M. Ramón\textsuperscript{a}, Anna Badia\textsuperscript{a}, Laura Giménez\textsuperscript{a}, Raquel Solano\textsuperscript{a}, David Collier\textsuperscript{d}, Andreas Karwautz\textsuperscript{e}, Janet Treasure\textsuperscript{d}
Objectives

- To examine whether individual and family eating patterns and food choices early in life were associated with EDs
- To assess whether there were differences across ED subdiagnoses in these domains
Method

◆ **Spanish Sample**
  ❖ 261 ED patients (AN=34%; BN=47%; EDNOS=19%)
  ❖ 160 controls

◆ **CCQ - Individual and Family Eating Patterns (Section 3)**
  ❖ 29 items assessing individual and family eating patterns before the age of 12 years (e.g., frequency of family meals, eating breakfast, etc.)
**ED vs Controls**

Logistic regression: effect of food style on the disorder

<table>
<thead>
<tr>
<th>Independent variables</th>
<th>$B$</th>
<th>$P$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Model: controls versus cases ($N = 421$)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sibling(s) lived at home</td>
<td>0.760</td>
<td>0.046</td>
</tr>
<tr>
<td>Grandparent(s) lived at home</td>
<td>0.489</td>
<td>0.086</td>
</tr>
<tr>
<td>Had first meal of day before lessons</td>
<td>−1.212</td>
<td>0.001</td>
</tr>
<tr>
<td>Food prepared specially for respondent</td>
<td>1.865</td>
<td>0.004</td>
</tr>
<tr>
<td>Father valued food more than others</td>
<td>0.567</td>
<td>0.028</td>
</tr>
<tr>
<td>Freq. ate fatty/sugary snacks (1)$^{b}$</td>
<td>0.689</td>
<td>0.006</td>
</tr>
<tr>
<td>Freq. ate fatty/sugary snacks (2)$^{c}$</td>
<td>1.349</td>
<td>0.001</td>
</tr>
</tbody>
</table>
ED subdiagnoses vs. controls

**Risk factors:**
- Grandparents lives at home: AN
- Food prepared specially for respondent: AN, BN
- Eating snacks: AN, BN
- Father values food more than others: BN
- Ate meals together < 3 times a day: EDNOS

**Protective factors:**
- Had first meal of day before lesson: BN, EDNOS
Summary

• AN – possibly more fussy
• BN EDNOS more irregular pattern eating
OCPD
Childhood temperament
Anxious/Avoidant

Parenting
Overinvolved
Conditional
Neglect

Food used instrumentally

Tease and criticise weight/shape/eating

Physical & Sexual Abuse

RAN  BPAN  BN  npBN  BED
G x E - Interaction effects
Differential susceptibility hypothesis (Belsky 1997)

• Some individuals are more affected than others by both negative and positive environmental influences or experiences

• Eg individuals with ↑ negativity respond differently according to sensitivity parental rearing (Belsky 1997, 2005, Belsky et al 2007, Belsky & Pluess 2009).

• Related to biological sensitivity to context (Boyce & Ellis 2005)
Differential susceptibility hypothesis: causes
(Belsky & Pluess 2009)

- Behavioral factor: - infant temperament.
- Physiology: Cortisol reactivity.
- Genetic: Serotonin transporter polymorphism
Evolutionary Background

• Good match between phenotypes and environment ► ▲Fitness.

<table>
<thead>
<tr>
<th>Anticipate Future</th>
<th>Actual Future</th>
<th>Good Match</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="image1" alt="Sun" /></td>
<td><img src="image2" alt="Sun" /></td>
<td>High Fitness</td>
</tr>
<tr>
<td><img src="image3" alt="Child" /></td>
<td><img src="image4" alt="Child" /></td>
<td>High Fitness</td>
</tr>
</tbody>
</table>
Evolutionary Background

- Badmatch between phenotypes and environment ▶ ▼ Fitness.

<table>
<thead>
<tr>
<th>Anticipate Future</th>
<th>Actual Future</th>
<th>Bad Match</th>
</tr>
</thead>
<tbody>
<tr>
<td><img src="sun.png" alt="Sun" /></td>
<td><img src="child.png" alt="Child" /></td>
<td>▼ Fitness</td>
</tr>
<tr>
<td><img src="child.png" alt="Child" /></td>
<td><img src="sun.png" alt="Sun" /></td>
<td>▼ Fitness</td>
</tr>
</tbody>
</table>
Plasticity in development allows offspring to adapt to anticipated environment and perhaps later to actual.
The Neurosensitivity Hypothesis
Variation in Developmental Plasticity

Dandelions
Fixed folk ▼ plasticity

Reduced sensitivity to environmental change

Orchids
Sensitive souls ▲ plasticity

Discordant Sibling Design

Andreas Karwautz

Gudrun Wagner

50% genes in common
Shared Environment in common
# Risk Factors in ED sibling

<table>
<thead>
<tr>
<th>Personal vulnerability</th>
<th>Childhood characteristics</th>
<th>Psychiatric disorders</th>
<th>Negative self-evaluation</th>
<th>Perfectionism</th>
<th>Extreme compliance</th>
<th>No close friends</th>
<th>Depressive disorders</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Environmental vulnerability</strong></td>
<td>Parental problems</td>
<td>Life-events</td>
<td>Sexual abuse</td>
<td>High expectations</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Dieting vulnerability</strong></td>
<td>Feeding problems in childhood</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Pudicity domain</strong></td>
<td>Pudicity related events</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Genetic vulnerability</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Cultural impact</strong></td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Sibling-related problems</strong></td>
<td>Rivalry</td>
<td>Peer-group popularity</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## 5HTT-genotype distribution

<table>
<thead>
<tr>
<th></th>
<th>AN-Patients</th>
<th>Healthy sisters</th>
</tr>
</thead>
<tbody>
<tr>
<td>L/L</td>
<td>45 (38.8%)</td>
<td>40 (37.0%)</td>
</tr>
<tr>
<td>L/S</td>
<td>50 (43.1%)</td>
<td>50 (46.3%)</td>
</tr>
<tr>
<td>S/S</td>
<td>21 (18.1%)</td>
<td>18 (16.7%)</td>
</tr>
</tbody>
</table>

No differences between patients and sisters: $\chi^2=0.239$, df=2, $p=0.887$

Lesch et al. 1996: 5HTTLPR genotype distribution in a caucasian population → 32% L/L, 49% L/S, 19% S/S

Genotype frequencies in Hardy Weinberg equilibrium.
Environmental Domains of Risk
(Karwautz et al 2011)

n = 128 sister pairs (n=256)
AN-R (min. 3 yrs.): n = 58 :AN-BP: n=70
Interaction: G x Parental Problems

(Karwautz et al 2011)

Figure 1: Interaction Gene x Parental Problems

Number of parental problems with SS genotype increases risk for AN
What are the clinical implications of eating disorders and motherhood?
The environment in Anorexia Nervosa
The environment in Anorexia Nervosa
Kitchen of patient with Bulimia Nervosa
The back seat of the car of a patient with bulimia nervosa
Eating Disorders (EDs) & Pregnancy

- Some women with EDs welcome pregnancy as a vacation from weight worries
- However, core psychological symptoms include a morbid fear of fatness & self-worth tied to weight, shape, or appearance
- The prospect of weight gain during pregnancy is terrifying

Micali et al., 2010
Eating Habits and Attitudes in the Post Partum Period

- Prospective (N=97) cohort during pregnancy and at 3 and 6 months postpartum
- Eating Disorder Examination (EDE).
  (Stein et al. Psychosomatic Med., 1996)
## Eating Habits and Attitudes in pregnant Cases of eating disorders

<table>
<thead>
<tr>
<th></th>
<th>Preconception</th>
<th>Late pregnancy</th>
<th>3 mos pp</th>
<th>6 mos pp</th>
</tr>
</thead>
<tbody>
<tr>
<td>Concern about shape***</td>
<td>0.91</td>
<td>1.14</td>
<td>1.34</td>
<td>1.08</td>
</tr>
<tr>
<td>Concern about weight****</td>
<td>0.96</td>
<td>0.80</td>
<td>1.34</td>
<td>1.63</td>
</tr>
<tr>
<td>Concern about eating**</td>
<td>0.13</td>
<td>0.04</td>
<td>0.15</td>
<td>0.09</td>
</tr>
<tr>
<td>Dietary restraint*</td>
<td>0.94</td>
<td>0.90</td>
<td>1.08</td>
<td>0.90</td>
</tr>
<tr>
<td>Global EDE***</td>
<td>0.60</td>
<td>0.58</td>
<td>0.79</td>
<td>0.77</td>
</tr>
</tbody>
</table>

** = p <0.05, *** = p< 0.01, ****=p<0.001

Pregnancy and neonatal outcomes in women with EDs

Table 3. Pregnancy Characteristics in Patients and Controls

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Patients (n = 49)</th>
<th>Controls (n = 67)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weeks of gestation</td>
<td>38.9 ± 1.8</td>
<td>39.2 ± 1.8</td>
<td>.43</td>
</tr>
<tr>
<td>Maternal weight gain (kg)</td>
<td>11.3 ± 3.9</td>
<td>12.1 ± 2.6</td>
<td>.21</td>
</tr>
<tr>
<td>Hyperemesis</td>
<td>33</td>
<td>9</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Anemia</td>
<td>49</td>
<td>12</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Gestational hypertension/</td>
<td>12</td>
<td>3</td>
<td>.07</td>
</tr>
<tr>
<td>preeclampsia</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrauterine growth restriction</td>
<td>8</td>
<td>0</td>
<td>.07</td>
</tr>
</tbody>
</table>

Values are mean ± standard deviation or percentage.

Kouba, 2005, Obstet Gynecol
Pregnancy and neonatal outcomes in women with EDs

**Table 5. Neonatal Characteristics in Patients and Controls**

<table>
<thead>
<tr>
<th>Neonatal Characteristics</th>
<th>Patients (n = 49)</th>
<th>Controls (n = 67)</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (g)</td>
<td>3,233 ± 606</td>
<td>3,516 ± 515</td>
<td>&lt; .01</td>
</tr>
<tr>
<td>Length (cm)</td>
<td>49.6 ± 2.7</td>
<td>50.2 ± 2.4</td>
<td>.18</td>
</tr>
<tr>
<td>Head circumference (cm)</td>
<td>33.7 ± 1.4</td>
<td>35.2 ± 1.6</td>
<td>&lt; .001</td>
</tr>
<tr>
<td>Apgar score &lt; 6 (5 min)</td>
<td>2</td>
<td>4</td>
<td>.64</td>
</tr>
<tr>
<td>Neonatal care</td>
<td>10</td>
<td>4</td>
<td>.28</td>
</tr>
<tr>
<td>Small for gestational age</td>
<td>12</td>
<td>1</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Microcephaly</td>
<td>8</td>
<td>0</td>
<td>&lt; .05</td>
</tr>
<tr>
<td>Malformations</td>
<td>2</td>
<td>0</td>
<td>.42</td>
</tr>
</tbody>
</table>

Values are given as mean ± standard deviation or percentage.

Kouba, 2005
Intrauterine and Postnatal Growth in Babies of Anorectic Mothers

Treasure and Russell  1988

Diagram showing growth curves for gestation (weeks) and weeks after birth.
Weight Chart of son of Mother with Anorexia Nervosa admitted to hospital

Russell et al 1998
Loss of teeth in son of mother with anorexia nervosa (due to sweetened pacifier).
Transgenerational passage BN, BED

- **Weight gain**
- $\uparrow$BED, $\downarrow$AN (Seiga Riz et al 2010)
- **Birth defects-BN**
- $\uparrow$miscarriages and foetal deaths (Lacey et al 1987).
Transgenerational Risk factors.

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NIHR Clinician Scientist and Honorary Consultant Psychiatrist
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Intergenerational risk

Risk

Maternal ED

Moderators
- Paternal factors
- Maternal factors (comorbidity active ED symptoms)
- Child characteristics

Mechanisms

Heritability of disorder

Perinatal factors

Exposure to mother’s maladaptive cognition, behaviour, affect

Outcome

Offspring ED

Adapted from Goodman & Gottlib, 1999
ED behaviours in pregnancy

**BN**

- Binge eating and vomiting
  
  *Lacey and Smith, 1987*
  *Lemberg and Phillips, 1989*
  *Blais et al, 2000*
  *Crow et al, 2008*

- Binge eating and purging but abstinence rates=
  
  *Crow et al, 2004*

**AN**

- Less improvement compared to BN
  
  *Blais et al, 2000*

- Non significant decrease in behaviours
  
  *Carter et al, 2003*
ED cognitions in pregnancy

- Improvement in body dissatisfaction and eating attitudes in pregnant women
  
  *Davies & Wardle, 1994; Rocco et al, 2005*

- Worsening in body dissatisfaction in ED women
  
  *Crow et al, 2004*

- Weight and shape concern improve
  
  *Crow et al., 2008*
Sample-ALSPAC

Avon Longitudinal Study of Parents and Children women enrolled at 8th week pregnancy and followed up to present date

Enrolled: 14,468

Missing 12/52 data: 2015

Remaining women: 12,453

Women reported history of Eating Disorders:
- AN: 175
- BN: 203
- AN+BN: 82

Two unexposed groups:
- Other psychiatric dis.: 1184
- Remaining sample: 10,775

57: recent
395: past
ED behaviours in pregnancy:

- Self-induced vomiting
- Laxative use
- Excessive exercise

* = p<0.001
Prevalence of ED in pregnancy:

N=739 random sample of pregnant women screened at 1st US scan
Affective disorders in ED mothers in pregnancy

Micali et al., 2011
ED and affective disorders in pregnancy and the post-partum

• **Depression**
  High prevalence rates in post-partum:
  • ~1/3 (Morgan et al., 2006; Morgan et al. 1999; Franko et al, 2001; Carter et al. 2003; Abraham, 1998)
  • and pregnancy: 40-60% (Mazzeo et al., 2006)

• **Anxiety**
??
Outcomes

- Anxiety (Crown-Crisp Experiential Inventory-CCEI)
  - Cut-off: >30
- Depression (Edinburgh Postnatal Depression Scale-EPDS)
  - Cut-off: >12
Probable Depressive disorder

% of women scoring above cut-off

AN=Other psychiatric>BN, unexposed

* p<0.0001
Anxiety pregnancy and post-partum

1: 18 weeks pregnancy; 2: 32 weeks pregnancy; 3: 2 months post-partum; 4: 8 months post-partum

* p<0.0001
8,880 Women recruited in pregnancy

6,493 Consented to post-natal participation

1,176 missing on pregnancy Q

5,317

104 foetal deaths

Lifetime AN (N=134)
Lifetime BN (N=215)
Lifetime AN+BN (N=102)
Lifetime other psychiatric disorders (N=1,070)
Unexposed (N=3,796)
Psychopathology in 2\textsuperscript{nd} trimester pregnancy
Brief symptom inventory (top centile)

* p<0.001, adjusted for maternal age, education, ethnicity
Perinatal complications and ED

Micali et al 2007
Solmi et al in press
Maternal ED and complications in offspring

- Low birth-weight
- ↓ Apgar scores
- ↑ Prematurity
- ↑ Perinatal mortality

Risk of miscarriages in women with BN
Abraham, 1998, Micali et al., 2007

Normal rates of miscarriages in 54 women with AN & BN
Blais et al., 2000
Meta-analysis of birth-weight in women with AN

Solmi et al, in prep
Transgenerational

- **Weight gain**
  - $\uparrow$BED, $\downarrow$AN (Seiga Riz et al. 2010)

- **Birth defects-BN**
  - $\uparrow$miscarriages and foetal deaths (Lacey et al. 1987; Micali et al., 2007).
Summary of results

- ED pregnancy symptoms higher in women with both past & recent ED compared to unexposed
- Evidence that women with AN ~ twice more likely to have a probable depressive disorder both in pregnancy and at 8 mo PP
- Recent meta-analysis suggests evidence of an effect of maternal AN on offspring birth-weight
Infant outcomes

Micali et al., 2009; 2011
Infant feeding

- Problems with feeding identified in women with ED:
  - Rapid sucking (Agras et al. 1999)
  - Mealtime conflicts and lower weight at 1 yr in infants of ED women (Stein et al., 1994)
  - Failure to thrive in the 1\textsuperscript{st} year of life in infants of women with history of AN (Brinch et al., 1988)

- Video-feedback interventions very helpful (Stein et al., 2006)
Persistent feeding problems in first 6 months of life
(covarying for birth weight, gestational age, breast feeding, maternal factors)

% of women reporting problems

- AN
- BN
- Other psychiatric controls
- controls

* p<0.001, **p<0.01
Persistent feeding problems in first 6 months of life

(covarying for birth weight, gestational age, breast feeding, maternal factors)

Persistent feeding problems in first 6 months of life

(covarying for birth weight, gestational age, breast feeding, maternal factors)

* p<0.001, ** p<0.05
Risk model for feeding difficulties

- Maternal ED
  - Early Feeding Difficulties 1/12
    - Maternal Distress @32 weeks preg
      - Child temperament
        - 0.19*
  - Maternal Distress @ 8 weeks PP
    - Late Feeding Difficulties 6/12
      - 0.25**
  - Maternal Distress @32 weeks PP
    - 0.08*  0.10*  0.12**

*p<0.001, **p<0.01, ***p<0.05
Psychopathology at age 3 and 1/2

Figure 1: SEM model of emotional problems at 3 ½ years in girls of AN mothers

Maternal AN → ED symptoms at 18 weeks gestation

Anxiety & depression in pregnancy

Anxiety at 32 weeks gestation

Depression at 32 weeks gestation

Emotional problems

Arrows indicate causal relationships. Numbers represent correlation coefficients:
- Maternal AN to ED symptoms: 0.05**
- Maternal AN to Anxiety & depression in pregnancy: 0.1*
- Maternal AN to Depression at 32 weeks gestation: 0.9*
- ED symptoms to Anxiety & depression in pregnancy: 0.3*
- ED symptoms to Depression at 32 weeks gestation: 0.8*
- Anxiety & depression in pregnancy to Emotional problems: 0.01
- Depression at 32 weeks gestation to Emotional problems: 0.2*
- Emotional problems to Anxiety & depression in pregnancy: 0.06†

** and † indicate statistical significance at p < 0.01 and p < 0.1, respectively.
Psychopathology at age 3 and 1/2

Figure 3: SEM model of conduct problems at 3 ½ in boys of BN mothers

RMSEA=0.02
CFI=0.99

*: p<0.0001; **p=0.001; ***p<0.05
Summary of results infant feeding and child psychopathology

• ↑ feeding difficulties in infancy and childhood

• These persist later on in childhood

• Affective disorders in pregnancy: important mediators

• Maternal ED and active symptoms in pregnancy directly and indirectly increase risk for child psychopathology in early childhood
Conclusions

• Maternal ED are common and have important effects of pregnancy, obstetric and infant outcomes
• Need for more intensive prenatal care in pregnant women with ED to optimise prenatal nutrition and foetal development (as per NICE guidelines in the UK)

• Need for adequate post-natal support re: feeding and emotional disorders
Clinical implications

- Need for more intensive prenatal care in pregnant women with ED to optimise prenatal nutrition and foetal development (as per NICE guidelines in the UK)

- Need for adequate post-natal support re: feeding and emotional disorders
Interventions during Pregnancy

• No specific information for people with eating disorders
Interventions during Childhood
Breaking the cycle of risk?

(Stein, A., Am.J Psychiatry, 163, 899-906)

• 80 mothers with bulimia nervosa or similar (infants were 4-6 months old).
• Video-feedback treatment-mother-child interaction vs counseling (13 sessions) Both guided CBT for BN.
• Video-feedback group ↓mealtime conflict
• Severe conflict 9/ 38 (23.7%) video vs 21/39 (53.8%) controls (OR=0.27).
Conclusion

• Eating disorders are neurodevelopmental disorders associated with genetic, epigenetic and environmental vulnerability.

• Women with ED have ↑factors known to ↑neurodevelopmental vulnerability eg. ↑anxiety ↑eating restriction/loss control & vomiting in pregnancy.

• Interventions for this high risk group are needed.
Thankyou

- Nadia Micali
- Abigail Easter
- Emma Taborelli
- Freya Corfield

- Frances Connan
- Iain Campbell
- Valentina Cardi
- Andreas Karwautz
- Gudrun Wagner
- Fernando Fernandez
- David Collier
- Angela Favero
Transgerational passage of behaviours
Tobacco use by the mother during pregnancy can result in

– premature birth and associated low birth weight,
– miscarriages,
– decreased placental blood flow
– subtle developmental delays

There are also data to suggest that heavy smoking may relate to later risk for conduct disorder in the child.
Interventions

• An intervention 0-5y (Busselton) to \( \uparrow \) Mo self worth \( \uparrow \) positive parenting strategies, \( \uparrow \) gentle physical interaction \( \rightarrow \) \( \downarrow \) BMI @27y (Cullen 1996)
Compulsive
Rigid

Anorexia

Impulsive
Weak Effortful control

Compulsive
Rigid

Binge

Phenotypes

Intermediate Phenotype

Environment triggers

Environment Activators

Genotype

Stress

Weak Social Processes,

Opioid, 5HT

Dieting
Intermittent Access
High Palatability Food

Child Adversity

‘s’ allele 5HTTLPR
Research Diagnostic Criteria RDoC(NIMH)

- Positive Valence
- Negative Valence
- Social Processes
- Attention
- Cognition
High sensitivity

Negative emotionality
FRY’S CHOCOLATE

J. S. FRY & SONS LTD., BRISTOL & LONDON
CHOCOLATE & COCOA MANUFACTURERS TO H. M. THE KING
300 GRANDS PRIX, GOLD MEDALS, &c.
Brewerton

- PTSD: associated with fast food, fizzy drinks, unhealthy diet Hirsh J 2011
- Palatable cafeteria diet ameliorates anx and dep behaviours and stress physiology associated with early adverse experiences MorrisMJ 2009
Stress and Adiposity: Meta-Analysis of Longitudinal Studies (Wardle et al 2011)

- Meta-analysis stress @ ↑adiposity \( (r = 0.014; \text{confidence interval (CI)} = 0.002-0.025, P < 0.05). \)

- Men > women.
When can perinatal and prenatal risk factors take place?

- Can relate to the pregnancy itself
- Can occur because the woman has a medical condition or injury that complicates the pregnancy
- Can result from environmental hazards that affect the mother or her fetus
- Can arise from maternal behaviors or lifestyles that have a negative effect on the mother or fetus
Neurodevelopmental Model

- Prenatal and perinatal insults
- Prenatal and perinatal programming (epigenetic mechanisms ie gene environment interaction which impact on later trajectory).
- Stress (over active HPA axis)
- Maternal care (insecure attachment)
- Nutrition (metabolic problems).
Inherited behavioral susceptibility to adiposity in infancy: a multivariate genetic analysis of appetite and weight

Llewellyn C 2012,
meta-analysis of single nucleotide polymorphisms related to adiposity identified 32 loci (small variance BMI): 33% mapped near hypothalamic regulators of energy balance (eg, TMEM18, KCTD15, SH2B1, GNPDA2, NEGR1, BDNF, POMC, FTO, and MC4R).
Intergenerational transmission of thinness (Whitaker et al 2011)

- The strongest predictor of child/adolescent thinness was parental weight status. The prevalence of thinness was highest (16.2%) when both parents were thinner and progressively lower when both parents were in the upper half of the healthy-weight range (7.8%) or were overweight (5.3%) or obese (2.5%), with no differences in the magnitude of maternal and paternal influences.
Behaviour change techniques used to decrease gestation weight change Gardner et al