Early life environment and neurodevelopment outcomes

Dr Deirdre Murray
Senior Lecturer, Dept of Paediatrics and Child Health
UCC
Outline

- How do we assess neurodevelopmental outcome?
- How do we grow a baby’s brain?
- What factors affect outcome?
THAT WASN'T REALLY AN AIRPLANE

THAT WAS JUST A SPOON
Developmental milestones

• Gross Motor
• Fine Motor
• Speech and Social interaction
• Developmental milestones a surrogate for later cognitive outcome
• Normal range is wide
• Significant delay always significant
• Isolated or global delay?
• Behavioural or cognitive or neuromuscular?
Cognitive outcome

• Subtle deficits
• Academic achievement
• Executive function

• Cognitive pre-requisites: working memory, processing speed, selective attention, response inhibition
What is executive function?

- Ability to organise and act on information
- Plan, organise, remember
- Prioritise, pay attention
- Use past experience and build on it

- Determines academic achievement
How do we predict later cognitive function?

• Developmental milestones

• Developmental screeners
  – Parental questionnaires
  – Ages and Stages, Denver Dev Assessment

• Developmental assessment
  – Developmental milestones and observed play
Neurodevelopmental assessment
0-3 years

Ages and stages questionnaire
Child behaviour checklist
Social and emotional growth chart

Bayley scales of infant development (BSIDIII)
Early neurodevelopmental assessment

1950s

Bayley Scales of Developmental assessment Version III
Neurodevelopmental assessment

> 5 years

Weshler Primary and Pre-school Scales of Intelligence IV

Weshler Intelligence Scales for Children

Kaufmann Brief IQ test: verbal and non-verbal IQ
“It takes a village to rear a child”

What does it take to grow a baby’s brain?
Infant brain growth

20 weeks

35 weeks

40 weeks
Cycles of myelination in the CNS during development.

<table>
<thead>
<tr>
<th>FETAL MONTHS</th>
<th>MONTHS OF FIRST YEAR</th>
<th>2 yrs</th>
<th>3 yrs</th>
<th>4 yrs</th>
<th>7 yrs</th>
<th>10 yrs</th>
<th>2nd decade</th>
<th>3rd decade</th>
<th>older</th>
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<tr>
<td>4 5 6 7 8 9 10</td>
<td>1 2 3 4 5 6 7 8 9 10 11 12</td>
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</tbody>
</table>

- Motor roots
- Sensory roots
- Sup. cerebellar ped.
- Mid. cerebellar ped.
- Optic rad.
- Somesthetic rad.
- Acoustic rad.
- Striatum
- Pyramidal tracts
- Great cerebellar commissures
- Reticular formation
- Assoc. areas

Baumann N, and Pham-Dinh D Physiol Rev 2001;81:871-927

Physiological Reviews
Human Brain Development

Neural Connections for Different Functions Develop Sequentially

- Sensory Pathways (Vision, Hearing)
- Language
- Higher Cognitive Function

First Year

Intrauterine toxins

Placental function

Genetic abnormalities

Congenital malformations

Maternal Nutrition

Intrauterine infection

Intra-uterine toxins

Perinatal hypoxic-ischaemia

Preterm birth
Preterm birth: 6% all births

Bigger is better

A baby’s brain at 35 weeks weighs only two-thirds what it will weigh at 40 weeks.

Source: March of Dimes

THE COLUMBUS DISPATCH
Near term/late preterm

- 70% of all preterms = 34-36+6 weeks
- Increased risk of neurodevelopmental disabilities (e.g., mental retardation, cerebral palsy x6)
- School-related problems
- Poor performance on academic achievement and neurocognitive tests.
In Utero growth

I’m thinking about going on the 5:2 diet
Fetal growth and effect on long term outcome?

Variable effect: depends on definition and severity.

\[ CP = OR \ 6.48 \ (4.2-11) \text{ if } < 3^{rd} \text{ percentile and} \]
\[ 3.81(2.7-5.5) \text{ if } < 10^{th} \text{ percentile} \]

- Blair and Stanley  J Obstet Gynae 1990

Small (6 IQ points), little effect if compared to siblings

- J Pediatr 1998

Higher incidence of school failure and “minimal brain dysfunction”

- Arch Pediatr Adolesc Med 2002

Effect on outcome after 33 weeks gestation

- Yanney, Marlow 2004 Seminars in Fetal and Neonatal Medicine
Early Childhood Neurodevelopment After Intrauterine Growth Restriction: A Systematic Review
Levine, et al.  
*Pediatrics* 2015; 135:1 126-141

Systematic review: 16 articles

11/16 found worse outcome in IUGR

Motor, cognitive, language 
Social development, attention and behavioural deficits
The CORK BASeline
Birth Cohort

Dr Deirdre Murray
Dept of Paediatrics and Child Health
Intrauterine growth restriction
Detailed neurodevelopment assessment
BP, Insulin resistance, 25-OH-D3
Skin prick testing

2500

Biobanking
TEWL
Body fat %
Anthropometry
Neonatal course

Feeding
Growth
Body fat %
Eczema, TEWL
Food allergy
General health
Childhood illness
Developmental screening
### The normal term newborn

<table>
<thead>
<tr>
<th></th>
<th>Mean</th>
<th>Std. Dev</th>
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<tr>
<td></td>
<td>n=996</td>
<td></td>
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<tr>
<td>G.A. at delivery (w)</td>
<td>39.75</td>
<td>1.15</td>
</tr>
<tr>
<td>Birthweight</td>
<td>3509.10</td>
<td>469.4</td>
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<tr>
<td>Head circumference</td>
<td>34.8</td>
<td>1.4</td>
</tr>
<tr>
<td>Length</td>
<td>50.4</td>
<td>2.0</td>
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<tr>
<td>% body fat</td>
<td>11.18</td>
<td>5.13</td>
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Outcome in small for gestational age babies

- August 2008 to February 2011 (n=1335)
- Body Fat composition, as measured by air displacement plethysmography was available for 66.7% (n=890)
- SGA babies 11.1% (n=148)
Methods

• Infants small for gestational age (80)
• Infants thin for gestational age (80)
• Controls stratified across remaining centiles (300)

• Outcome BSID III and CBCL at 2 years to newborn status
Outcome at 2 years

• Adjusted for maternal age, occupation, smoking status, marital status, years of schooling and socioeconomic status.

Small and thin:
• Cognitive deficit: 3 times more likely
• Motor deficit: 5.7 times more likely
• Language deficit: 8 times more likely
Infant Feeding and Childhood Cognition at Ages 3 and 7 Years
Effects of Breastfeeding Duration and Exclusivity


Prospective cohort study (Project Viva), 1312 Project Viva mothers and children.

**Results**  Adjusting for sociodemographics, maternal intelligence, and home environment in linear regression-
-longer breastfeeding duration was associated with higher Peabody Picture Vocabulary Test score at age 3 years (0.21; 95% CI, 0.03-0.38 points per month breastfed)
-higher intelligence on the Kaufman Brief Intelligence Test at age 7 years (0.35; 0.16-0.53 verbal points per month breastfed; and 0.29; 0.05-0.54 nonverbal points per month breastfed).

Causal relationship of breastfeeding duration with receptive language and verbal and nonverbal intelligence later in life.
Environmental exposure

Maternal Education vs genetic potential

Infant attachment
Neuroscience, Molecular Biology and the Childhood Roots of Health Disparities: Building a New Framework for Health Promotion and Disease Prevention

Shonkoff J JAMA 2009;301(21):2252-2259

Those reporting emotional abuse in childhood increased risk of major depressive illness 61% vs 18.5%

Early stress: decreased hippocampal volume, decreased pre-frontal cortex Memory, anxiety, aggression
Parental substance abuse
Dysfunctional schools
Personal maltreatment
Chronic neglect
Family violence
Maternal Depression

Decreased cognition
Altered emotional states
Altered decision making

Altered brain architecture

Emotional instability
Substance abuse
Aggression
Poor academic performance

Parental substance abuse
Dysfunctional schools
Personal maltreatment
Chronic neglect
Family violence
Maternal Depression
Early environmental factors

- Parental genes & Environment
- Maternal nutritional or stress hormone levels
- Early nutrition

In utero environment

Pre-maturity

Exposure Maternal Education Environment

Outcome

Birth asphyxia sepsis
Improving outcome

- Influence of multiple factors
- Term gestation
- Normal birth weight
- Breastfeeding
- Good early growth
- Maternal education
- Stress free environment
Children’s Discovery centre

Thank you!!