Nutrition's Impact on Childhood Cognitive Function, Learning, and Development

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Premises

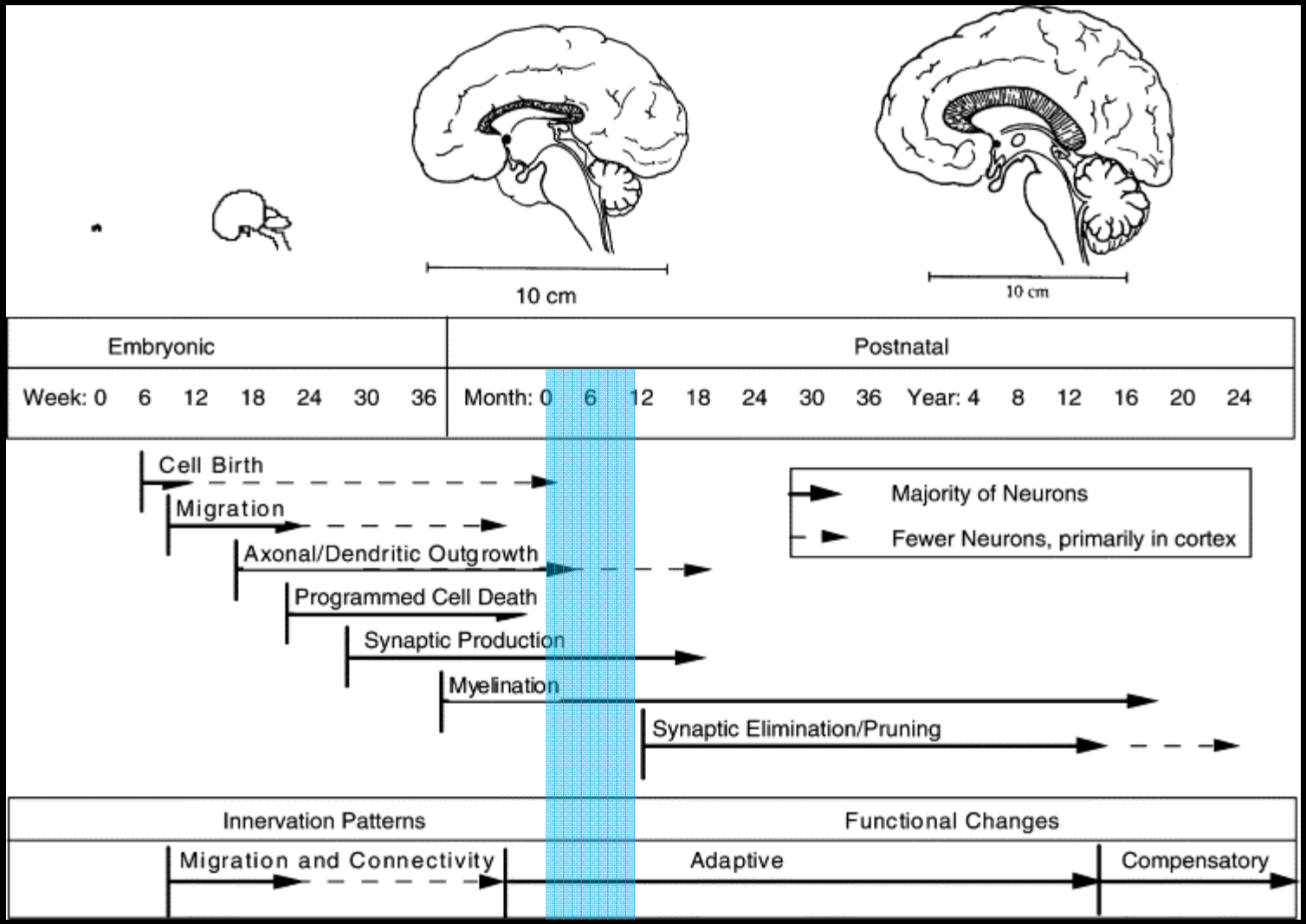
- From conception forward across the life span nutrition is critical for brain and behavioral development.
- Understanding the influence of nutrients on brain development and behavior requires consideration of complex brain-behavior-environmental interactions.
- Measures of brain structure and function in children are interrogating a work in progress.

Presentation Overview

Areas of focus will include biobehavioral correlates of:

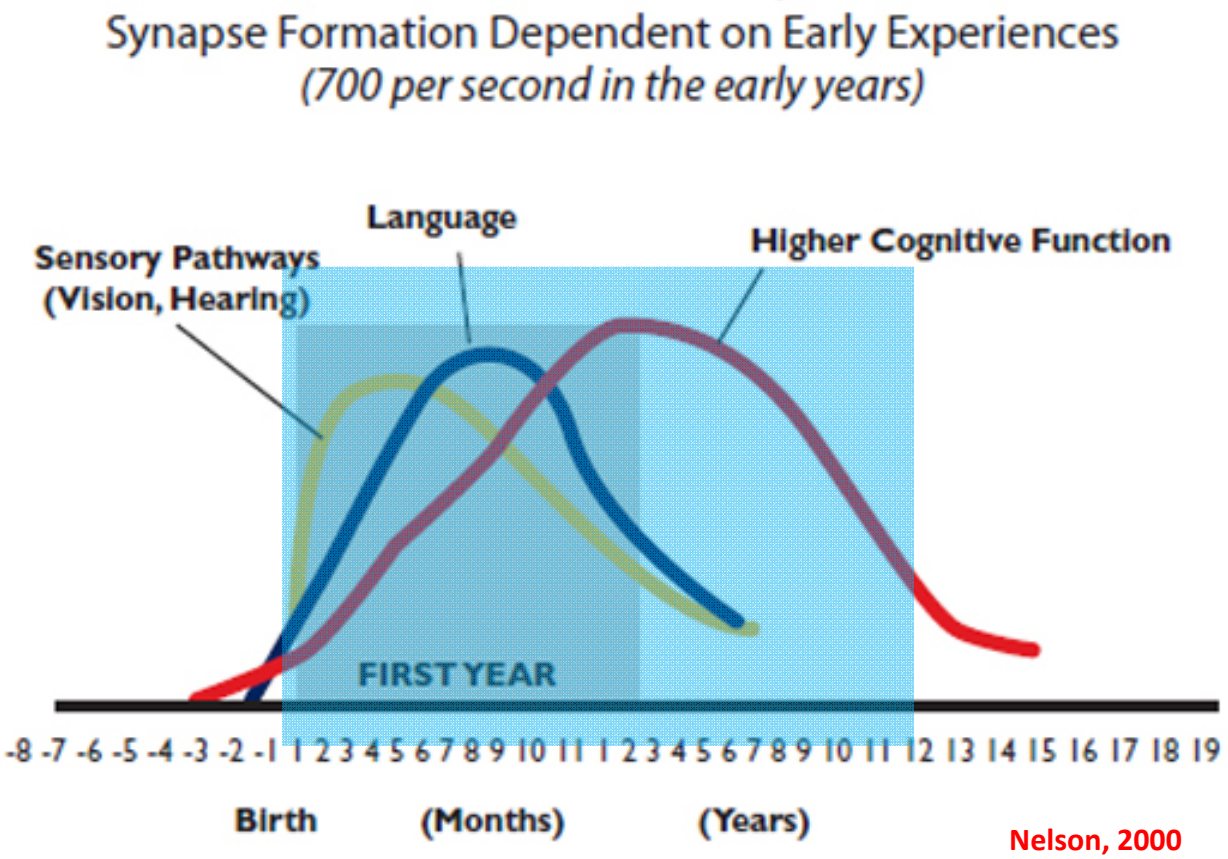
- Early postnatal diet
  - Infants
  - Preadolescents
- Breakfast – Preadolescents
- Childhood obesity

Human Brain Development



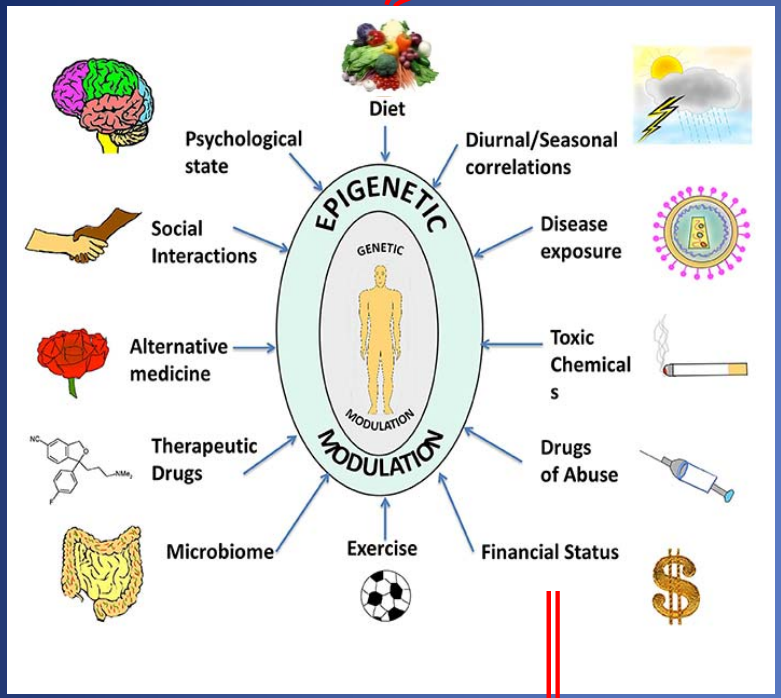
Andersen, 2003

Human Brain Development



Nelson, 2000

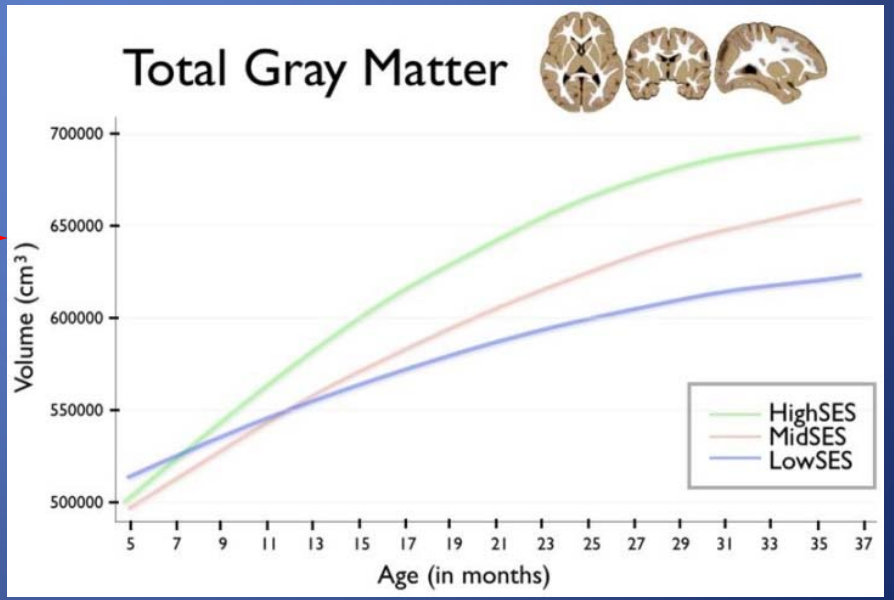
EPIGENETIC INFLUENCES



Adapted from Kanherkar et al., 2014

Dietary factors may influence brain development and function via epigenetic processes

Attig et al., 2010
Bloomfield, 2011
Canani et al., 2011
Georgieff et al., 2015
Kanherkar et al., 2014
McKay and Mathers, 2011
Verduci et al., 2014
Zeisel, 2009



Hanson et al., 2013

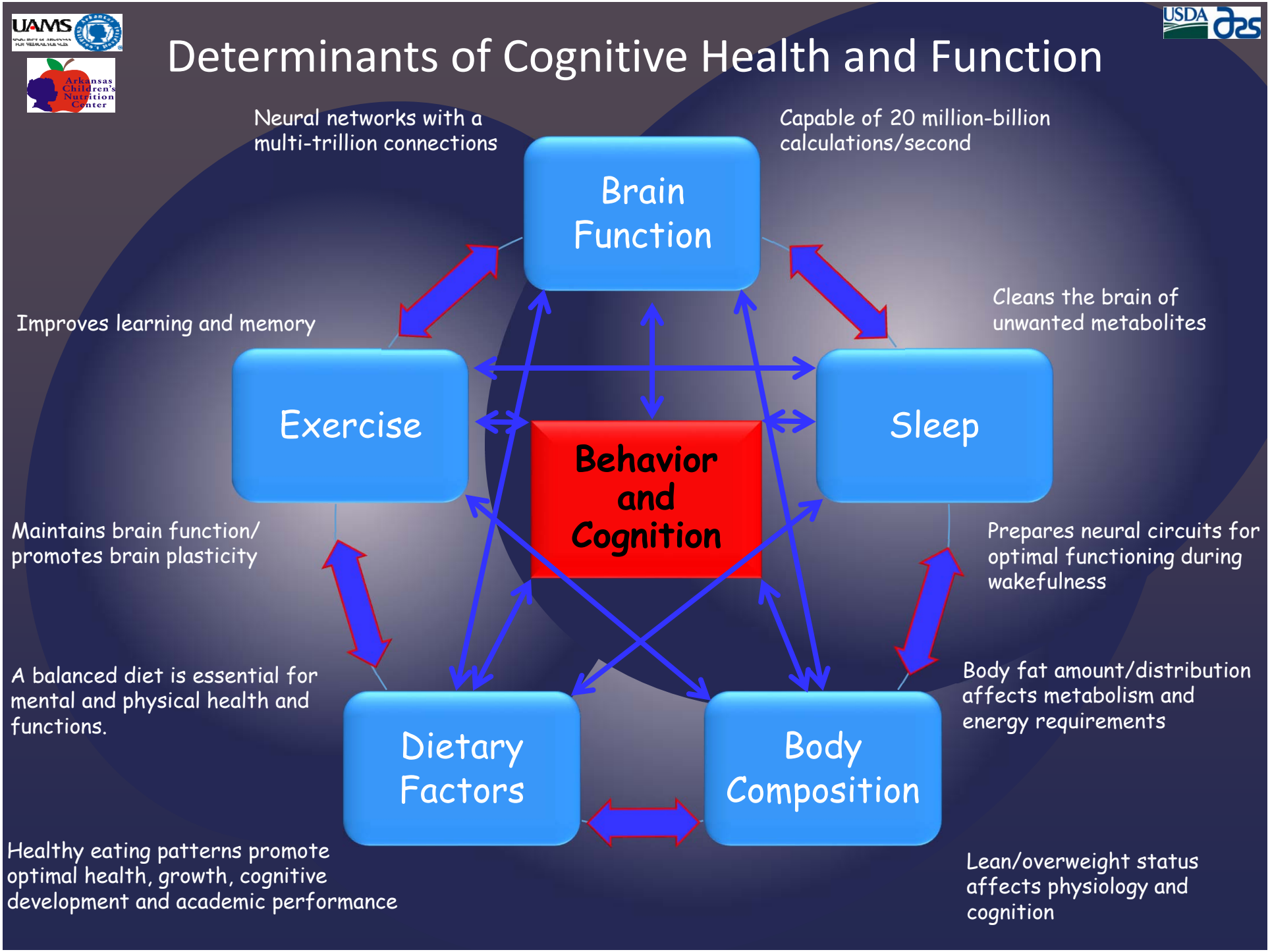
Environmental experiences modify gene expression

Functional consequence: organism responds differently to its environment

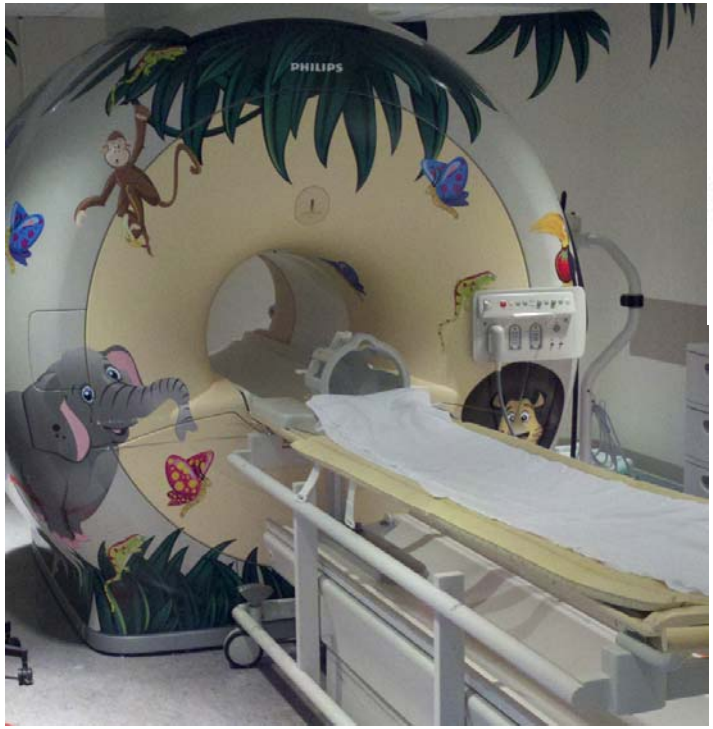
Offers explanations for indvidual differences and trait characteristics

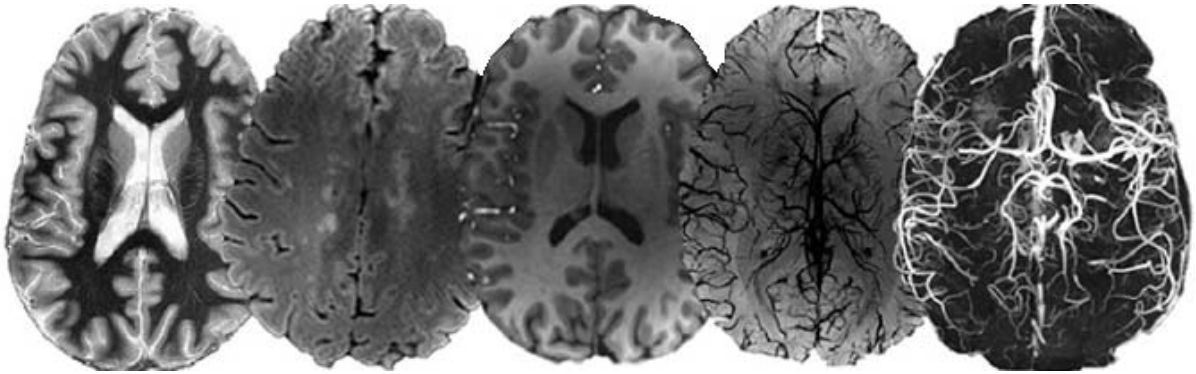
Provides new opportunities for modification of conditions and behaviors

Determinants of Cognitive Health and Function

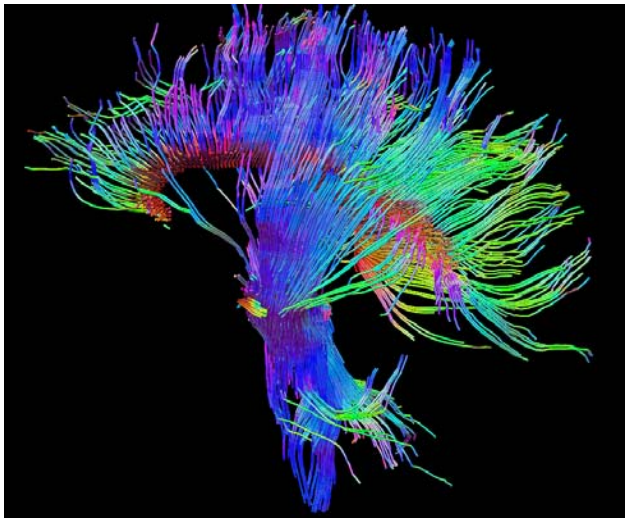


Magnetic Resonance Imaging (MRI)

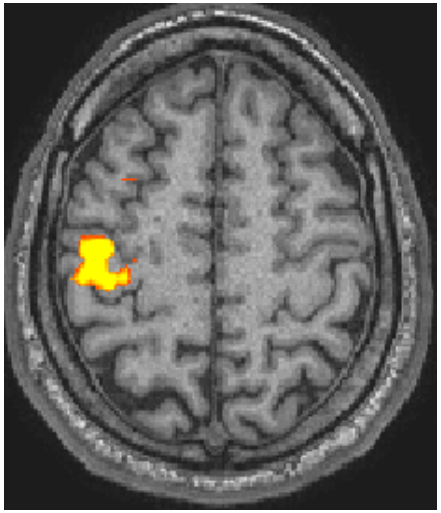




Structural MRI



DTI Fiber tracking

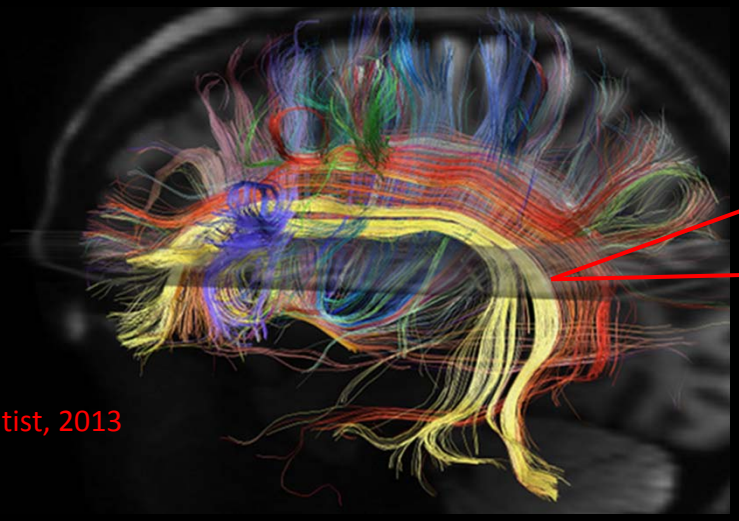


Functional MRI

- Brain Structure
  - size and shape of specific brain regions
  - integrity of brain white and grey matter
- Brain Function
  - functional connectivity during resting
  - activation in the brain during tasks

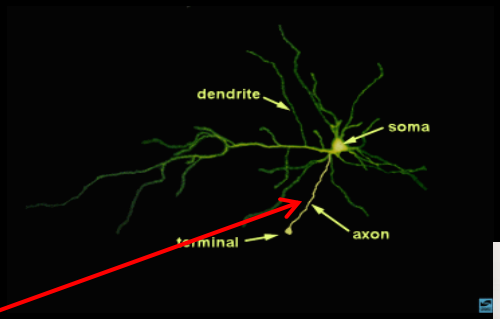
NUTRIENTS AND BRAIN DEVELOPMENT

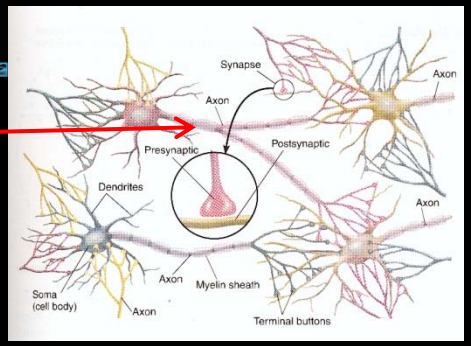
Myelinated fibers



The Scientist, 2013

Neurons and Networks





Myelin

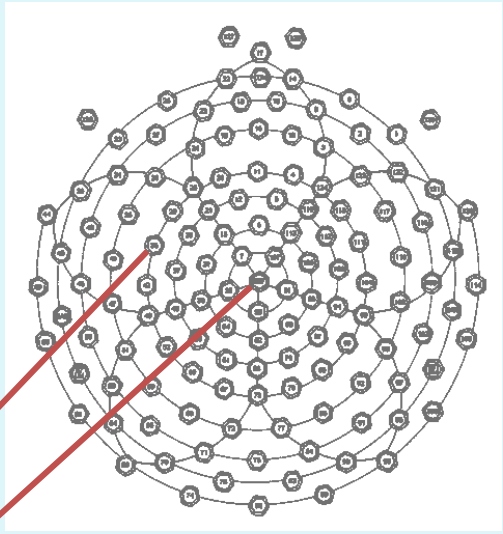
Iron
LC-PUFAs
Choline

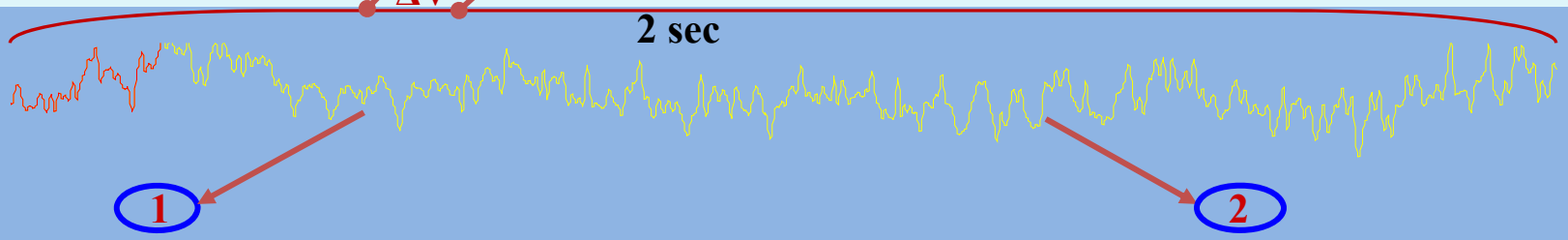
Cell proliferation, synaptogenesis

Protein
Iron
LC-PUFAs
Glucose

Georgieff et al., 2015; Wullschleger et al., 2006

High Density Recording of Brain Electrical Activity

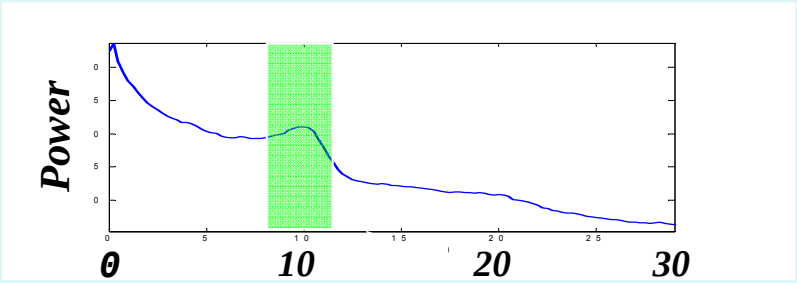




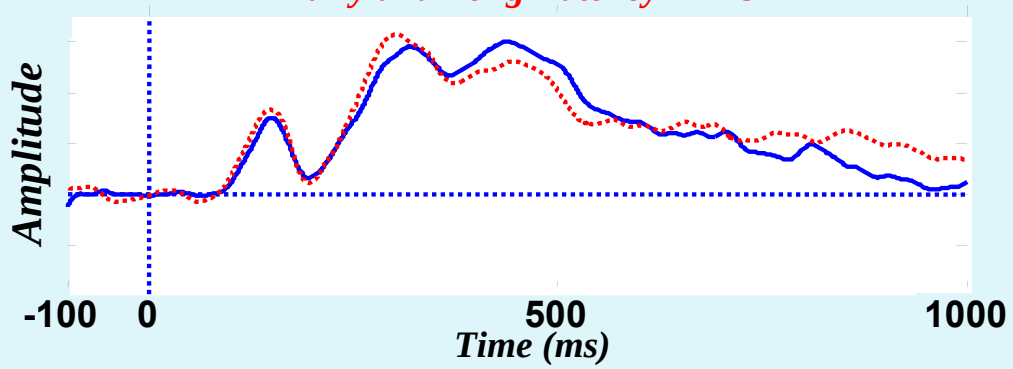
Frequency composition, but not distribution across time

Average all trials together which eliminates signals not stimulus locked.

Power Spectral Density



Early and Long-Latency ERPs



Early Infant Diet: Brain/Cognitive Correlates During Infancy and Childhood

The majority of U.S. infants are initially breastfed (BF), but by the age of 6 months most transition to milk-based (MF: 75%) or soy protein-based (SF: 25%) formula.

Bhatia & Greer, 2008; Grummer-Strawn et al., 2008

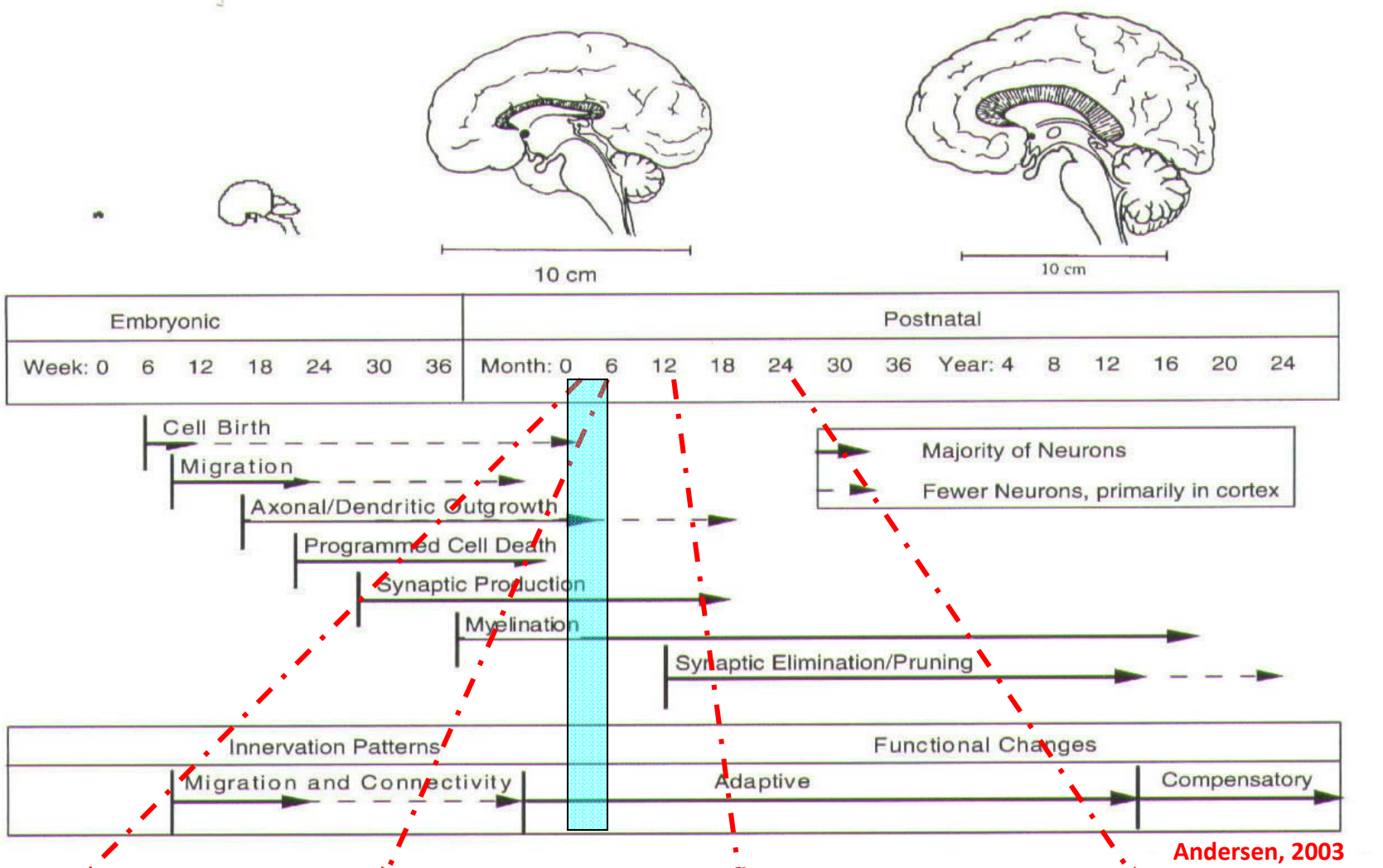
infant diets vary significantly in factors that influence CNS and behavioral development:

- **feeding process: breast vs. bottle** (Burgard, 2003)
- **composition of biologically active components**
  - **omega-3 fatty acids** (Heird, 2007)
  - **sialic acid** (Wang, 2009)
  - **choline** (Wurtman, 2009)
- **sources for**
  - ***carbohydrates*** **(BF, MF: lactose; SF: sucrose and/or corn syrup)**
  - ***protein*** **(BF, MF: casein and whey; SF: soy)**

Bhatia & Greer, 2008; Joeckel & Phillips, 2009; Lönnerdal, 2003

- **These differences present conditions for organizational and activational effects on the developing CNS with potential epigenetic consequences**

Human Brain/Behavior Development



Social orientation

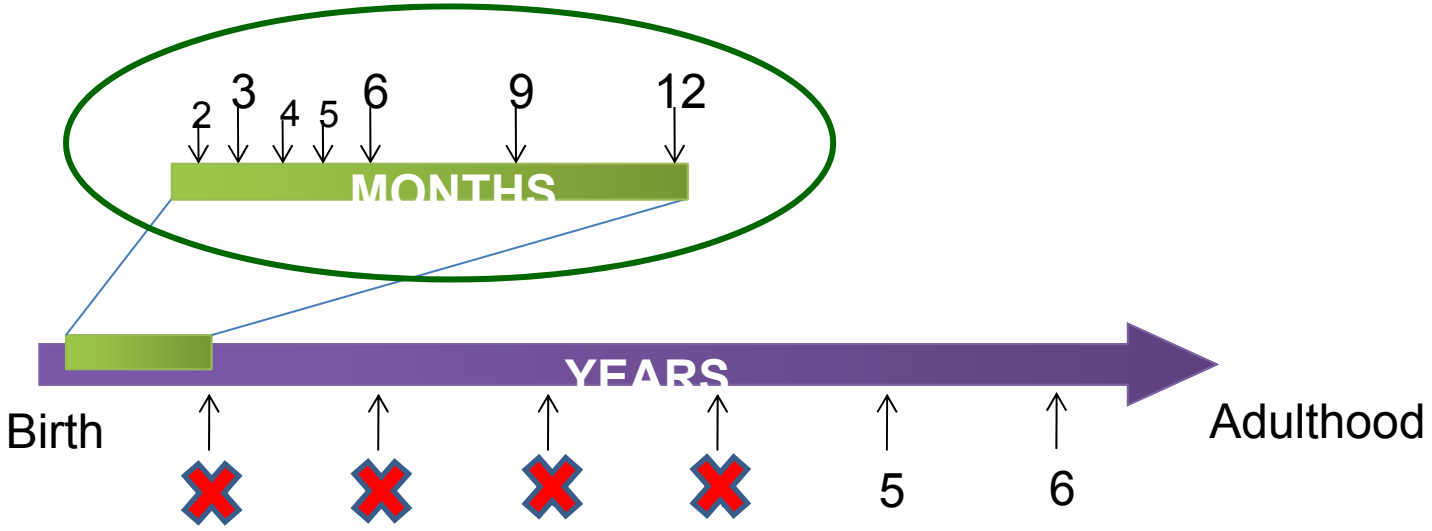
Modulation of affect, arousal, attention; early memory

Separation distress; working memory; acoustic highlighting of words

Maturation of sensory and motor functions; early speech; joint attention

THE BEGINNINGS STUDY

A prospective longitudinal study of the influences of infant diet on the physiological, cognitive, and behavioral development of children from 3 months to 6 years of age who were fed breast milk, cow milk formula or soy formula as infants (200/group).



Diet, Metabolism, and Body Composition Assessments

(Except for food records kept by parent, all administered to or obtained from child or parent)

	3m	6m	9m	1y	2y	3y	4y	5y	6y
Food Frequency Questionnaire -Moms	X	-	-	-	-	-	-	-	-
Diet assessment- Breast-fed Moms only	X	X	-	-	-	-	-	-	-
Food Records	X	X	X	X	X	X	X	X	X
Anthropometric Data	X	X	X	X	X	X	X	X	X
DXA	X	X	X	X	X	X	X	X	X
NMR	X	X	X	X	X	X	X	X	X
PeaPod/BodPod	X	X	-	-	-	-	-	-	X
BIA	-	-	-	-	X	X	X	X	X
Ultrasound	-	X	-	X	X	-	-	X	-
Urine- Milk-fed and Breast-fed	X	X	-	-	X	-	-	X	X
Urine- Soy-fed	X	X	-	-	X	-	-	X	X
Blood- Soy-fed	X	X	-	-	-	-	-	-	-

Psychophysiological Assessments (Brain Function Laboratory)

(Administered to child)

	3m	6m	9m	1y	2y	3y	4y	5y	6y
Baseline	X	X	X	X	X	X	X	X	X
Finger-Length Pattern Measurement	X	X	X	X	X	X	X	X	X
Spontaneous Sleep Recordings	X	X	X	X	-	-	-	-	-
Startle Test	X	X	X	X	X	X	X	X	X
Auditory Language Discrimination	X	X	X	X	X	-	-	-	-
Auditory Language Discrimination Extension	-	-	-	-	-	X	-	-	-
Semantic Incongruity	-	-	-	-	-	X	X	X	X
Face Recognition	-	-	-	-	-	-	X	X	X
Hearing Screening	-	-	-	-	-	-	-	-	X
Auditory Brainstem Response	-	-	-	-	-	-	-	-	X

Home, Family, and Behavioral Assessments

(Completed by parent or administered to parent)

	3m	6m	9m	1y	2y	3y	4y	5y	6y
Family Inventory of Life Events and Changes (FILE)	X	-	-	X	X	X	X	X	X
Edinburgh Handedness Inventory	X	-	-	-	-	-	-	-	-
Hollingshead: Four Factor Index of Social Position(s)	X	-	-	X	X	X	X	X	X
Family Adaptability and Cohesion Evaluation Scales-II	X	-	-	X	X	X	X	X	X
Minnesota Multiphasic Personality Inventory-2	-	X	-	-	-	-	-	-	-
Wechsler Abbreviated Scale of Intelligence (WASI)	X	-	-	-	-	-	-	-	-
Symptom Assessment-45 Questionnaire (SA-45)	X	X	X	X	X	X	X	X	X
Carey Temperament Scales	-	X	X	X	X	X	X	X	X
Child Behavior Check List (CBCL)	-	-	-	-	X	X	X	X	X
Behavior Rating Inventory of Executive Function – Preschool Version (BRIEF-P)	-	-	-	-	X	X	X	X	-
Behavior Rating Inventory of Executive Function – Parent Form (BRIEF)	-	-	-	-	-	-	-	-	X
Process	X	X	-	X	X	X	-	-	-

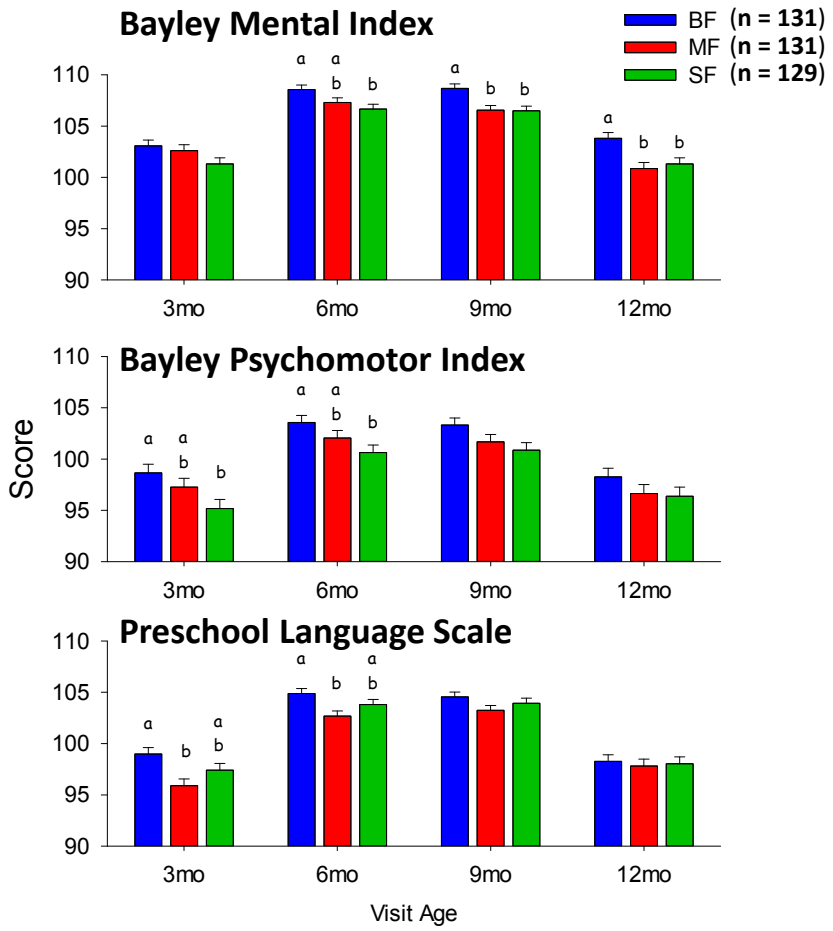
Psychological / Behavioral Assessments

(Administered to child)

	3m	6m	9m	1y	2y	3y	4y	5y	6y
Edinburgh Handedness Inventory	-	-	-	-	-	-	-	-	X
Bayley Infant Development Scales	X	X	X	X	X	-	-	-	-
Reynolds Intellectual Assessment Scales (RIAS)	-	-	-	-	-	-	X	X	-
Wechsler Preschool and Primary Scale of Intelligence	-	-	-	-	-	-	-	-	X
NEPSY	-	-	-	-	-	X	X	-	-
Grooved Pegboard Test	-	-	-	-	-	X	X	X	X
Preschool Language Scale-3	X	X	X	X	X	X	X	X	X
Motor Free Visual Perception Test, Third Edition (MVPT-3)	-	-	-	-	-	-	-	-	X
Developmental Test of Visual Motor Integration, 5th Ed. (VMI)	-	-	-	-	-	-	-	X	X
Children's Memory Scale (CMS)	-	-	-	-	-	-	-	-	X
Clinical Evaluation of Language Fundamentals 4th Ed. (CELF-4)									X

Breast-fed children show cognitive advantages

Infants



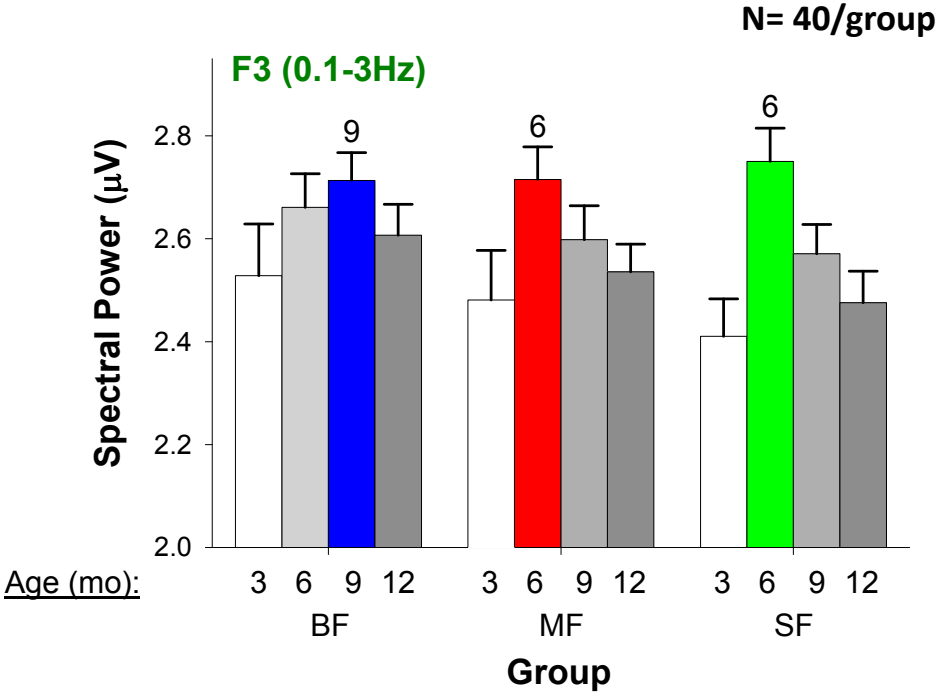
Andres et al., 2012

Children

- Receptive Language; Verbal and Non-verbal Intelligence (3 and 7 yrs)
  Belfort et al., 2013
- Academic Performance (12 yrs)
  Dalmeijer et al., 2015
- IQ - Meta-analysis (12 yrs)
  Horta et al., 2015
- IQ (1-7 yrs)
  Jedrychowski et al., 2012
- IQ; Academic Performance (6.5 yrs)
  Kramer et al., 2008
- Verbal/Cognitive IQ and Perceptual Reasoning (6 and 8 yrs)
  Oddy et al., 2003

Maturation of brain electrical activity and heart rate control differs in breast-fed and formula-fed infants

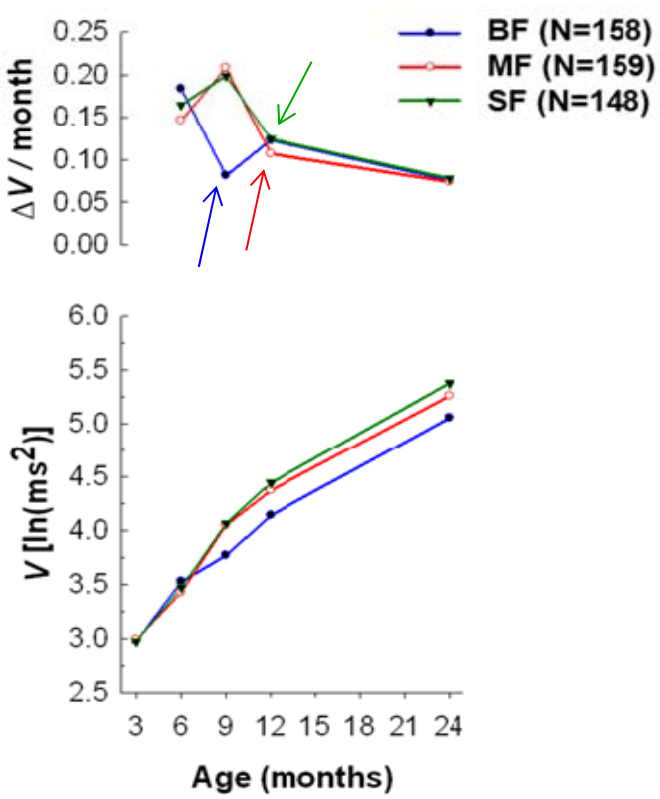
EEG



- There are diet-related differences in the temporal pattern of EEG development.
- Differences in temporal development reflect current neurodevelopment that may influence future neurodevelopment.

Jing et al., 2010

Vagal Tone



- The slowing of *V* development may be a pivotal point in parasympathetic maturation.
- This occurs earlier in breast-fed than formula-fed infants.

Pivik et al., 2013

Language Development

4 years – 6 years

Sentences – Distinguishing Meaning from Nonsense

2 years

Semantic Incongruity – Linking Words with Objects

3 months

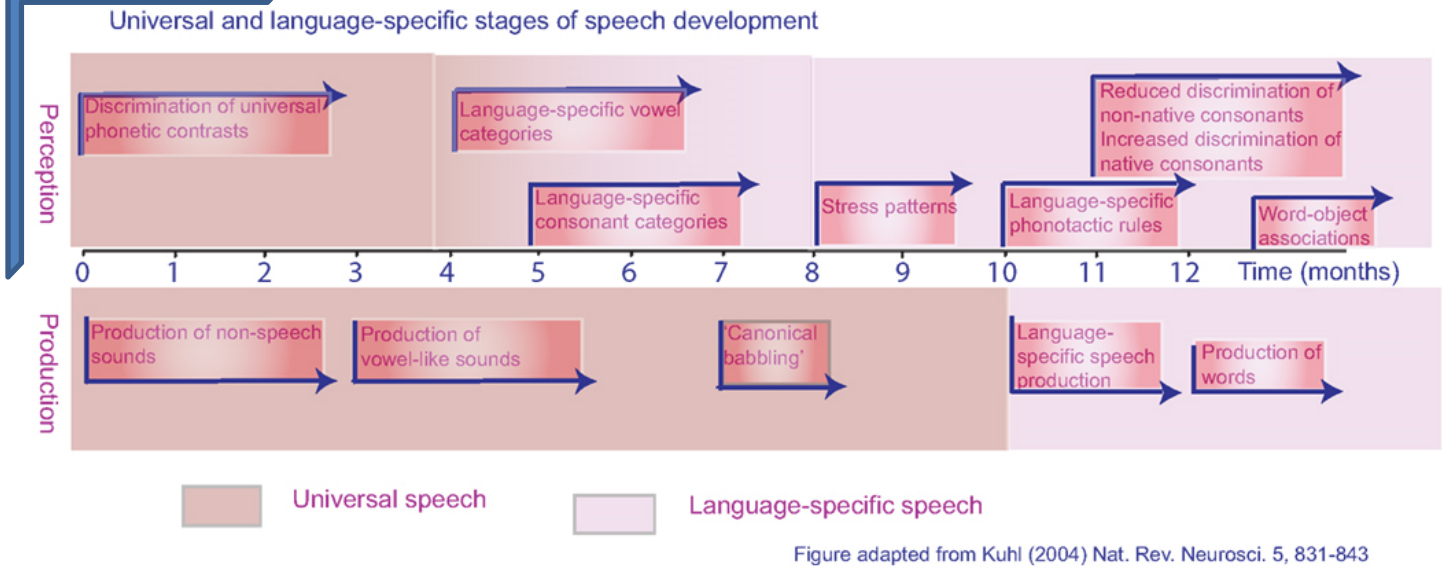
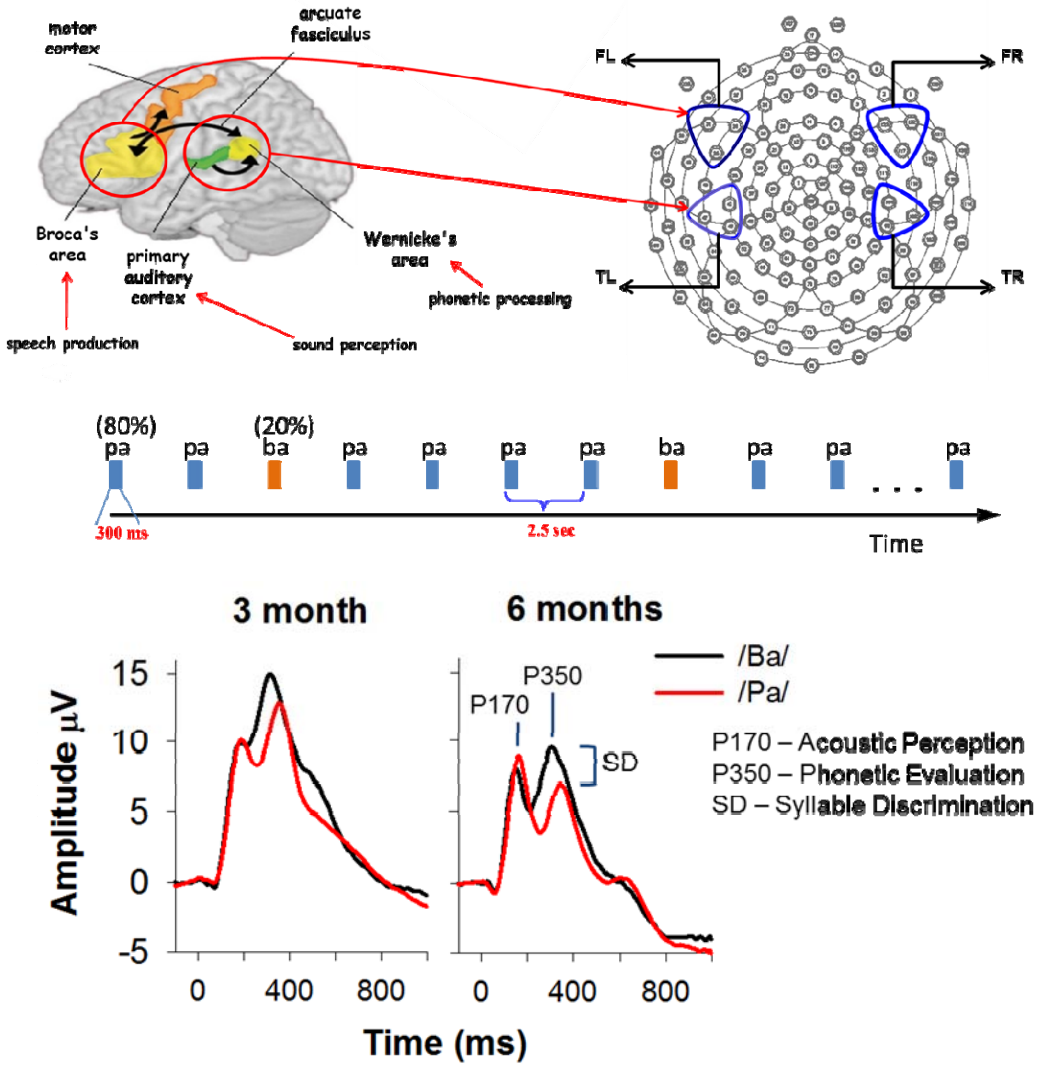


Figure adapted from Kuhl (2004) Nat. Rev. Neurosci. 5, 831-843

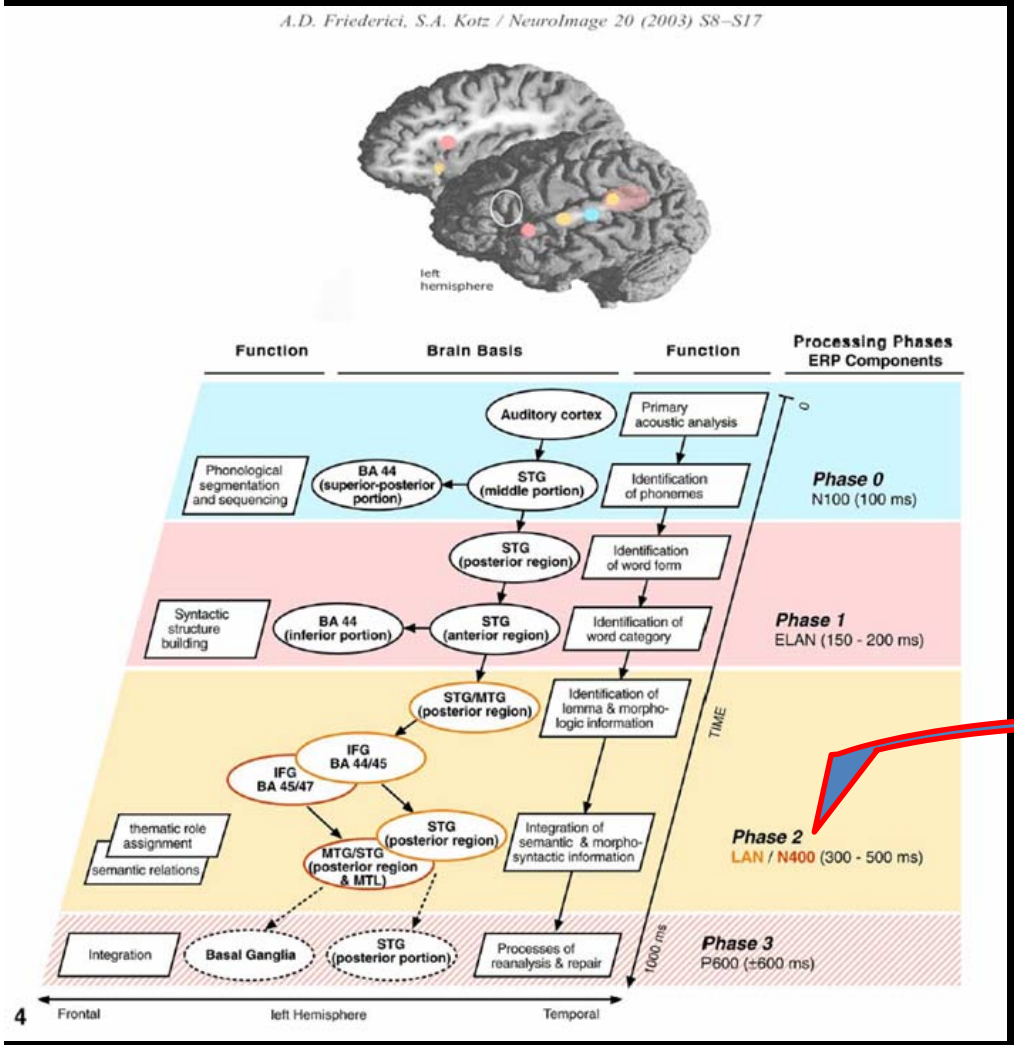
Early infant diets differentially influence processes essential for language acquisition

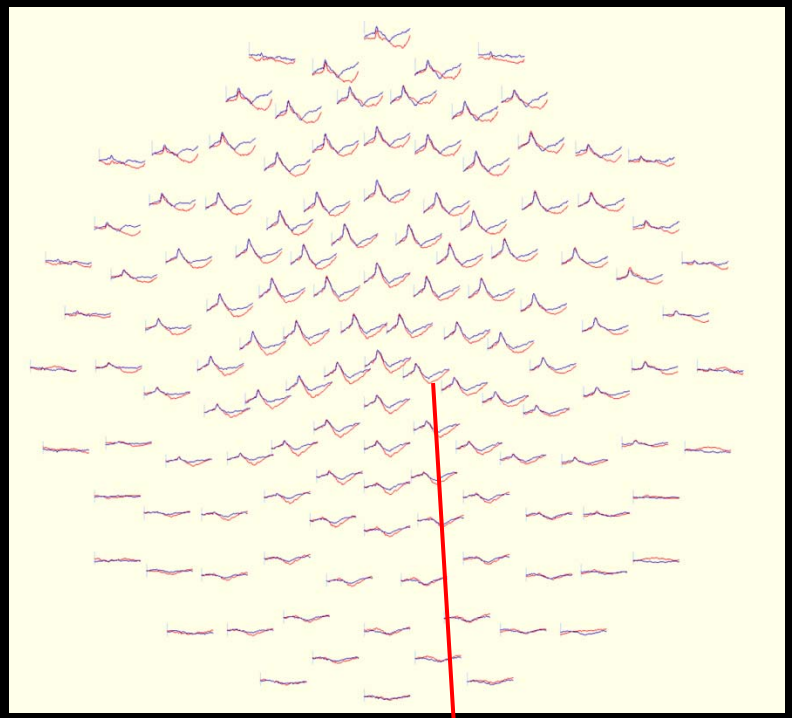


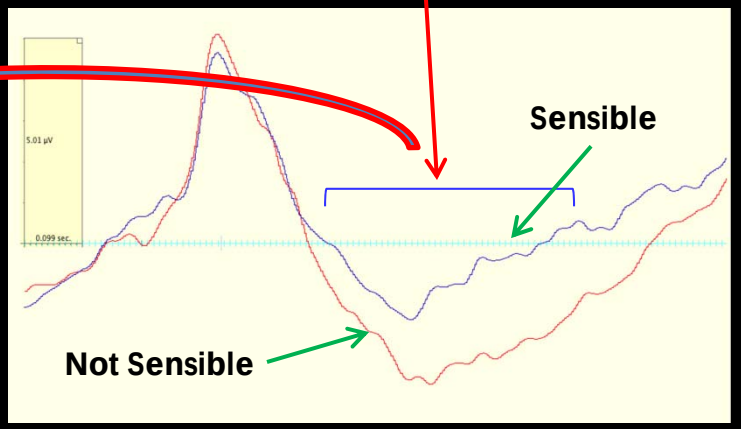
- greater syllable discrimination in breast-fed than formula-fed infants.
- a general absence of differences between formula-fed groups.

Pivik et al., 2012

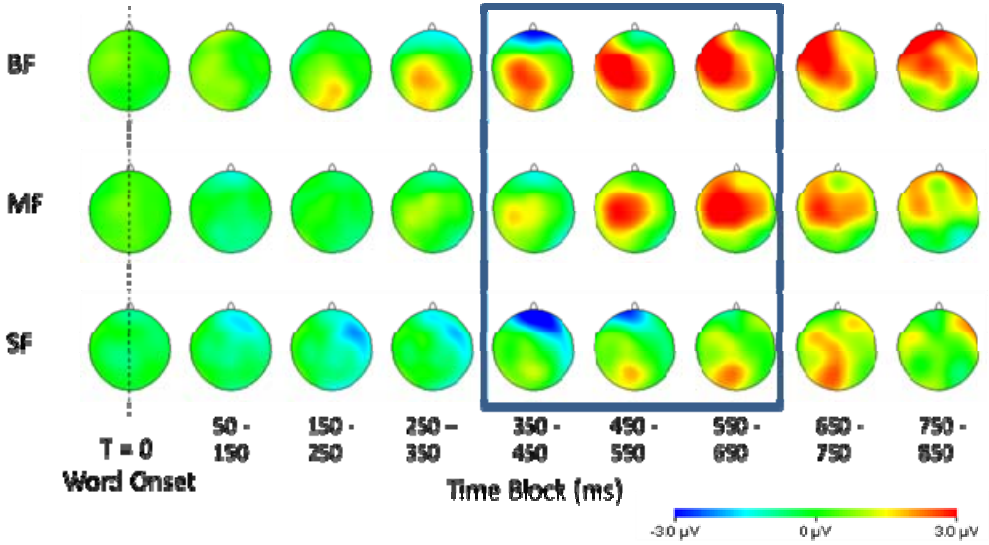
Sentence Comprehension In Half A Second

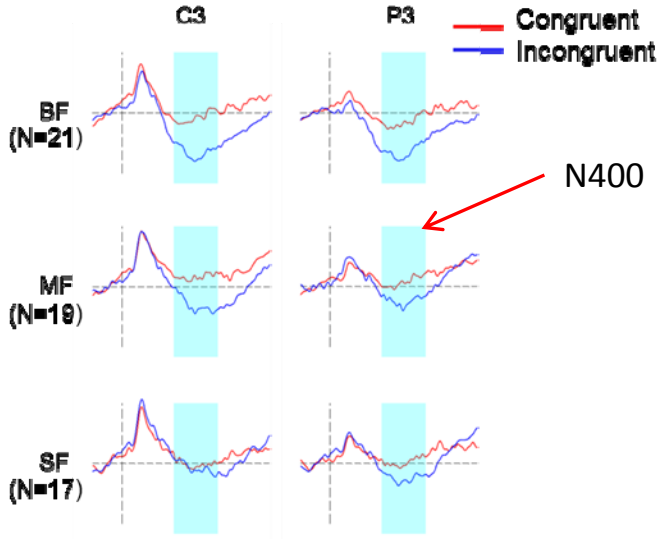




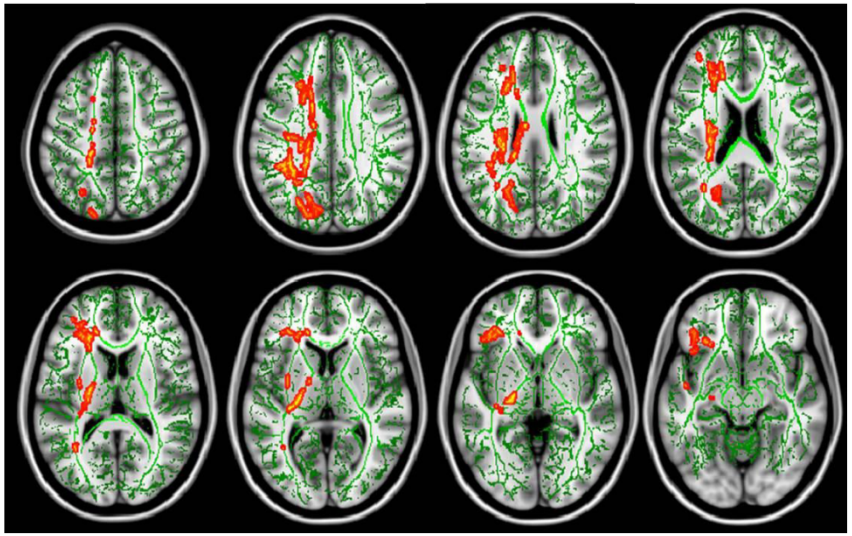


Early infant diets differentially influence the development of brain processes underlying later language comprehension in children





Pivik et al., 2014



- responses to incongruent words are greater in breast-fed than formula-fed groups, but similar in formula-fed groups
- congruent word responses were similar across groups
- white matter development (orange) is greater in breast fed than formula-fed children
- amount of myelination is positively correlated with standardized IQ and language test scores

Ou et al., 2014

Preadolescents and Breakfast

Brain glucose utilization between the ages of 4-10 years is twice that of adults

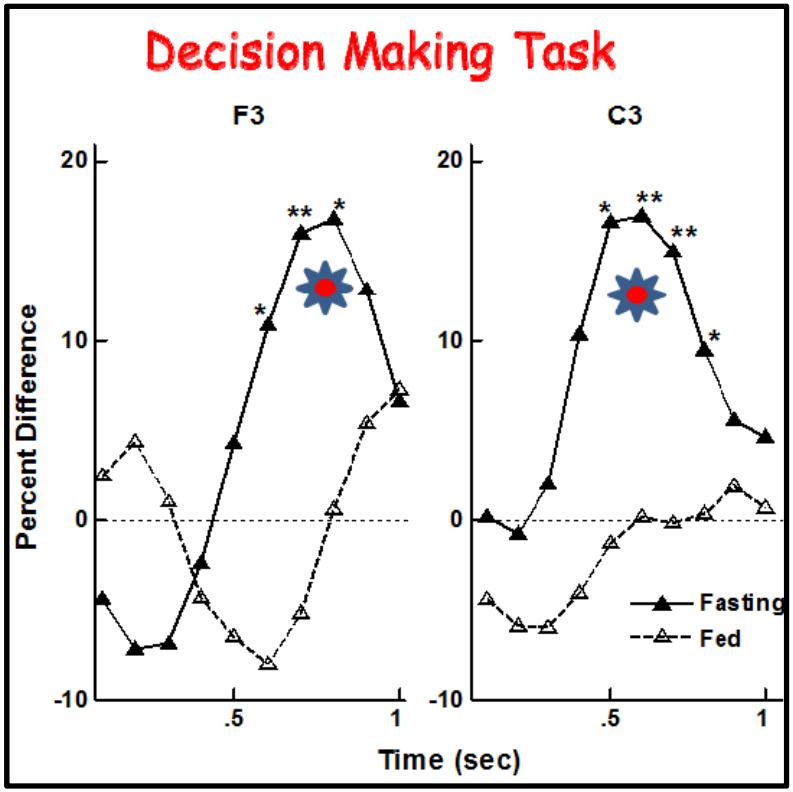
High metabolic rates and energy demands in children make them particularly sensitive to nutritional deficiencies—even on a short-term basis. Chugani, 1987,1998

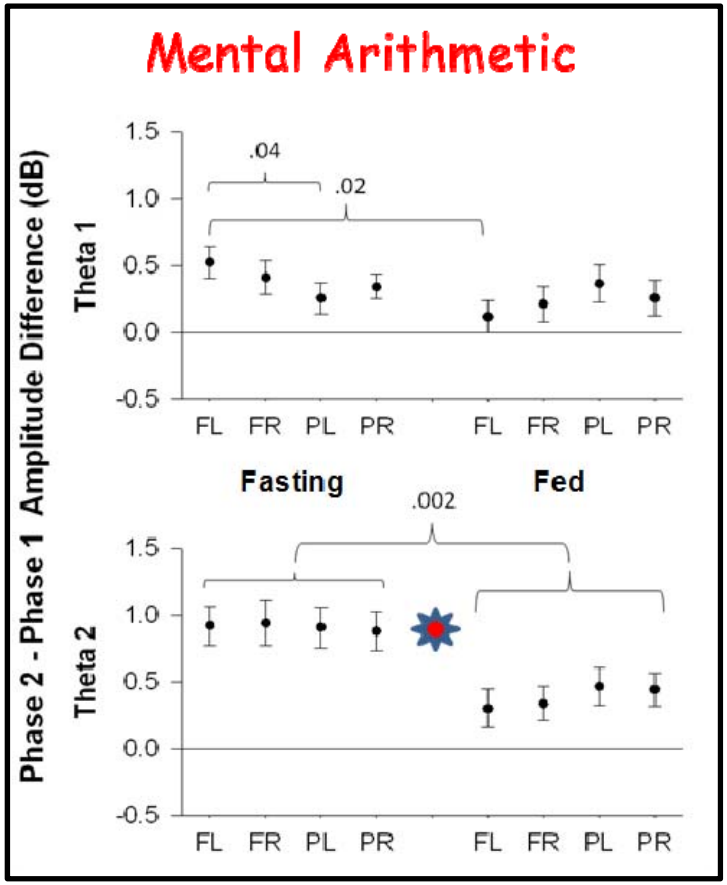
Skipping breakfast negatively impacts learning and performance in children by affecting processes involving attention, discrimination, memory, and reaction time.

Benton et al., 1998; 2001;2003
Kleinman, 1999
Wesnes et al., 2003

- **Understanding these nutritional and cognitive/behavioral interactions is necessary for optimizing processes important in successful school performance.**

Eating or skipping breakfast affects immediate learning and performance





- Eating breakfast enhances the efficiency of neural networks engaged during executive function tasks in school-aged children.

Pivik et al., 2007,2012

Childhood Obesity Compromises Cognition

Decreased academic performance, memory, attention, verbal and motor abilities in obese compared with normal weight children

Davis et al., 2011; Li et al., 2008
Shore et al., 2008; Smith et al., 2011

Impairments of executive function appear to represent a core cognitive feature of obesity in children and adults

Braet et al., 2007; Cserjesi et al., 2007, 2009
Gunstad et al., 2007; Smith et al., 2011

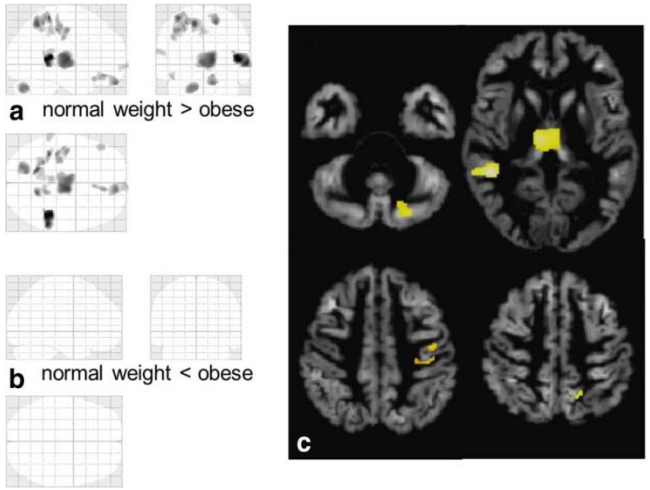
- **It is likely that executive function dysfunction contributes to the development and maintenance of obesogenic behaviors**

Brain structure and function are reduced in obese children

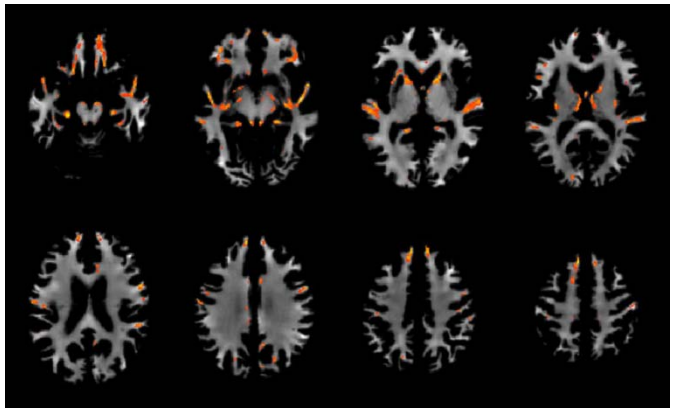
Structure

Obese children have less gray and white matter.

Gray Matter

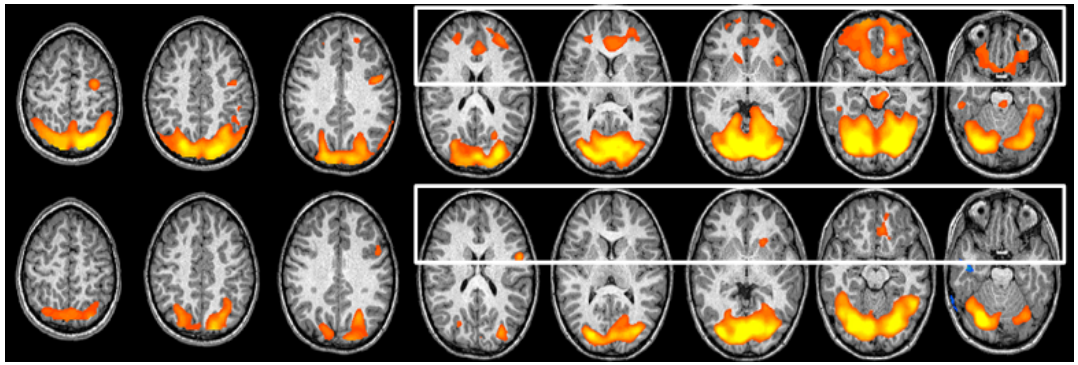


White Matter



Function

Frontal brain activation is reduced in obese children when performing an executive function inhibitory (go/no-go) task.



Ou et al., 2015

Brain response measures (ERPs) document executive function deficits related to inhibition and the ability to self-regulate.

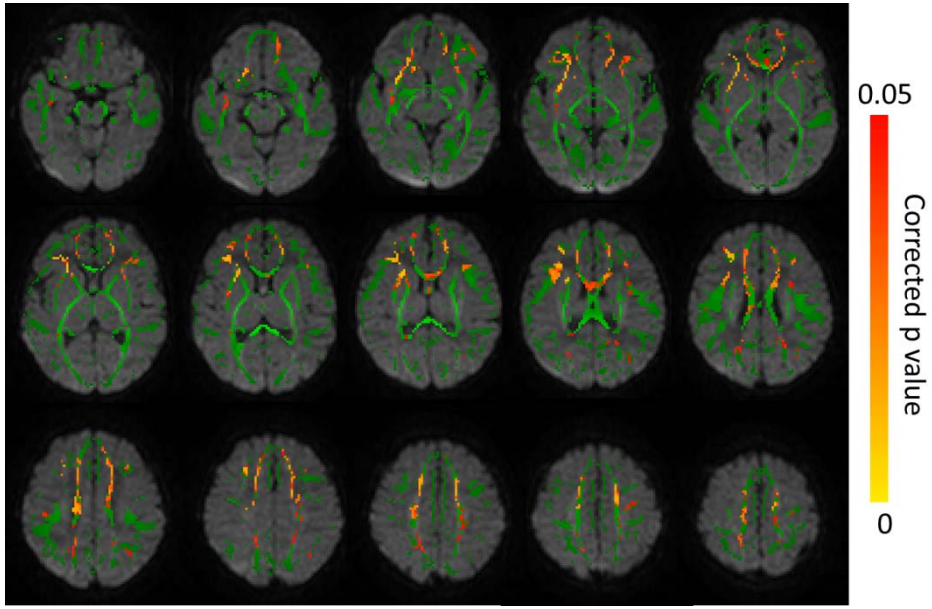
Kamijo et al., 2012, 2014
Skoranski et al., 2013

Normal weight

Obese

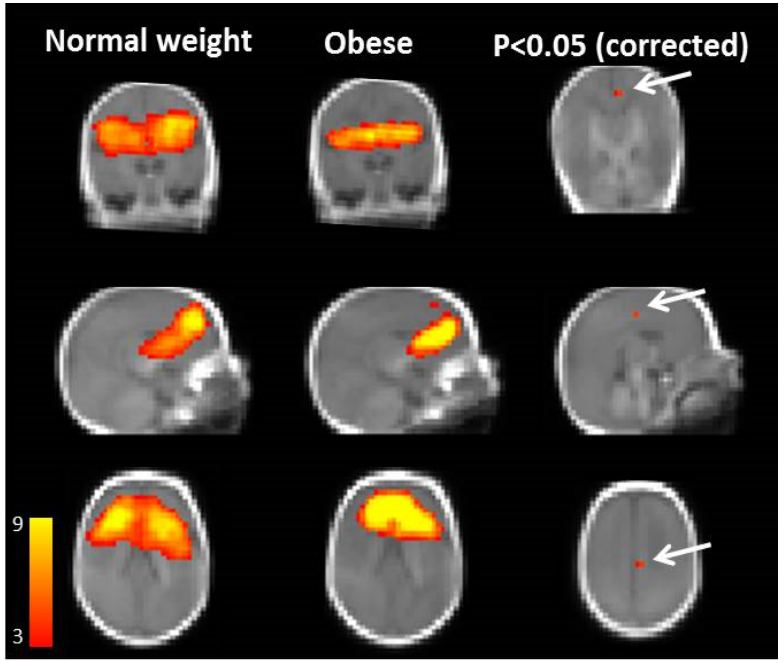
Maternal Obesity Impacts Newborn Brain Development and Function

White Matter



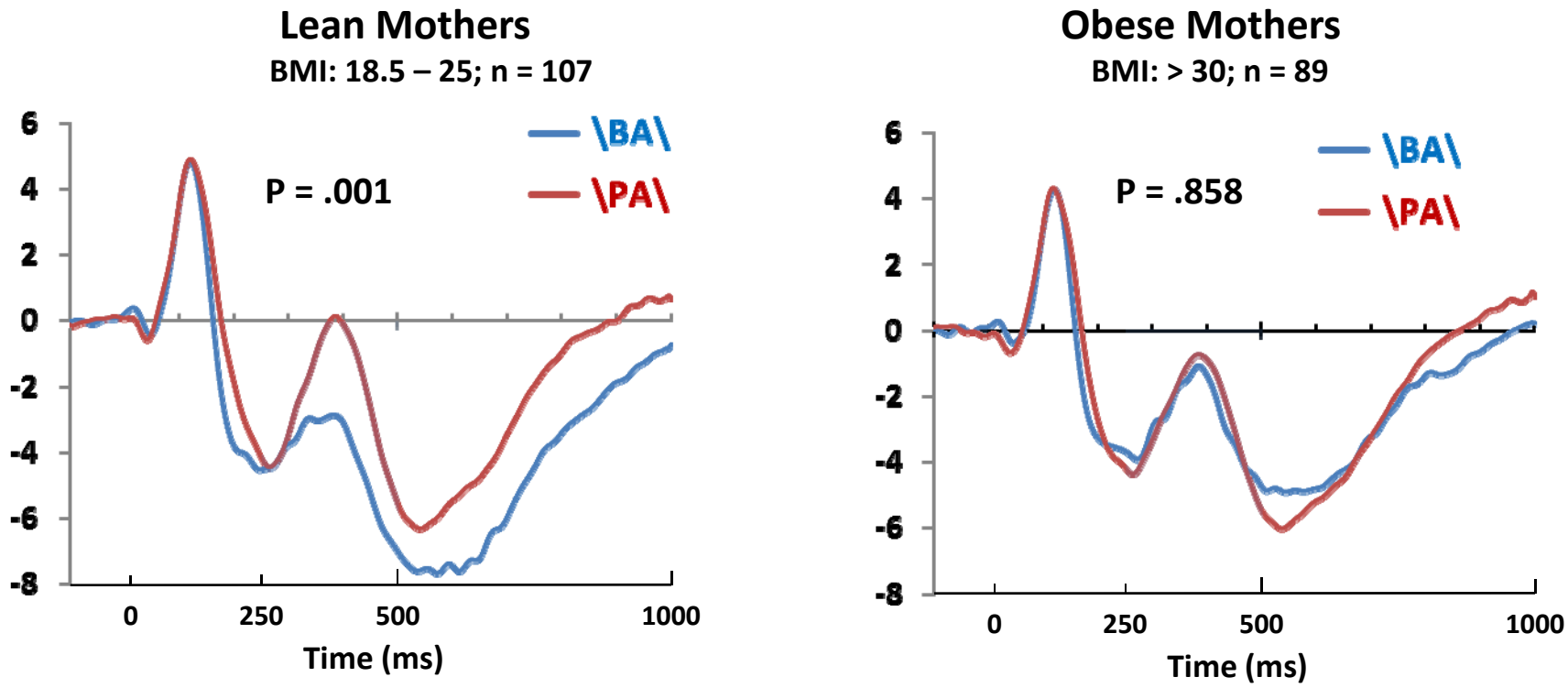
Orange/yellow: regions where newborns of obese mothers have less white matter development

Neural networks



Orange/yellow: resting-state functional connectivity of the prefrontal network is reduced in newborns of obese mothers. Ou et al., 2015

Maternal Obesity Impacts Brain Function and Cognition in Children



Frontal brain responses show syllable discrimination in 2 year olds born to lean mothers but not those born to obese mothers.

Children (1-7 yrs old) of mothers with excessive weight gain in pregnancy (>17kg) showed reduced cognitive development than those of mothers who gained less (<14-17 kg)

Jedrychowski et al., 2012

Information Gaps, Solutions, and Outcome Possibilities

Need for: **routine consideration of nutritional status and dietary factors in neurodevelopmental and neurocognitive research in healthy infants and children.**

- **Studies in children rarely consider nutrition-related factors**

Addressed by: **an integrated scientific approach that combines methods for assessing brain structure and function with dietary-related factors, environmental variables, and individual subject characteristics.**

- **Our growing understanding of brain development and function as the product of epigenetic effects of environmental factors modulated by immediate state influences mandates this strategy.**

Benefits: **a better understanding of how these interactions may be tailored to optimize neurodevelopment and promote cognitive functioning and health in children.**

- **Provide dietary and life style guidance as children pass through critical behavioral and cognitive developmental stages**
- **Identify risk factors for childhood obesity that may inform effective prevention strategies.**

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