Does crucial development only occur in the first two years of life?

4 November 2014

#ScienceSeries

EARLY INTERVENTION FOUNDATION

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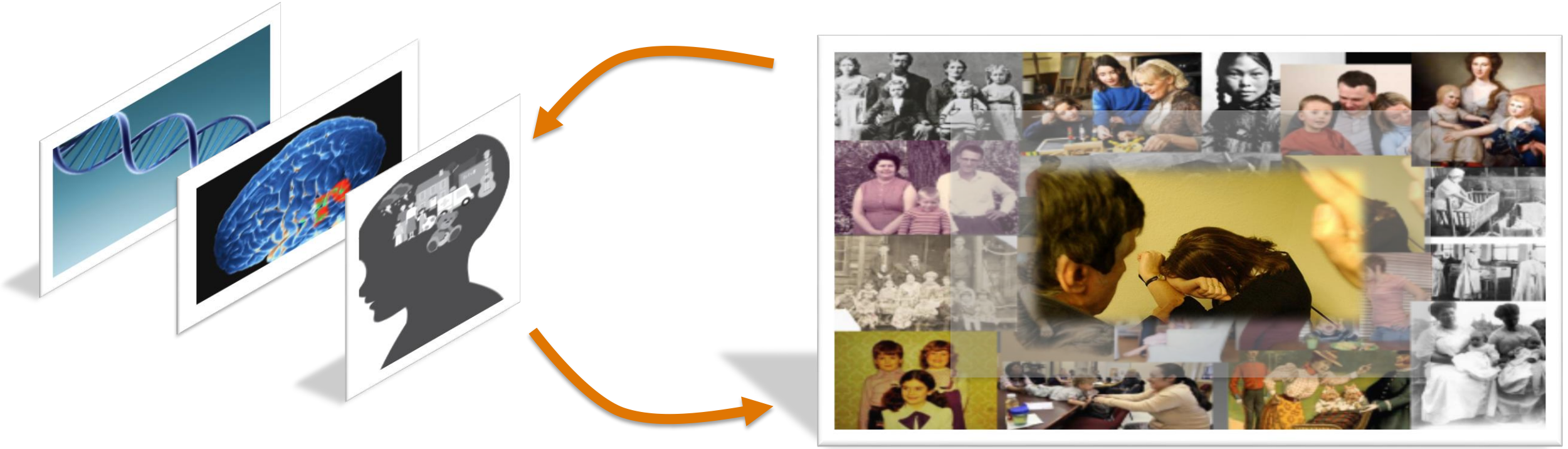
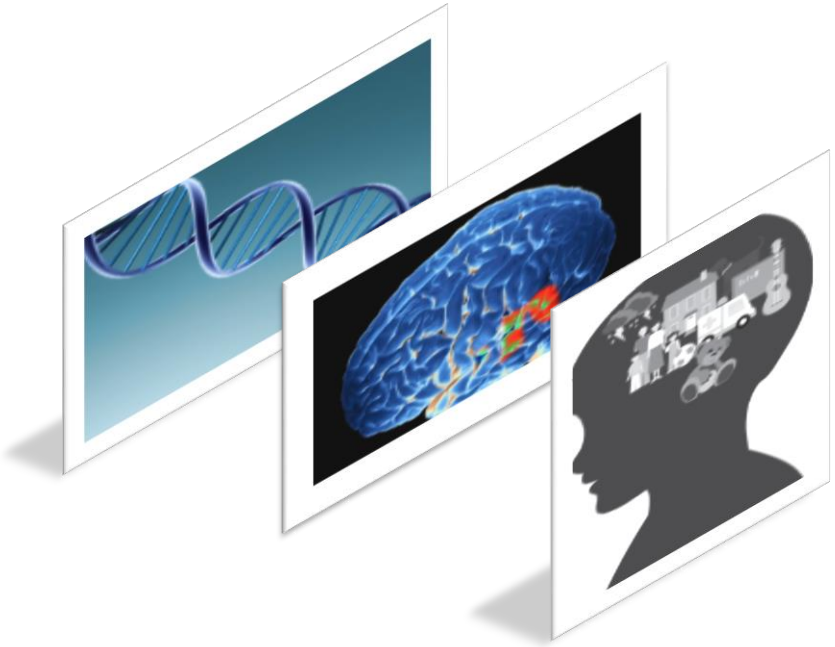
Does crucial development only occur in the first two years of life?

Early Intervention Foundation - November 2014

Eamon McCrory & Essi Viding

Infancy……Childhood……Adolescence……Adulthood

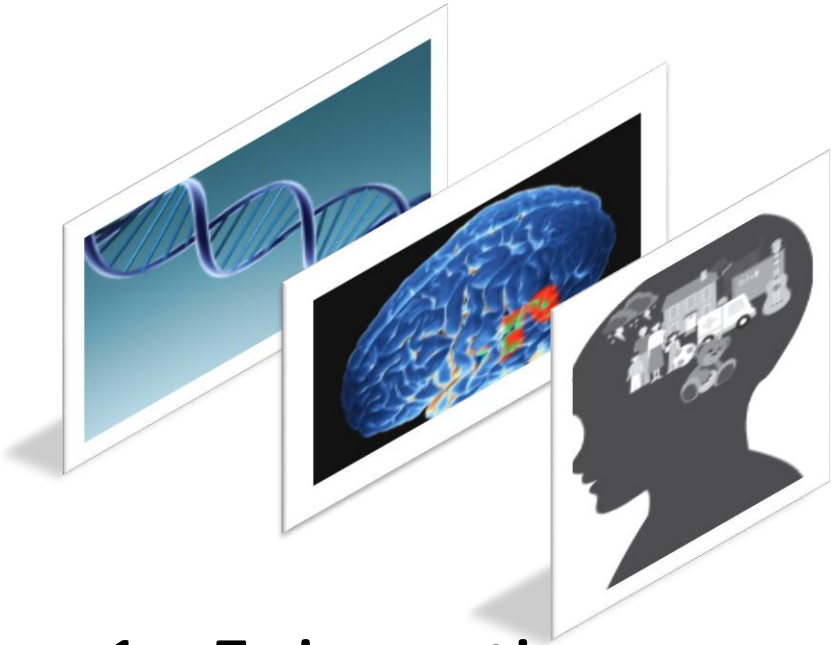




- ↑ Psychiatric disorders e.g. anxiety, depression
- ↓ Attainment
- ↓ Economic productivity
- ↑ Physical health problems e.g. asthma, hypertension, heart disease and diabetes

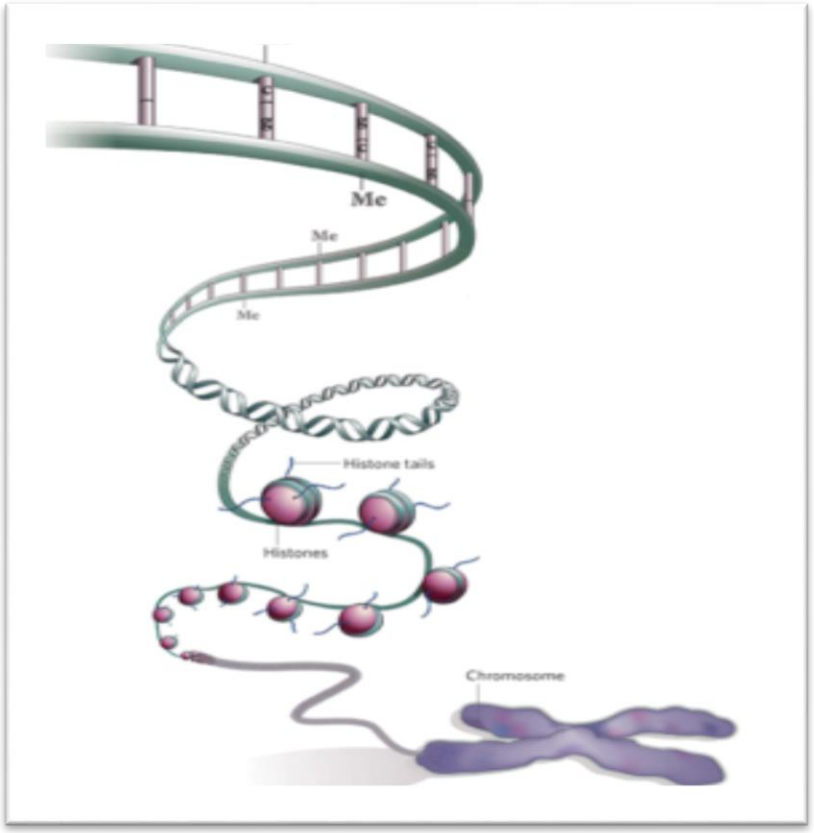
What do we know about the process of biological embedding?

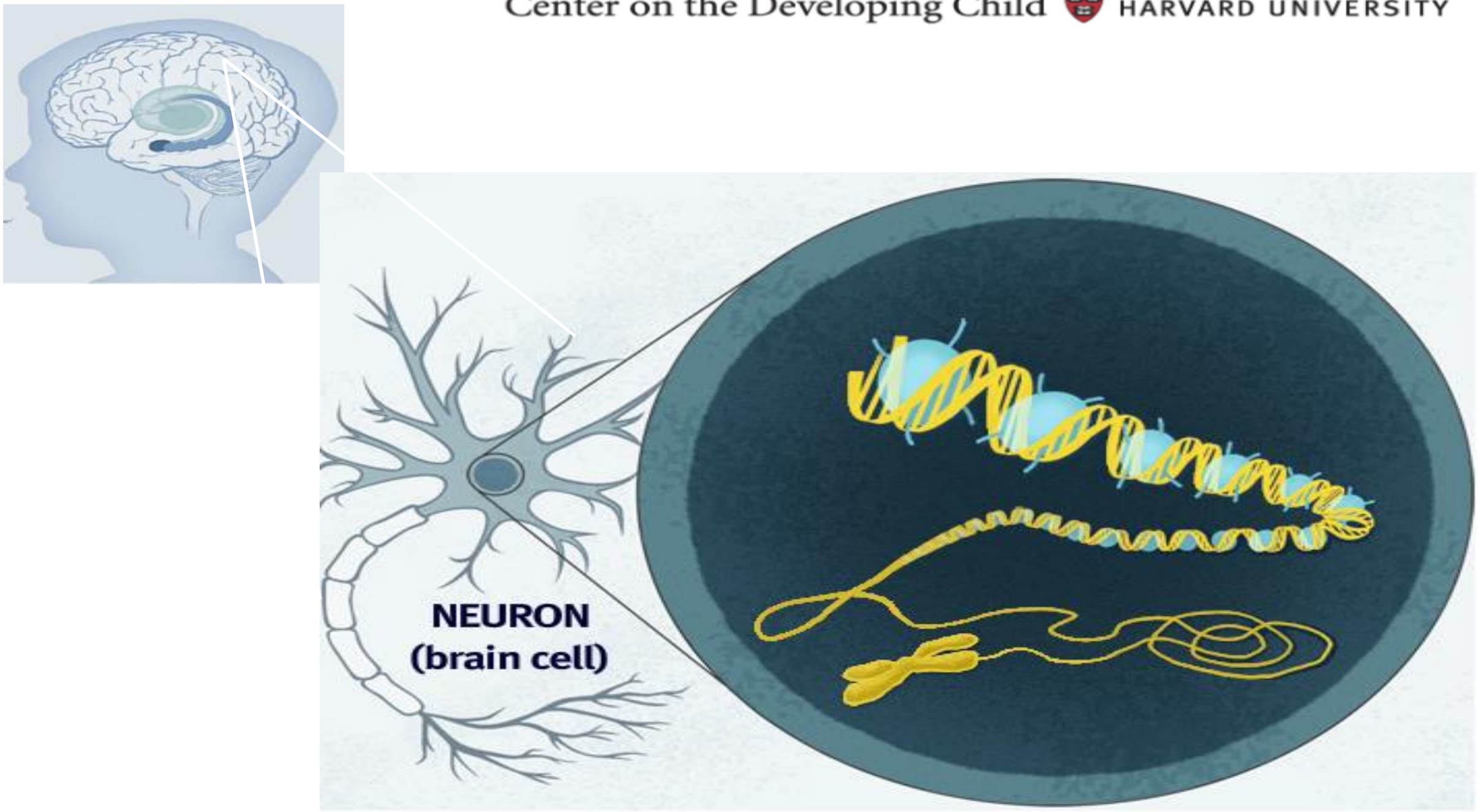
Infancy.....Childhood.....Adolescence.....Adulthood

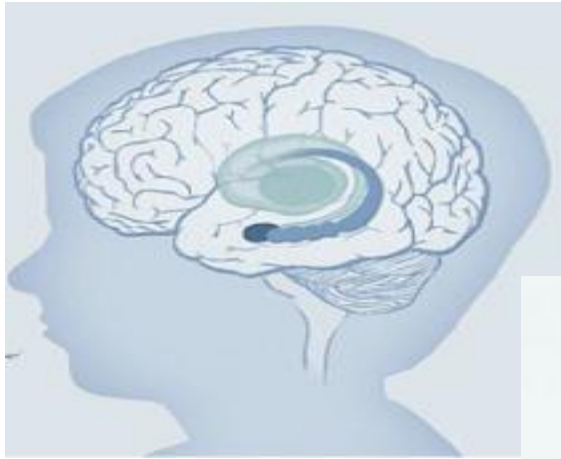


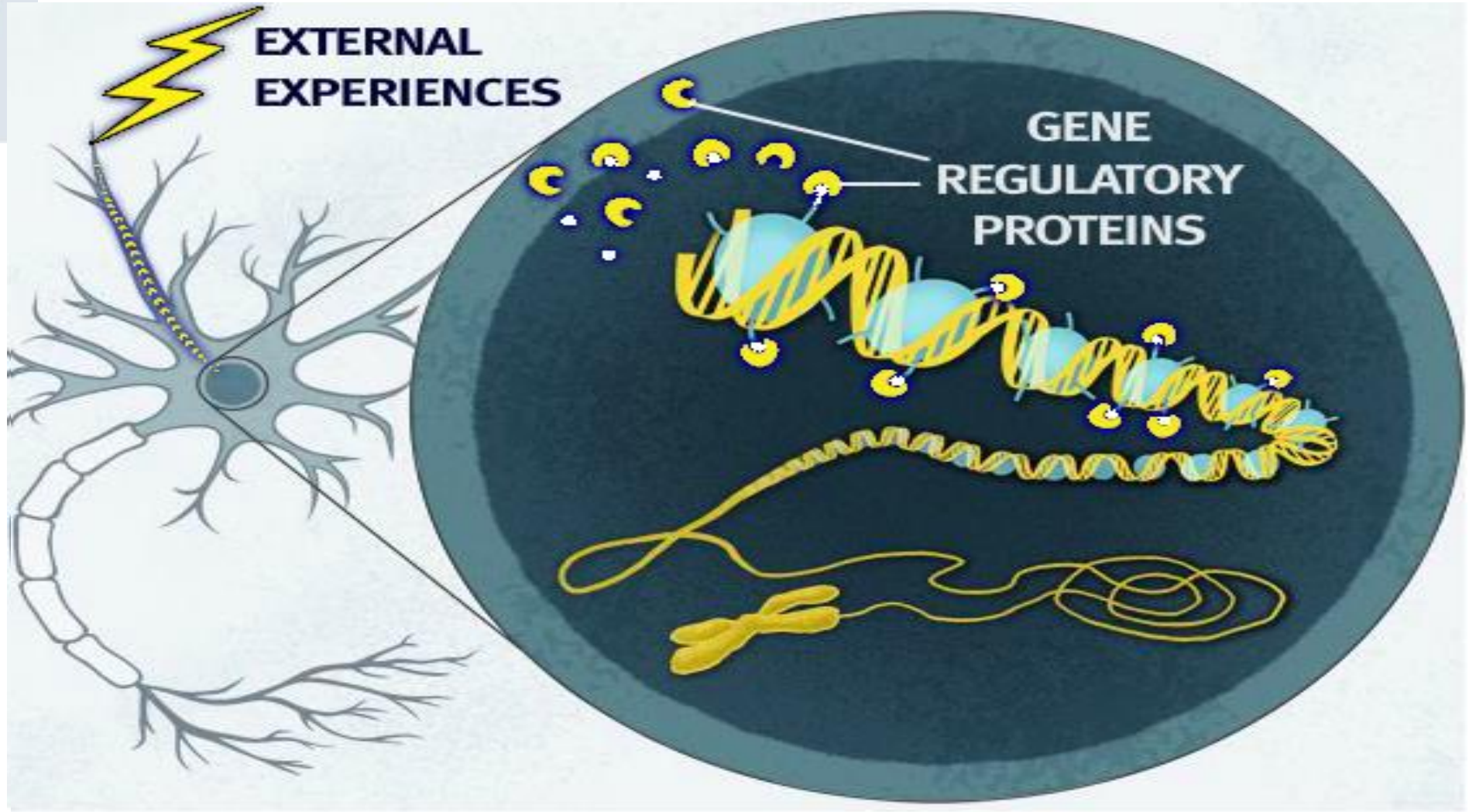
1. Epigenetics
2. Brain Development
3. Challenges

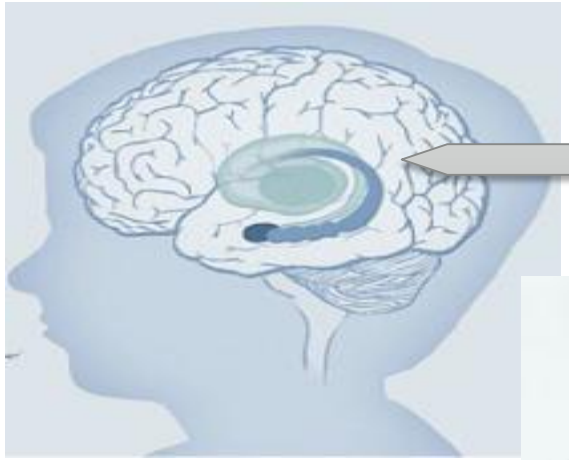
1. Epigenetics

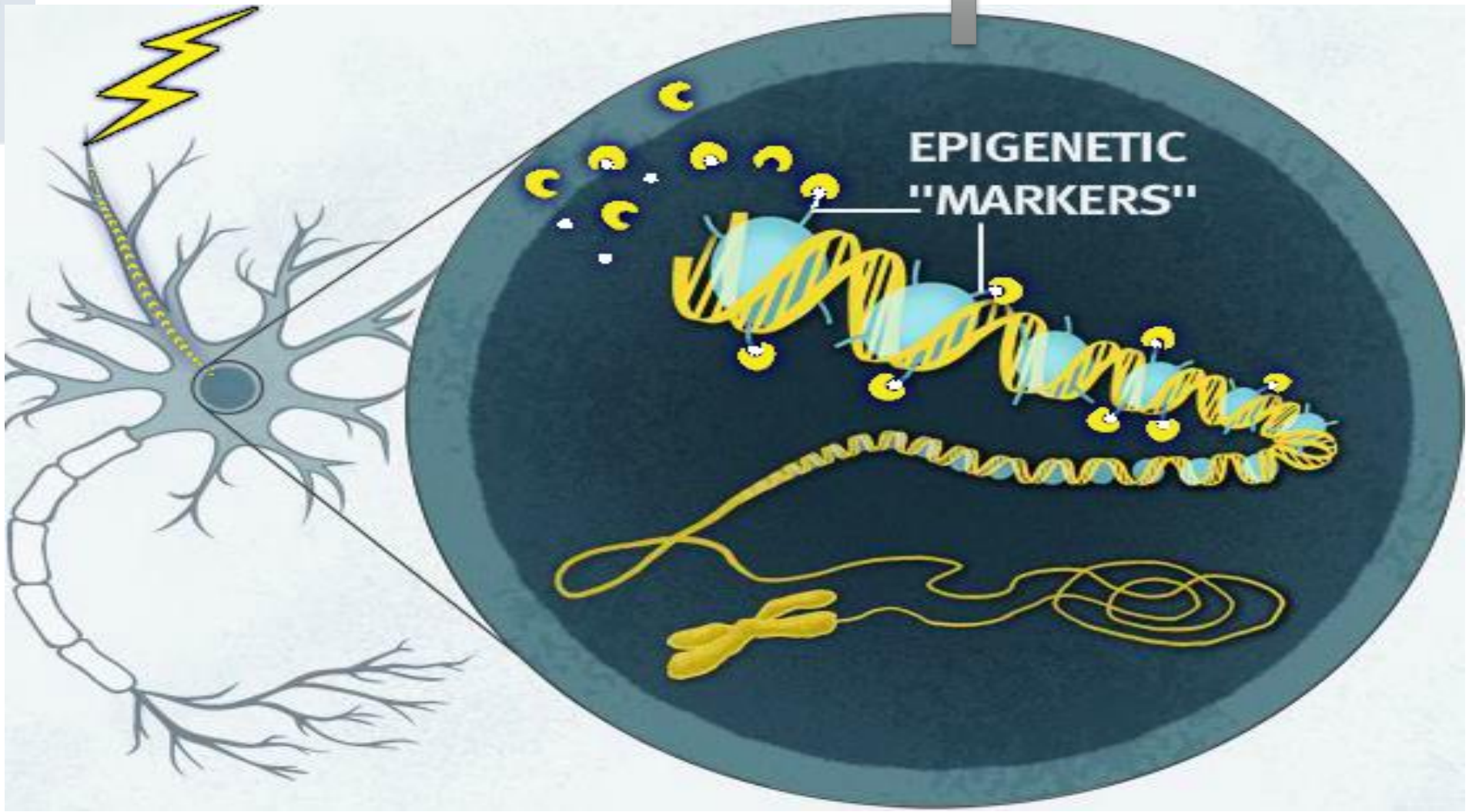



NEURON
(brain cell)




EXTERNAL
EXPERIENCES
GENE
REGULATORY
PROTEINS




EPIGENETIC
"MARKERS"

- Nutritional, toxin or drug exposure can all modify an individual's epigenome.

- Epigenetic instructions that change how and when certain genes are turned on or off can cause temporary or enduring health problems. By and large, however, epigenetic modulation serves adaptive regulatory processes.

- Environmental experiences – both those that are highly stressful as well as those which are supportive – can cause epigenetic changes that alter the systems that mediate response to adversity later in life.

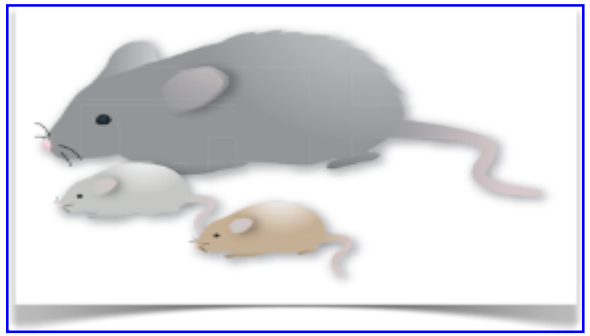
Animal Studies

Michael Meaney's animal studies

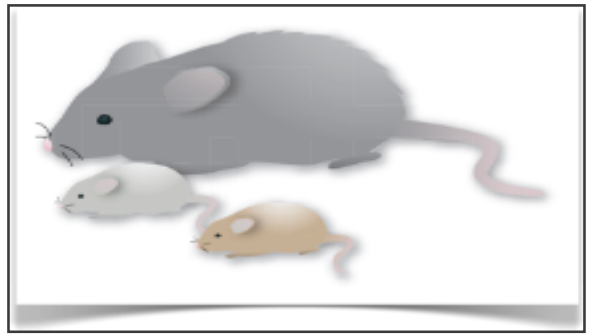
Pups experiencing High Levels Licking Grooming

Pups experiencing Low Levels Licking Grooming

High Nurturing

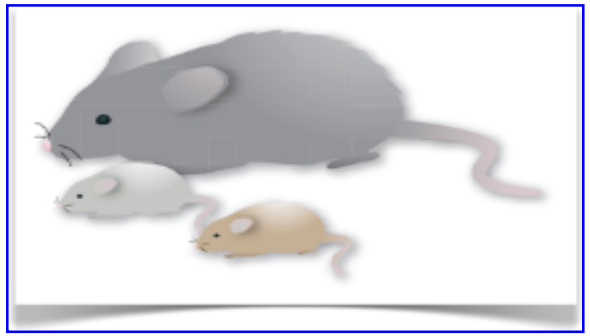


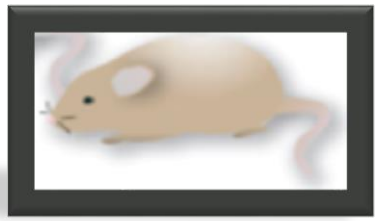
Low Nurturing

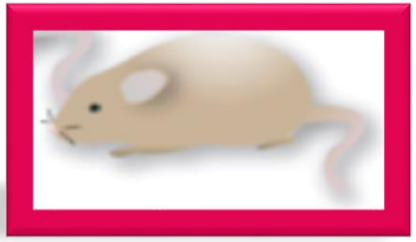


Meaney & Szyf, 2005; Weaver et al., 2004; Hyman, 2009

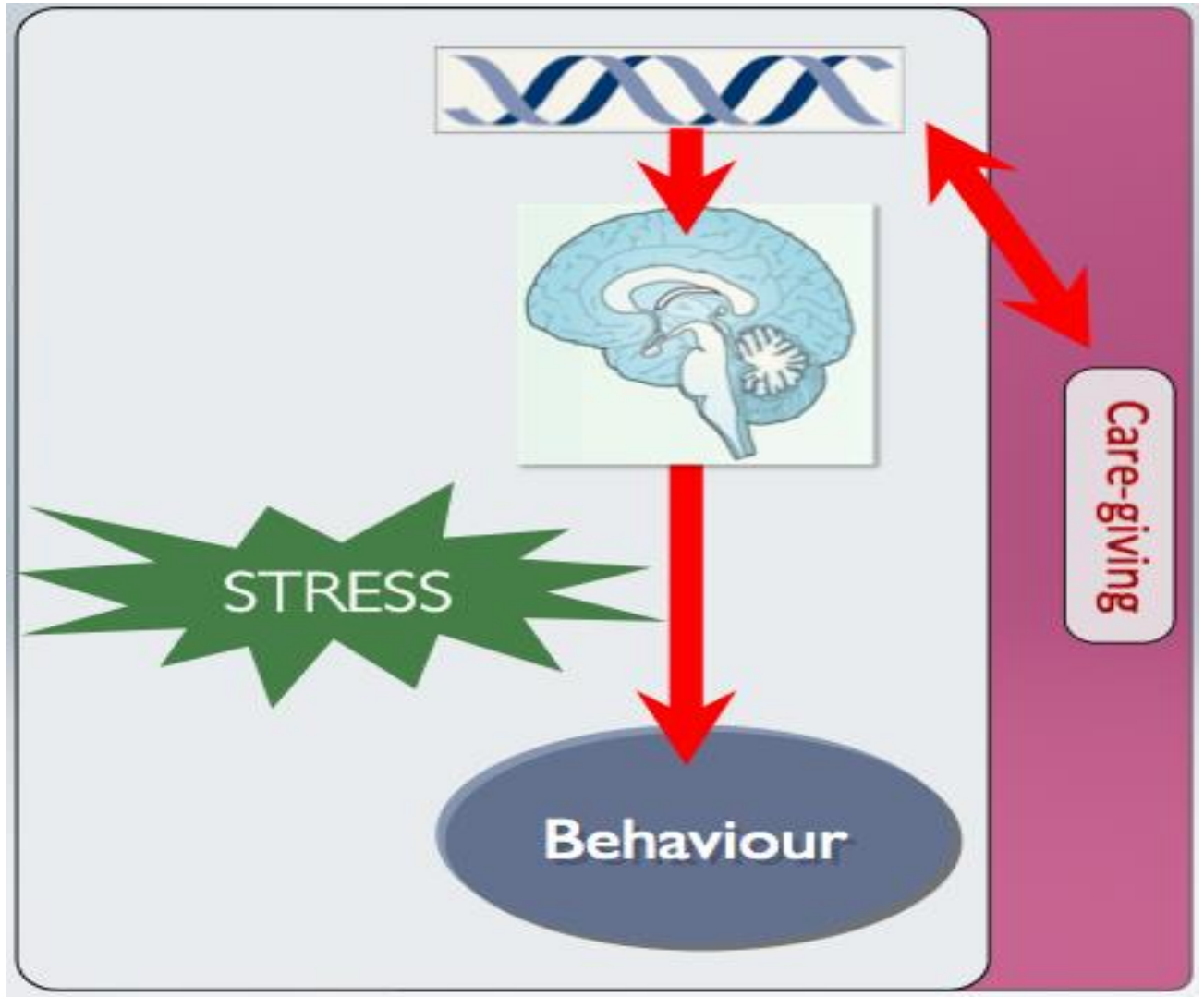
High Nurturing







Meaney & Szyf, 2005
Weaver et al., 2004
Hyman, 2009


STRESS
Behaviour
Care-giving

- Animal studies examining the impact of prenatal stress on brain development have found substantial down regulation in gene expression in region specific patterns. *Mychasiuk et al., 2012*

human studies

Oberlander et al.,

- Epigenetic mechanisms have therefore being postulated as one mechanism that mediates the link between maternal prenatal stress and infant outcome.

- Preliminary evidence

BUT…

- Developmental processes have evolved to be robust to a wide variety of experiences in the normal range – much needs to be learned about key stressors and key periods of vulnerability.

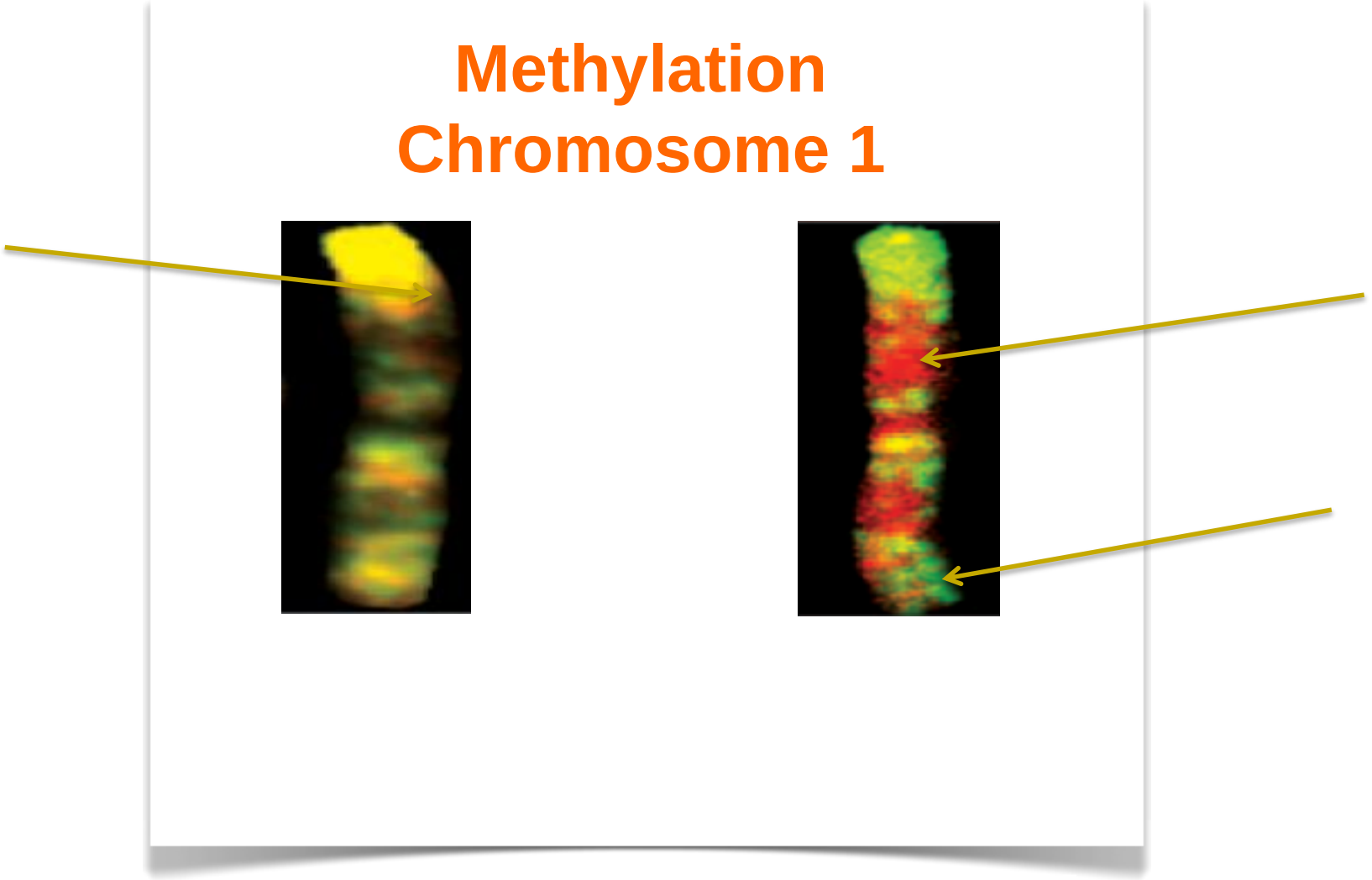
- Epigenetic modification helps optimize functioning to the environmental conditions that an in infant is likely to face early in development.

- Little is known about the impact of stress exposure versus the absence of experience-dependent inputs often characterized by neglect.

- Do what degree are epigenetic changes reversible? Does reversibility vary across genes, and interact with genotype and other environmental experiences?

- And finally, epigenetic changes occur across the lifespan:

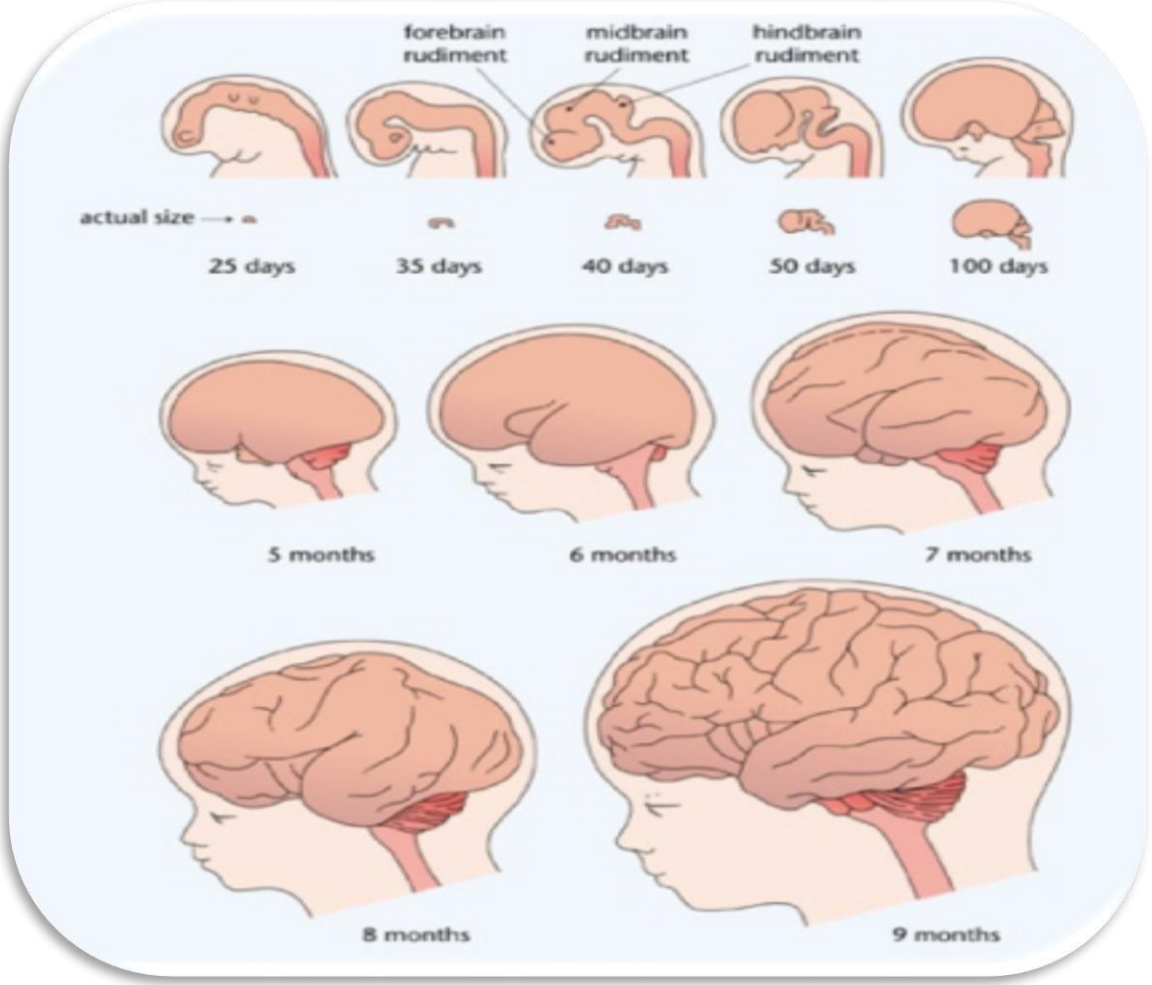
Epigenetic modulation continues across the lifespan….



2. Brain Structure and Function

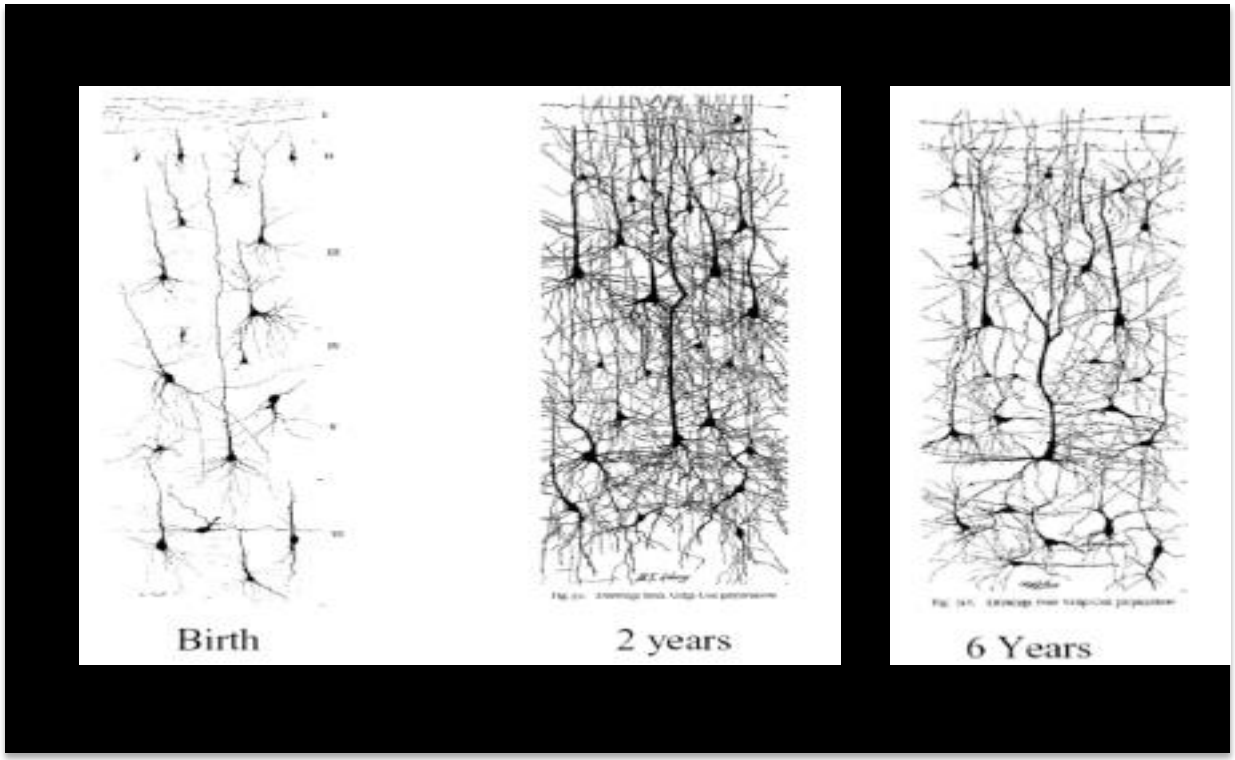
- Brain structure can be measured by a wide variety of indices, including:
  - volume
  - cortical thickness
  - folding
  - connectivity
  - neurotransmitter levels
  - receptor densities

- The brain undergoes a period of rapid growth during gestation.
- Proliferation and migration of cortical neurons largely take place in the fetal period
- The complex pattern of cortical folding is largely in place at birth when most neurons are already present (approx. 100 billion)
- By age 2 years, brain is 80% of adult size

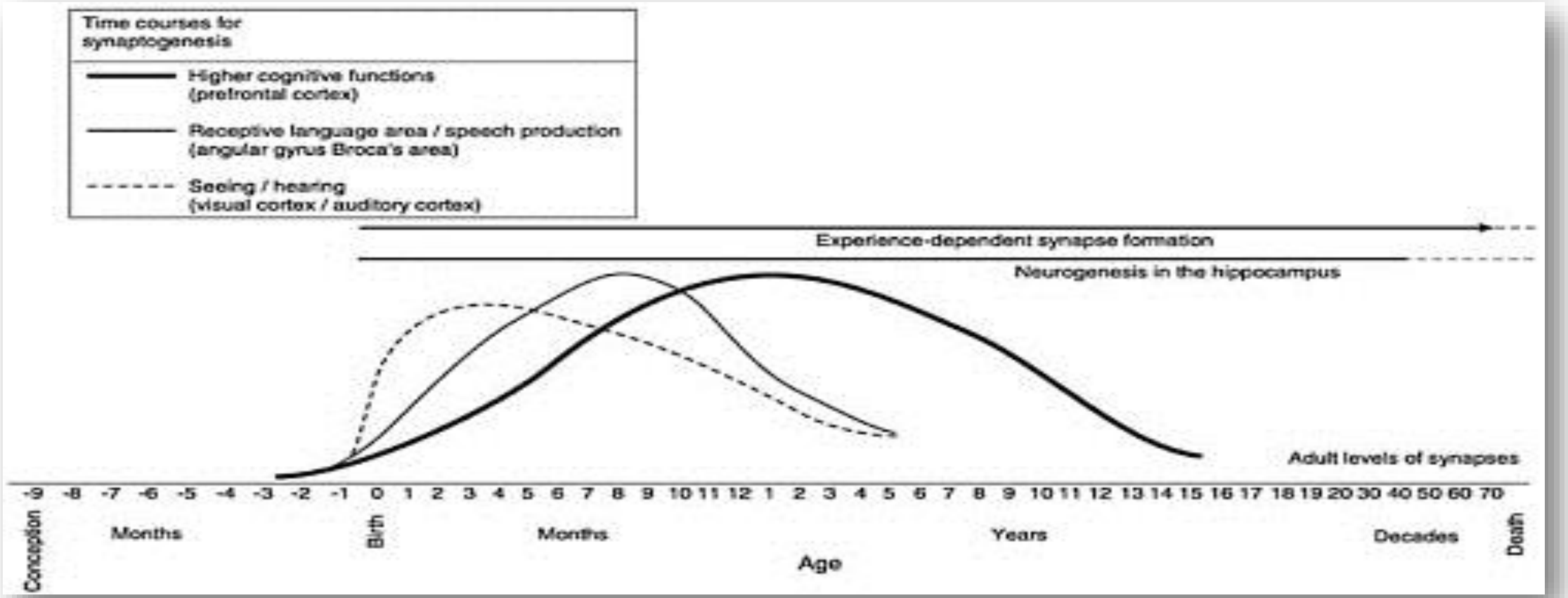


Proliferation and pruning

- A key developmental process involves the overproduction of neurons and neuronal connections or synapses.
- Soon after birth, there is a dramatic increase in the number of synapses, throughout the human brain (synaptogenesis).
- Connections and pathways are ‘pruned’ over childhood



Varies by brain region across development.



In the frontal cortex of overproduction occurs at around one year of age, and it is not until middle to late adolescence that adult numbers of synapses are obtained

White matter increases linearly across development.

Plot of Conel's uncorrected original data on layer II (dashed lines) and layer VI (solid lines) myelinated fiber density (no. per 0.005 mm2) versus postnatal age (months) for the von Economo areas he studied.

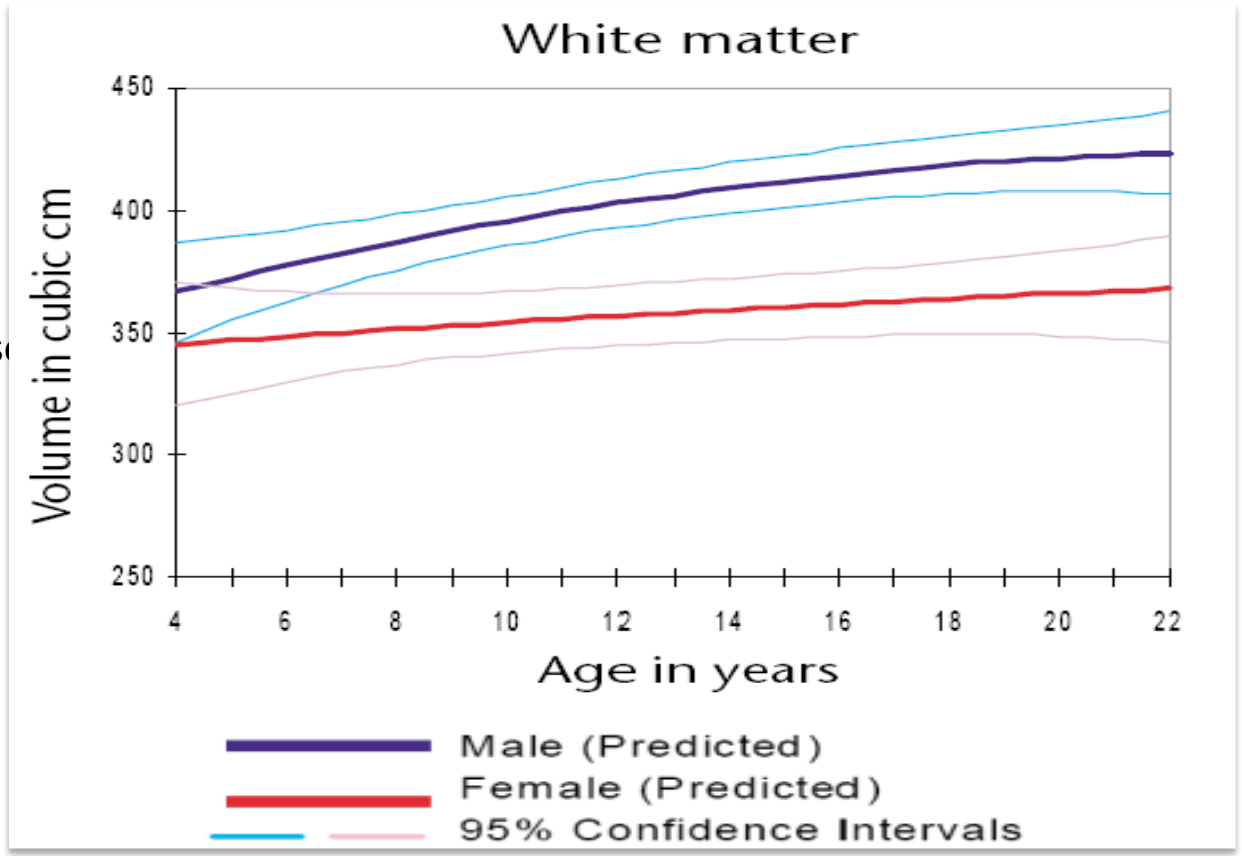
- There is a steady increase in white matter in certain brain regions during childhood and adolescence including the frontal cortex

- These increases appear linear with increasing age (Giedd et al., 1999).

- Age-related changes in white matter density observed along these pathways may reflect increases in axon diameter or myelination.

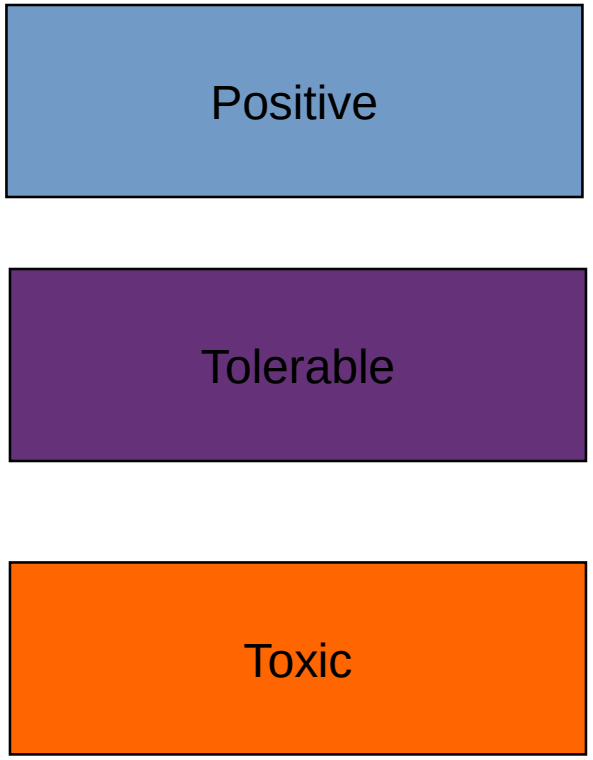
- This might reflect ↑ speed of nerve cell conduction, possibly contributing to:

➢ More efficient cortical communication?
➢ Greater capacity for complex thought?



http://developingchild.harvard.edu/resources/reports_and_working_papers/

Early Childhood Stress Influences Developmental Outcomes



Serve and Return Interaction Between Children and Caregivers

- Young children naturally reach out for interaction through babbling, facial expressions, gestures, and words, and adults respond with the same kind of vocalizing and gesturing back at them.

- This “serve and return” behavior is critical for building healthy brain architecture.

- If the responses are unreliable, inappropriate, or simply absent, as in experiences of neglect, the developing architecture of the brain may be disrupted, and later learning, behavior, and health may be impaired.

Maltreatment is associated with region specific reductions in grey matter density

THE JOURNAL OF CHILD PSYCHOLOGY AND PSYCHIATRY

ACAMH

Journal of Child Psychology and Psychiatry *:* (2012), pp **–**

doi:10.1111/j.1469-7610.2012.02597.x

Reduced orbitofrontal and temporal grey matter in a community sample of maltreated children

Stéphane A. De Brito[1,2], Essi Viding[1,3], Catherine L. Sebastian[1,3], Philip A. Kelly[1,2], Andrea Mechelli[4], Helen Maris[1,2] and Eamon J. McCrory[1,2]

[1]Division of Psychology and Language Sciences, University College London, London, UK;[2]The Anna Freud Centre, London, UK;[3]Institute of Cognitive Neuroscience, University College London, London, UK;[4]Department of Psychosis Studies, Institute of Psychiatry, King's College London, London, UK

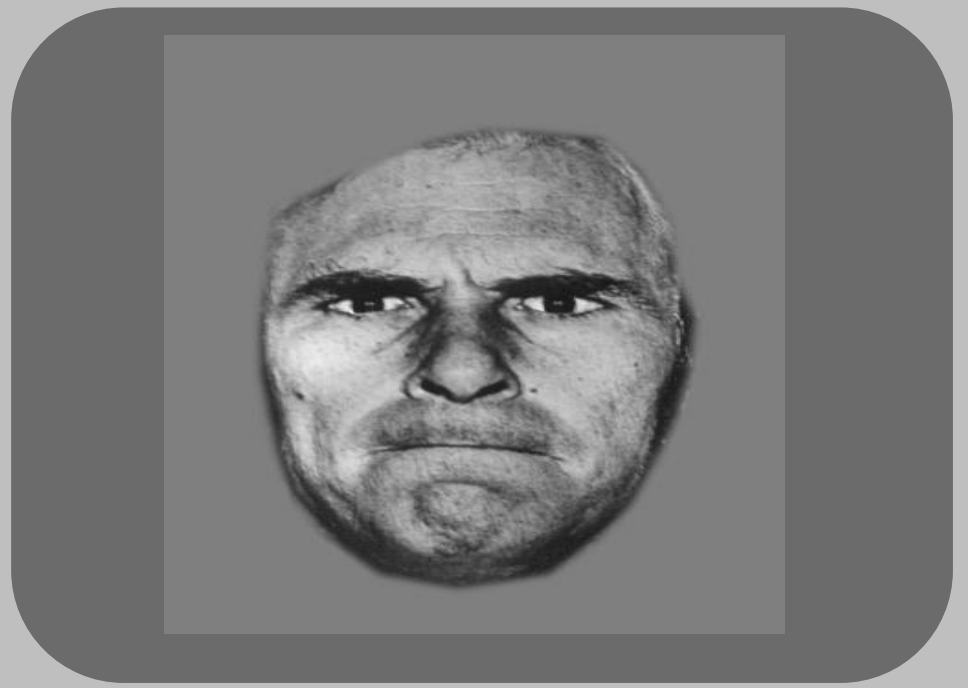
There is also an increase functional reactivity in regions implicated in threat detection and response

Dec 2011

Current Biology

Heightened neural reactivity to threat in child victims of family violence

Eamon J. McCrory[1,2,*], Stéphane A. De Brito[1,2,*], Catherine L. Sebastian[1], Andrea Mechelli[3], Geoffrey Bird[4,5], Phillip A. Kelly[1,2], and Essi Viding[1]



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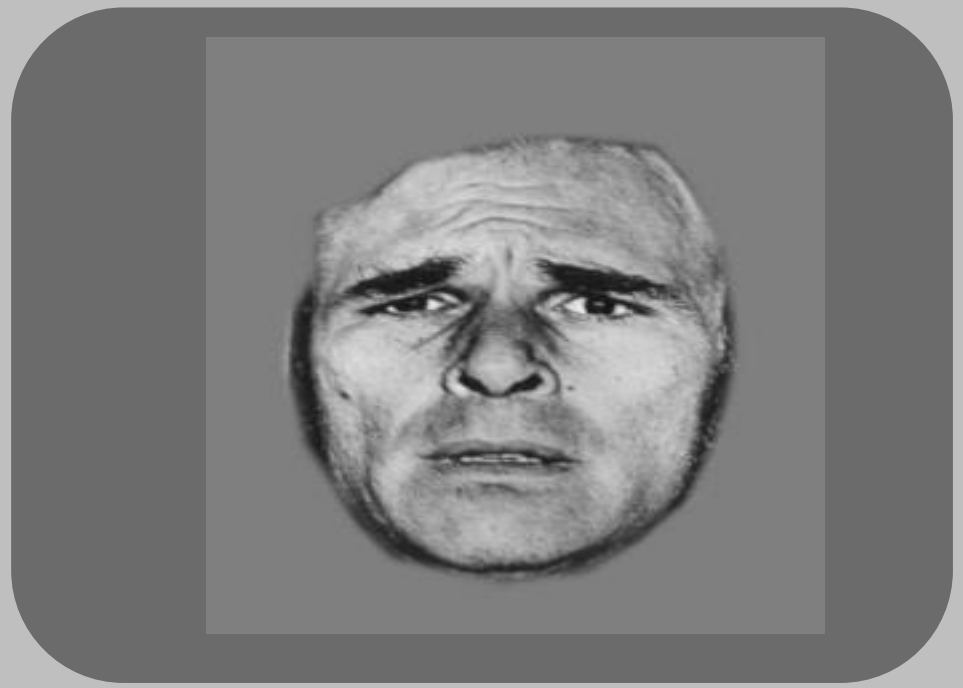
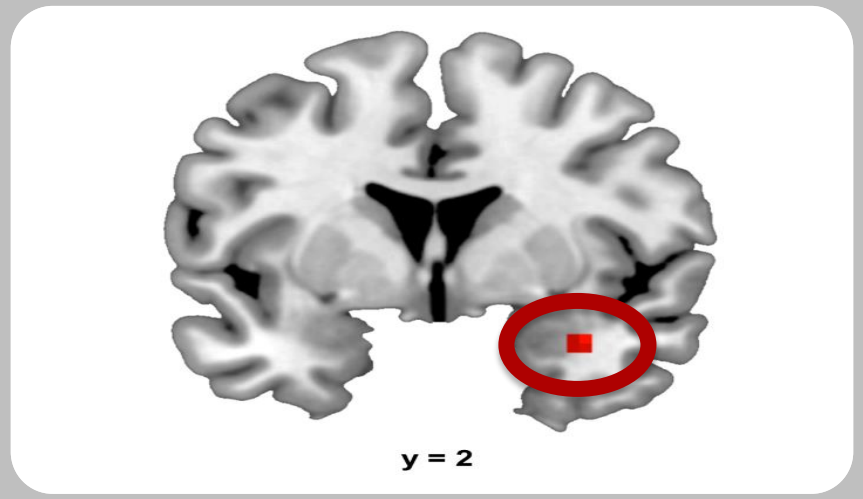
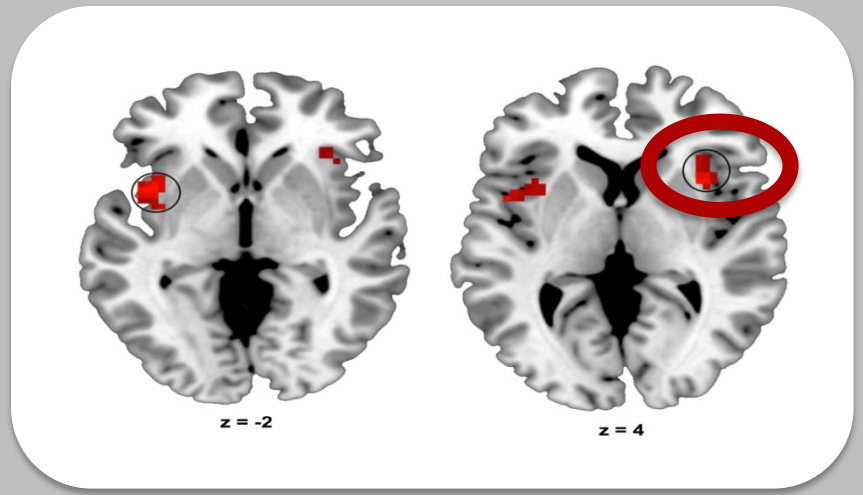


Children





McCrory et al., (2011)

Amygdala

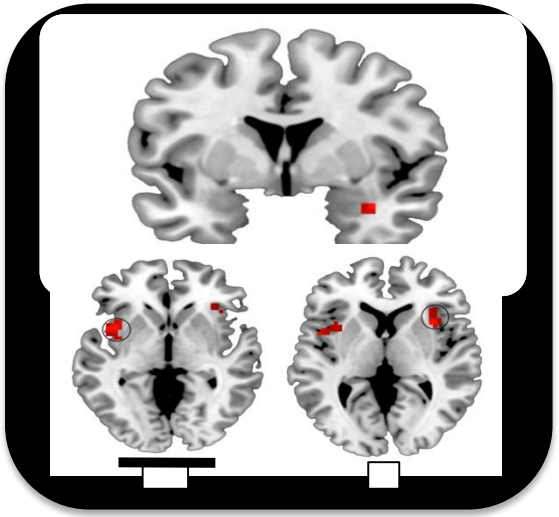
Anterior insula

Soldiers

Wingen et al., (2011)

- Functional and sturctural correlates of maltreatment imply that children have adapted to the demands of their early environment.
- Such apparent adaptations may confer short-term functional advantages in enhancing a child's vigilance to threat in an environment where they are not adequately protected by a caregiver, who may themselves be a source of threat.
- However, there may be 'real-time' costs in limiting attentional capacity for mastering age-appropriate skills in social /academic domains (chains of risk).
- These brain changes are likely to also increase Latent Vulnerability for mental health problems across the life span.

Maltreatment



Stress

Increased risk of Psychopathology

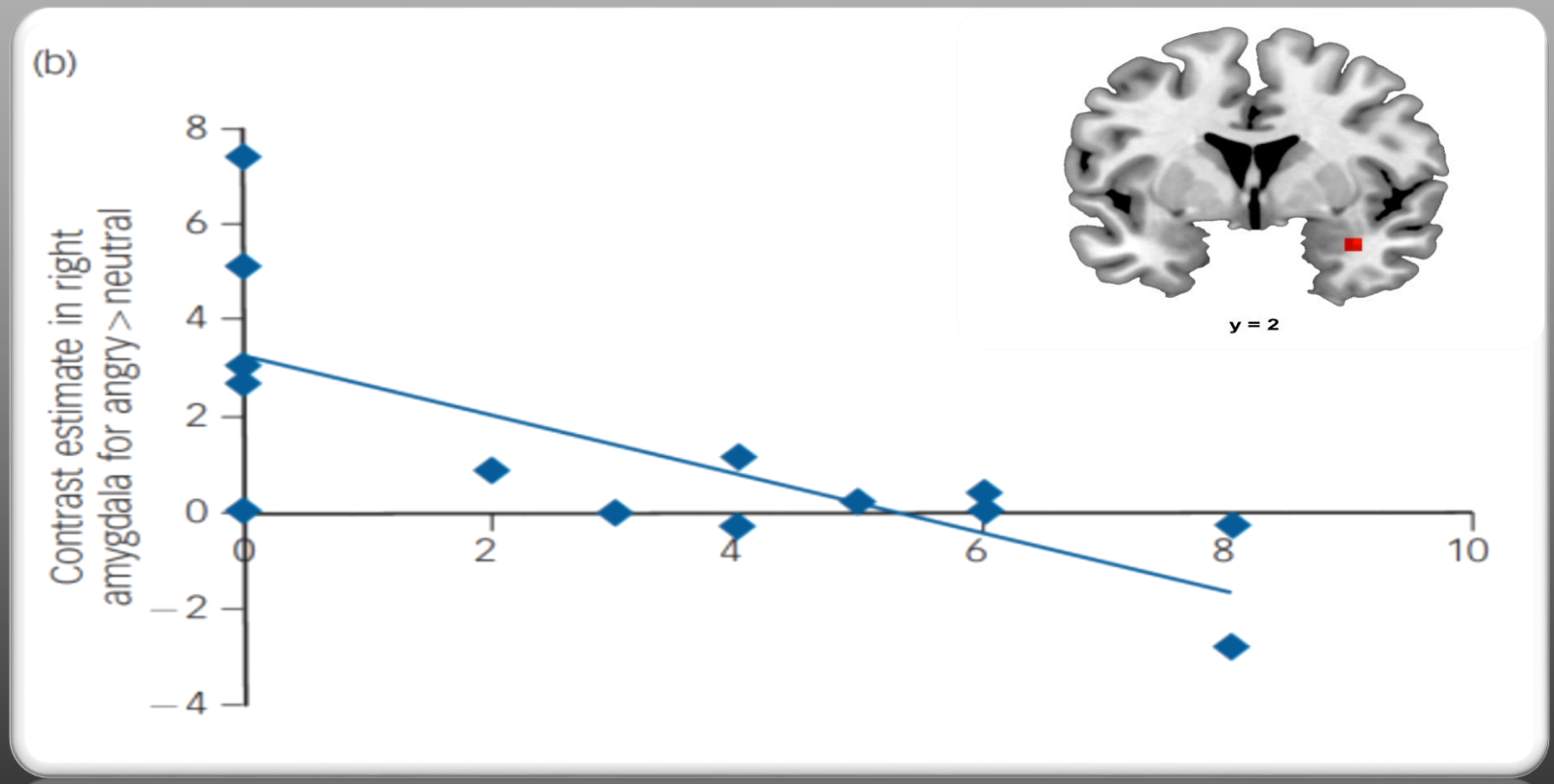
Challenges:

Is the child’s path set after the first two years?

Does age of onset make a difference?

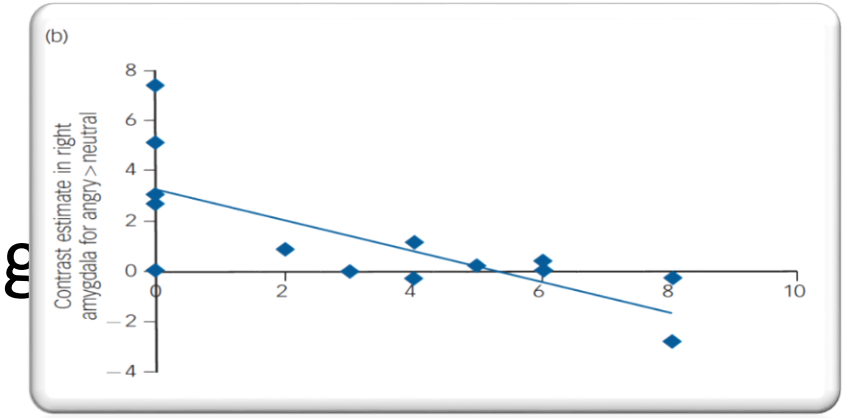
Early Adversity

Amygdala activation



McCrory, DeBrito, Kelly, Bird, Sebastian, Mechelli, Samuel, & Viding, 2013

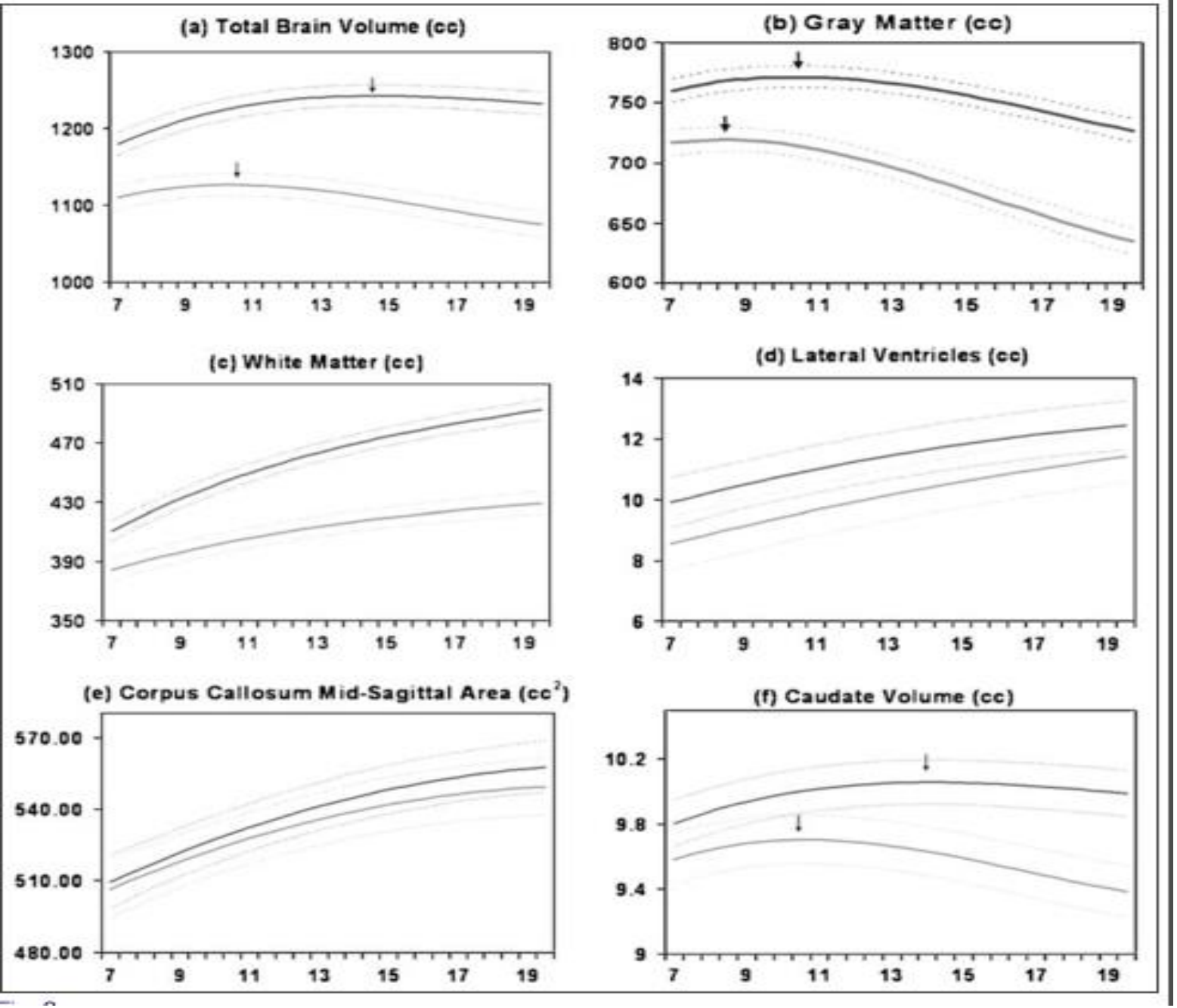
- Difficult to separate the effect of timing
  - duration,
  - severity/multiple incidents

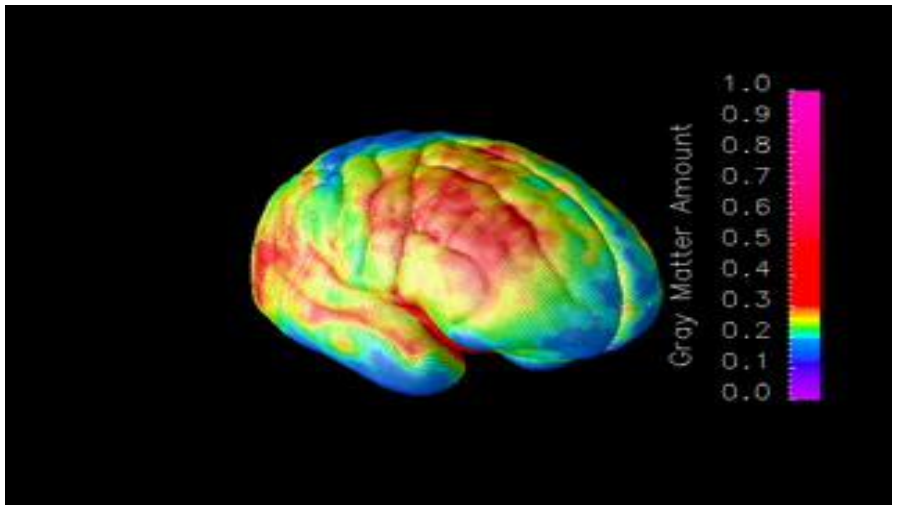


- Studies to date have not been able to tease apart the effects of early adversity and the duration/severity

- No doubt early experiences are important for brain development

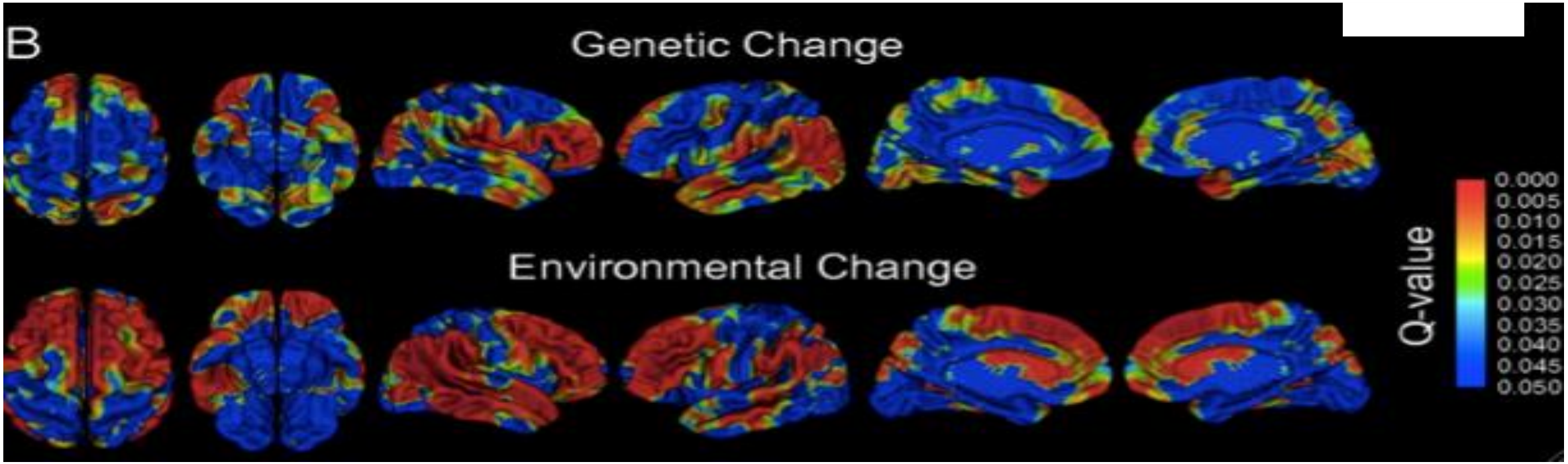
- But brain development is not on a fixed trajectory after the first few years of life





Gotay et al., 2009

Probability maps depicting regional differences in the significance of variance components.



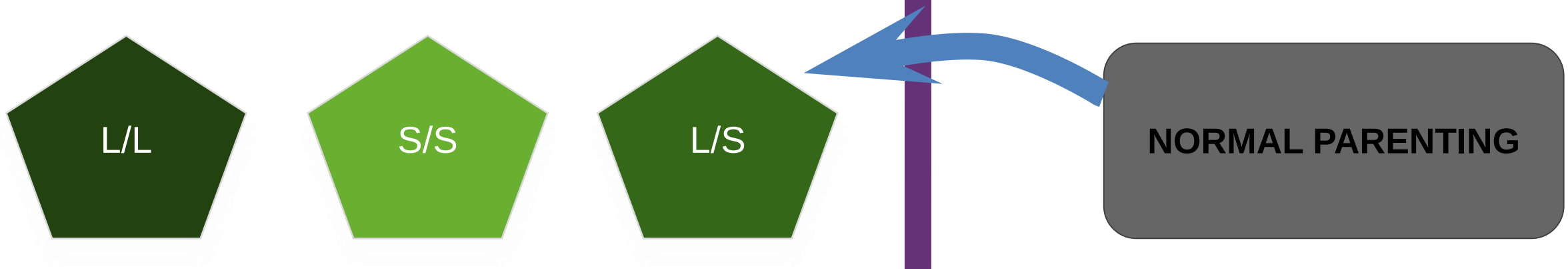
Schmitt J E et al. PNAS 2014;111:6774-6779

- Varied outcomes after early adversity
  - Increased risk, but not deterministic

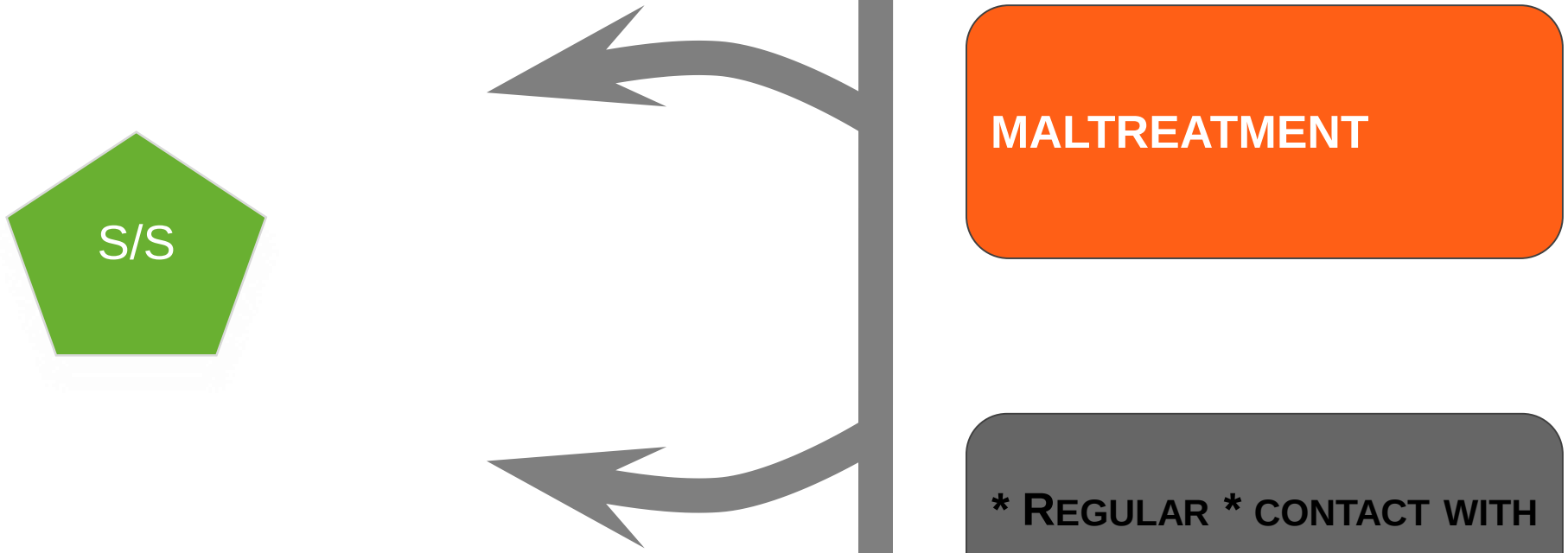
- Individual characteristics can increase the likelihood of vulnerable/resilient outcome
  - Temperament
  - Cognitive ability
  - Attractiveness

- Affect the likelihood of subsequent life stressors; gene-environment correlation

- There are also substantial differences in environments that are encountered post adversity, which may exert protective effects

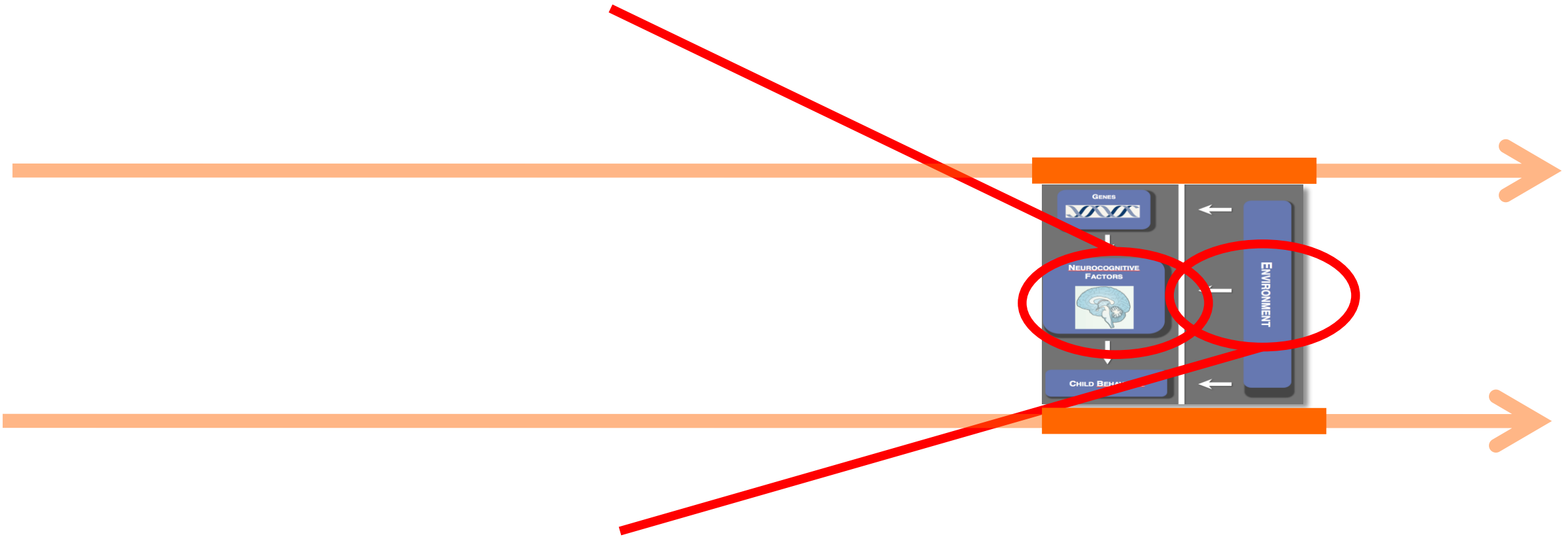

L/L
S/S
L/S
NORMAL PARENTING

MALTREATMENT

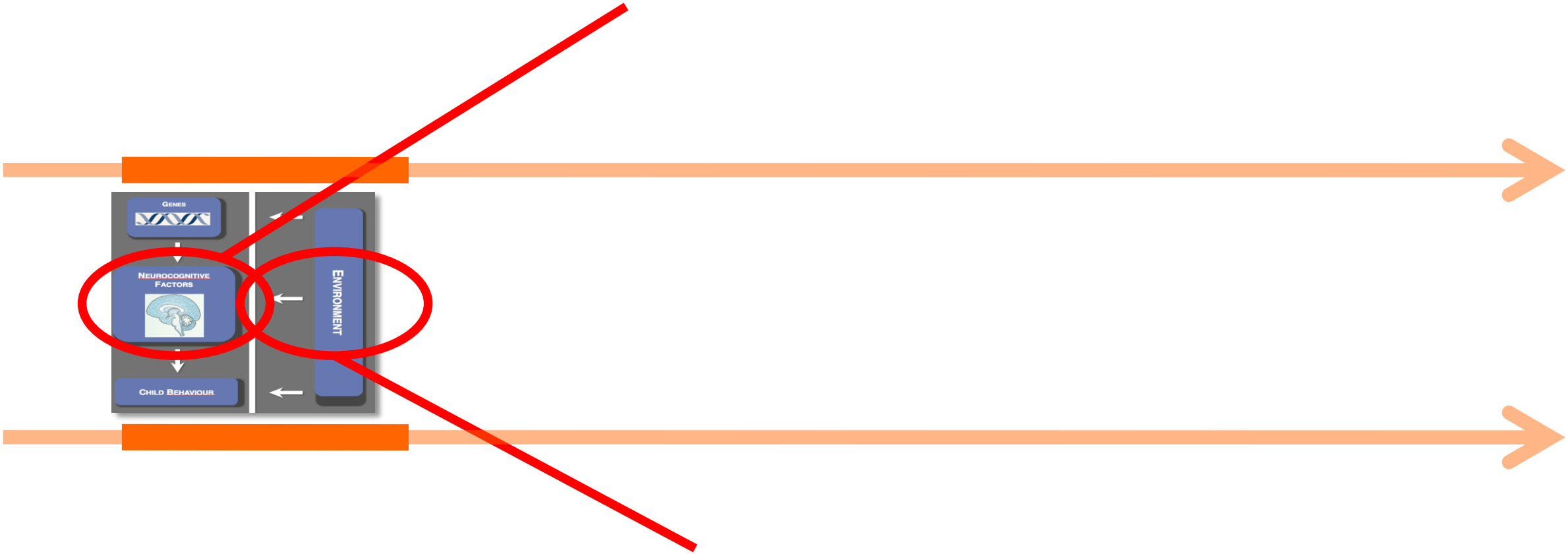

S/S
MALTREATMENT
* REGULAR * CONTACT WITH A TRUSTED ADULT

Different factors are likely to be of more or less importance at different stages in development.

Adolescence



Infancy


Genes
Neurocognitive Factors
Child Behaviour
Environment

Also important to remember:

- Early adversity is typically accompanied by a host of other risk factors, e.g. food insecurity, poor nutrition, community violence, educational disadvantage

- Interventions will likely need take a holistic/systemic approach

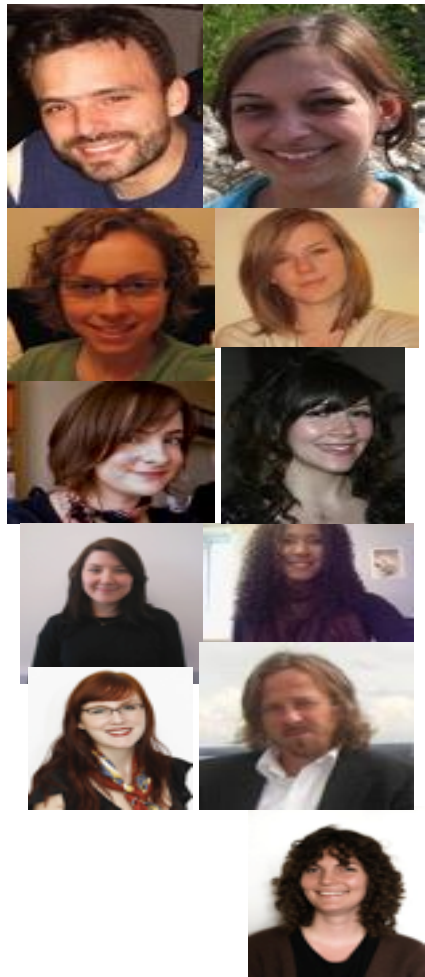
Summary

Arguably, the brain is particularly responsive to experiences and environments during early development, which influences how well or poorly its architecture matures and functions.

But brain development is not on a fixed trajectory after the first few years of life; there is evidence of ongoing plasticity and malleability, especially in relation to higher order functions.

Developmental Risk and Resilience Unit

UCL



Center on the Developing Child HARVARD UNIVERSITY

Excellent set of working papers from the US highlighting policy gaps and implications:

http://developingchild.harvard.edu/resources/reports_and_working_papers/