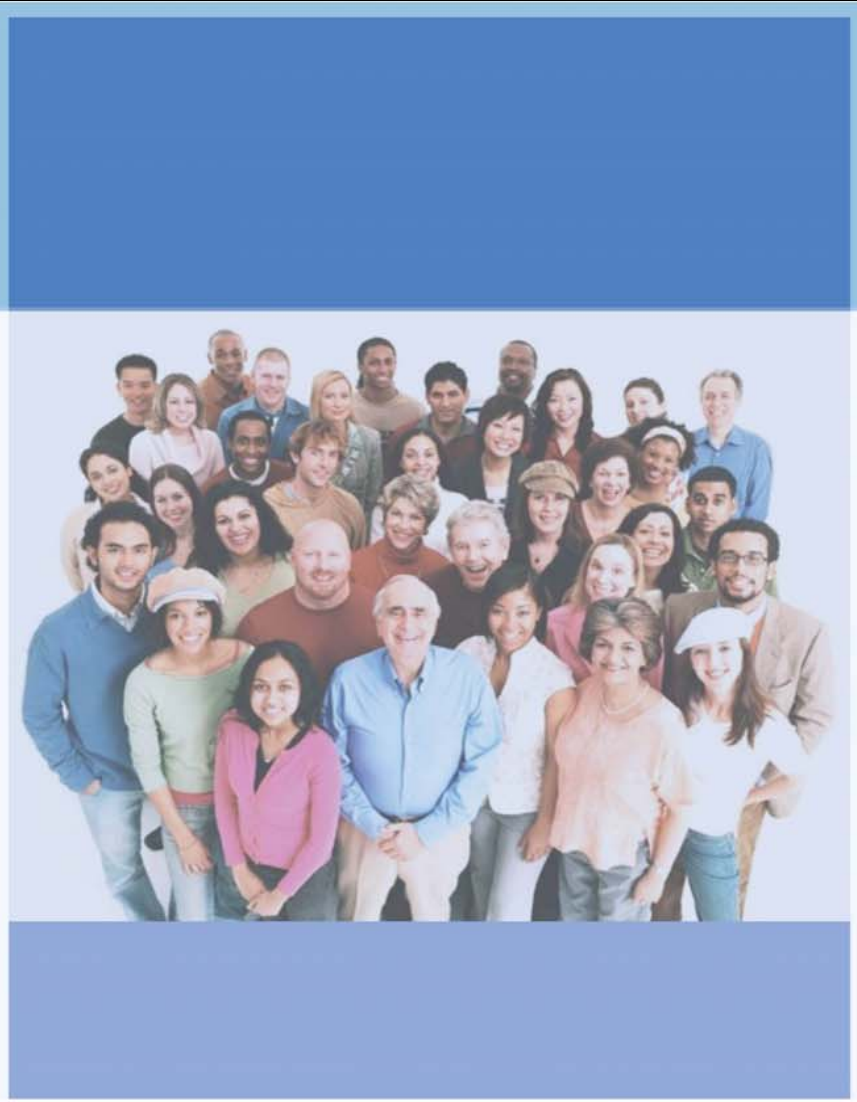
RECOVERY FROM ADDICTION



# Factors Influencing Brain Development and Behaviour

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Canadian Centre for Behavioural Neuroscience
University of Lethbridge

October 18, 2010 - October 22, 2010
Banff, Alberta

Alberta family wellness initiative

Norlien Foundation

# Key Points

1. Behaviours emerge as the brain develops.

2. Brain development is prolonged.

3. Brain structure and function is altered by a wide range of pre- and postnatal factors.

4. Brain and behavioural development is modulated by gene expression, which in turn is modulated by experience.

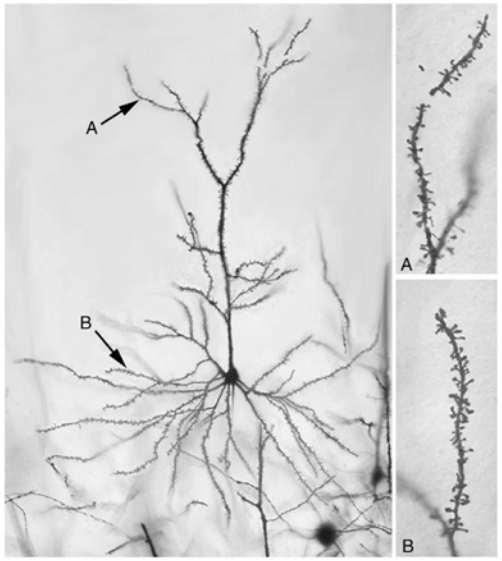
# How does the brain work?

1. The nervous system's function is to create behaviour in a perceptual world created by the brain.

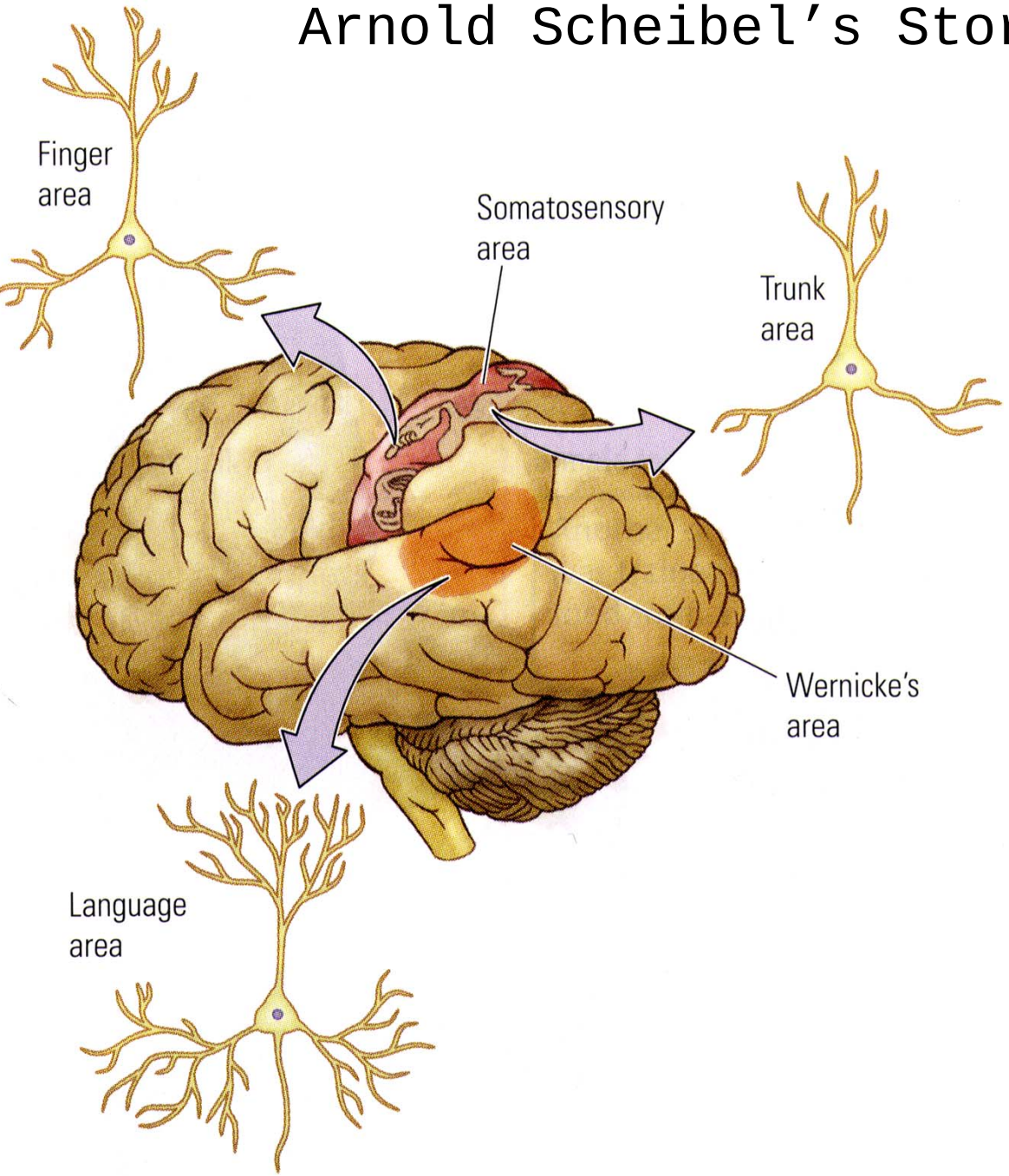
# How does the brain work?

1. The nervous system's function is to create behaviour in a perceptual world created by the brain.

2. It does this with neurons and networks.



# Arnold Scheibel's Story




## Cell Structure

1. Complexity of computations
2. Education
3. Occupation
4. Sex Effect

# How does the brain work?

1. The nervous system's function is to create behaviour in a perceptual world created by the brain.

2. It does this with neurons and networks.

3. Connections change with experience, a property known as *plasticity*.

# Principles

Brain changes result in behavioural change.

This change is known by names such as learning, memory, addiction, maturation, ageing, recovery, fatigue, dementia, depression, PTSD, etc.

# How can this happen?

Experience alters brain activity, expression of genes, brain chemistry, behaviour, and so on.

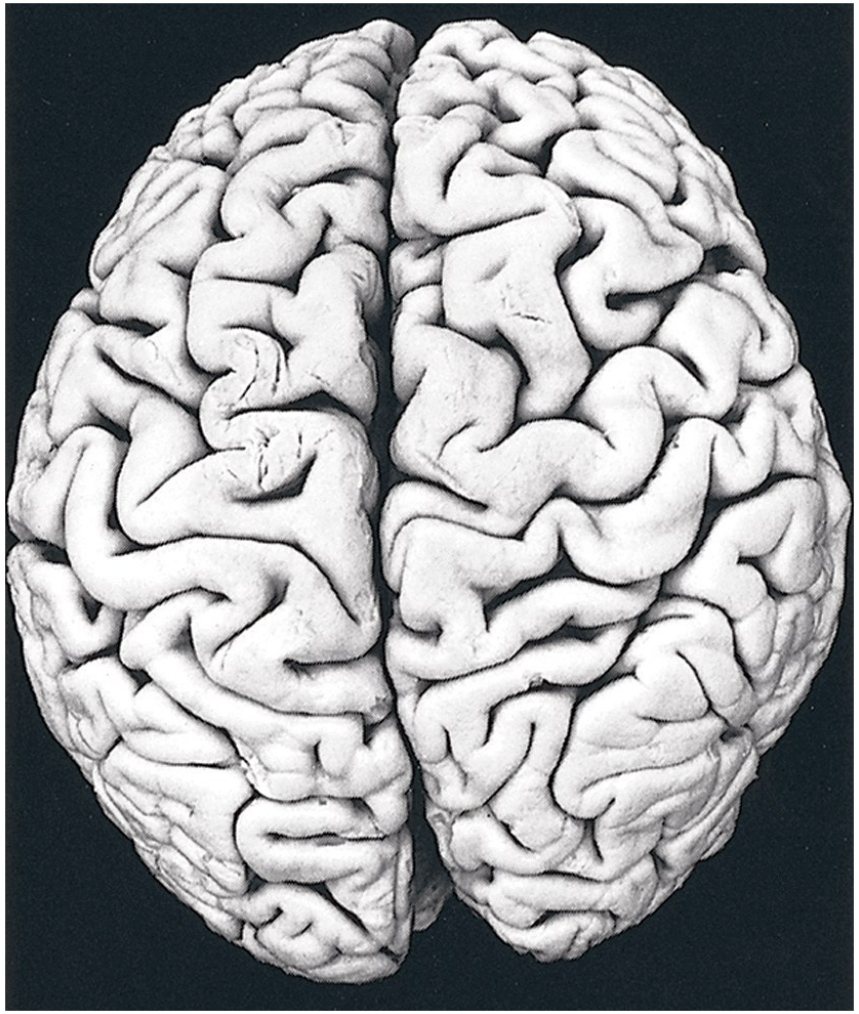
Any one of these can alter connectivity and thus function.

# What is experience?

*Everything* that you encounter both pre- and postnatally as well as in adulthood…

Examples:  sounds, touch, light, food, thoughts, drugs, injury, disease…

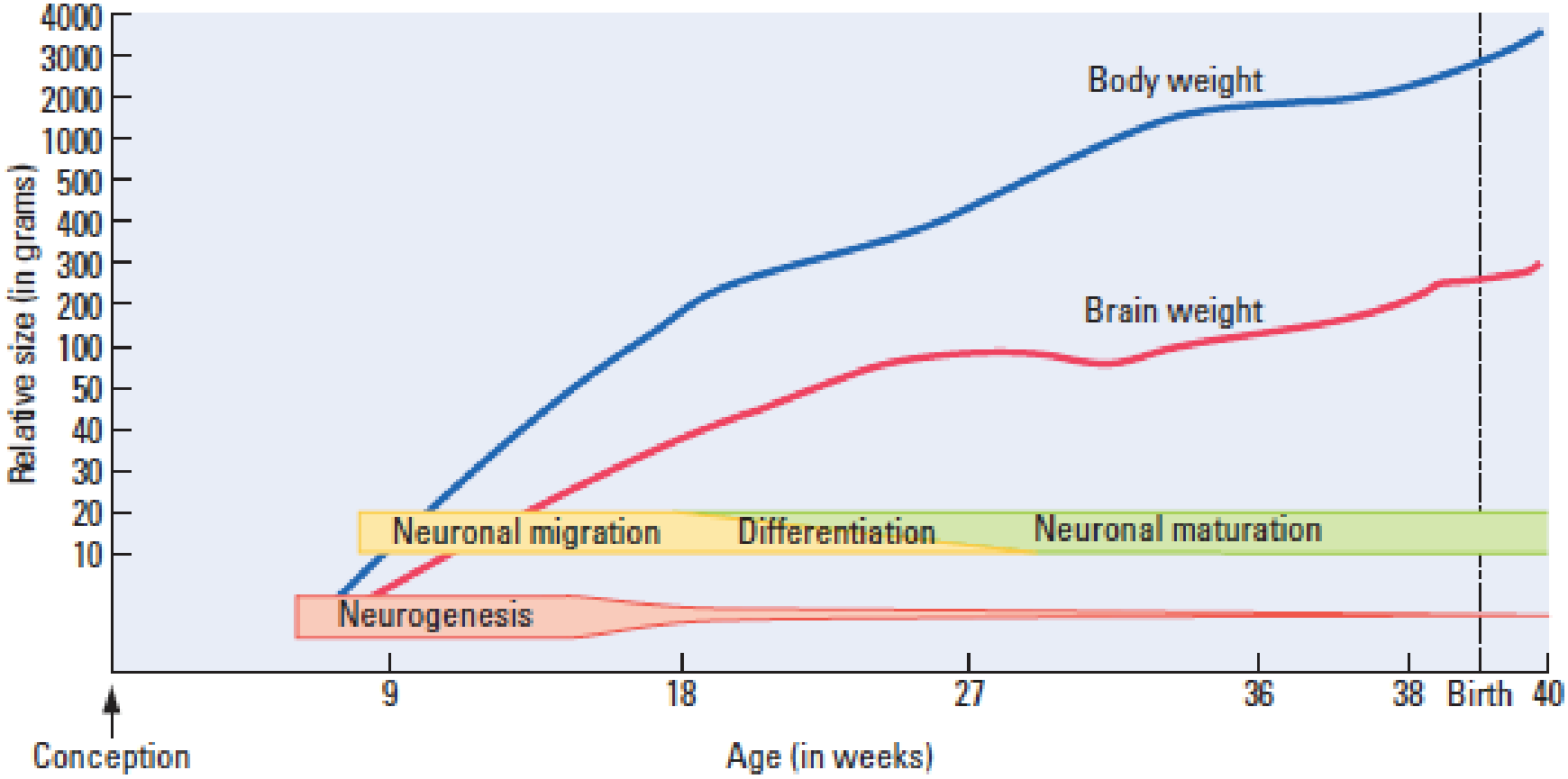
# Developing the cerebral hemispheres



80 billion neurons
$10^{14}$ connections
=
An engineering marvel…

Your brain is sculpted by a lifetime of experiences, especially in the first few years of life.

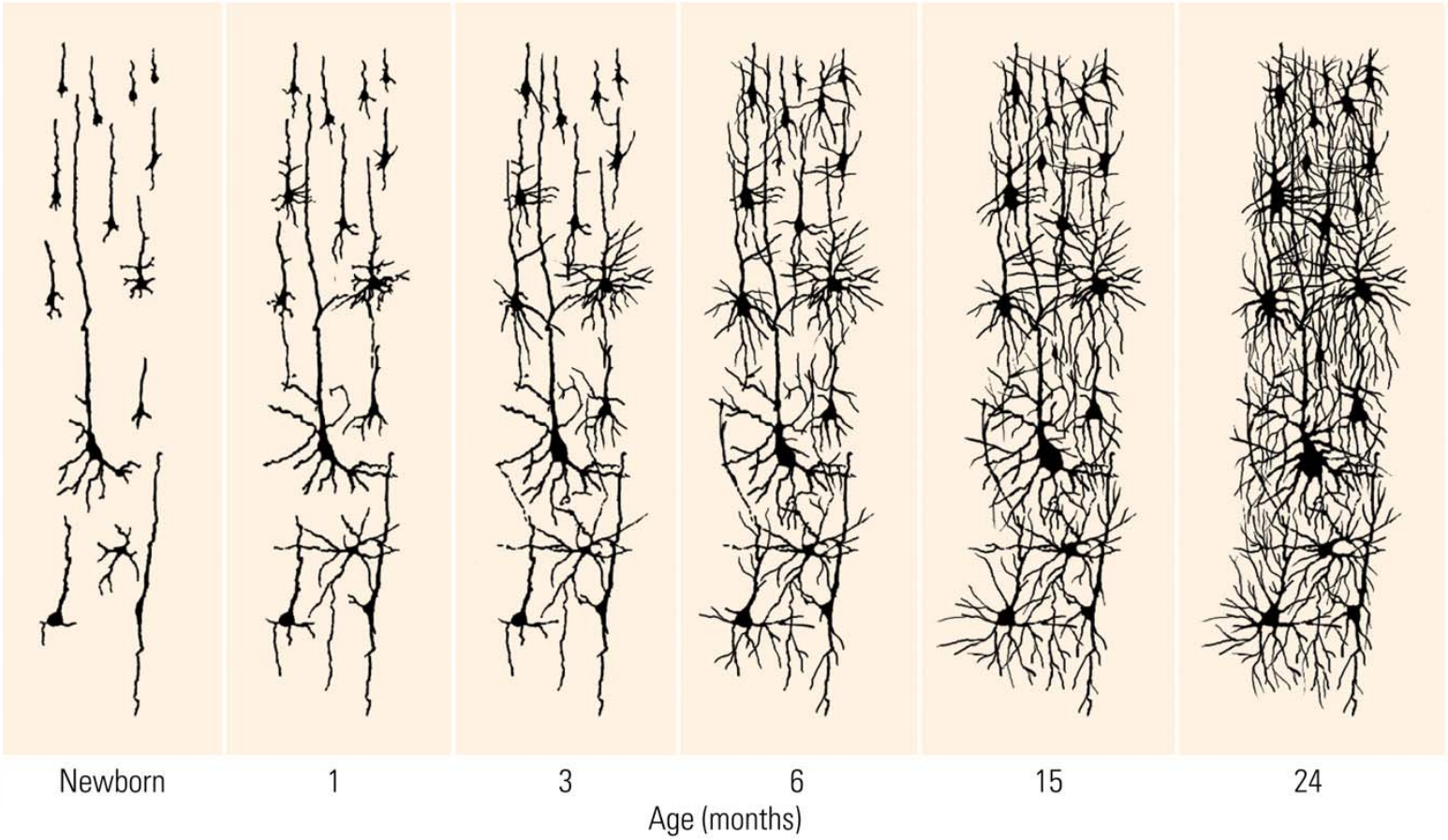
# Gross Development of the CNS



## TABLE 7-1 Stages of Brain Development

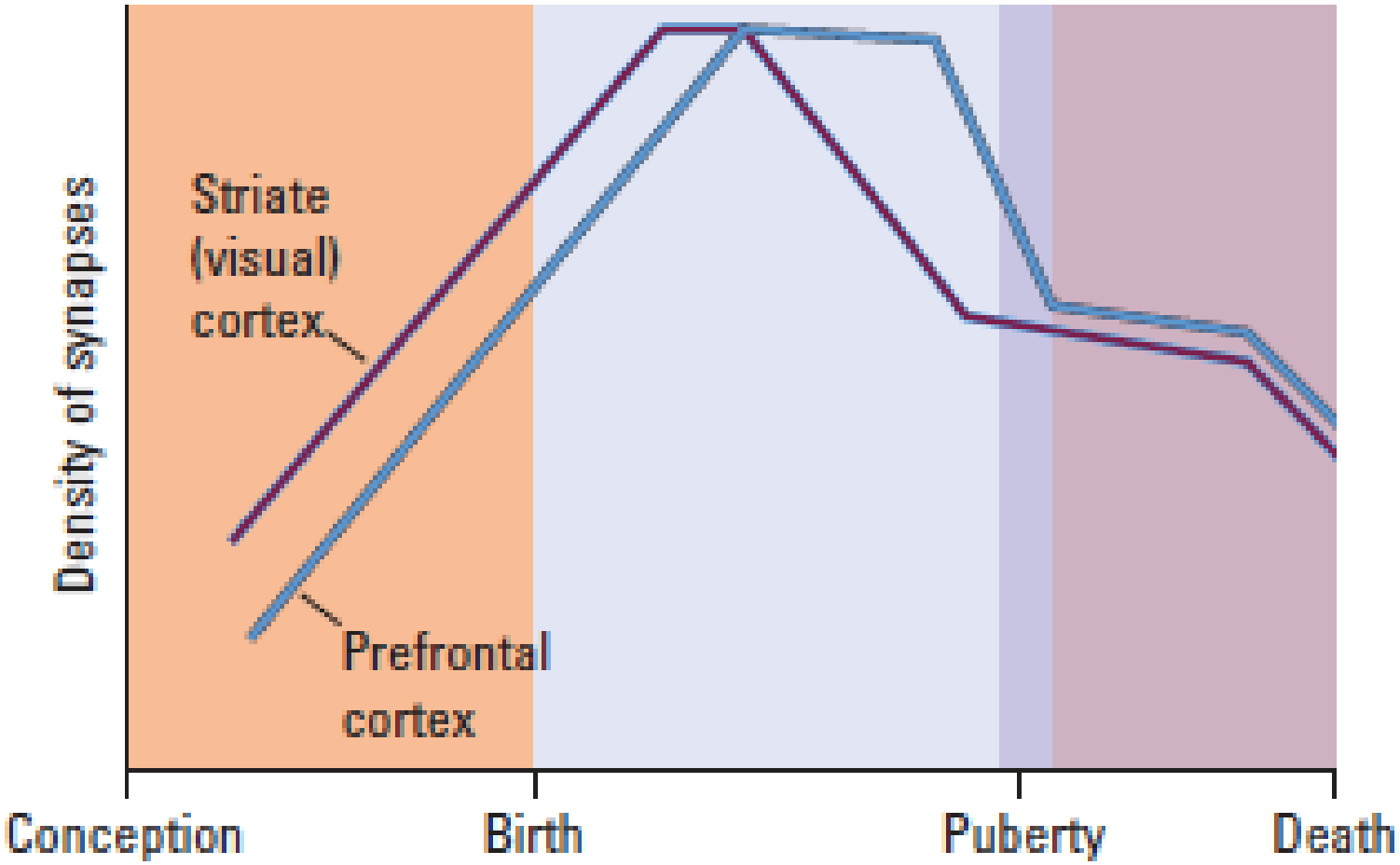
1. Cell birth (neurogenesis; gliogenesis)
2. Cell migration
3. Cell differentiation
4. Cell maturation (dendrite and axon growth)
5. Synaptogenesis (formation of synapses)
6. Cell death and synaptic pruning
7. Myelogenesis (formation of myelin)

# Brain Cells develop connections over the first 2 years

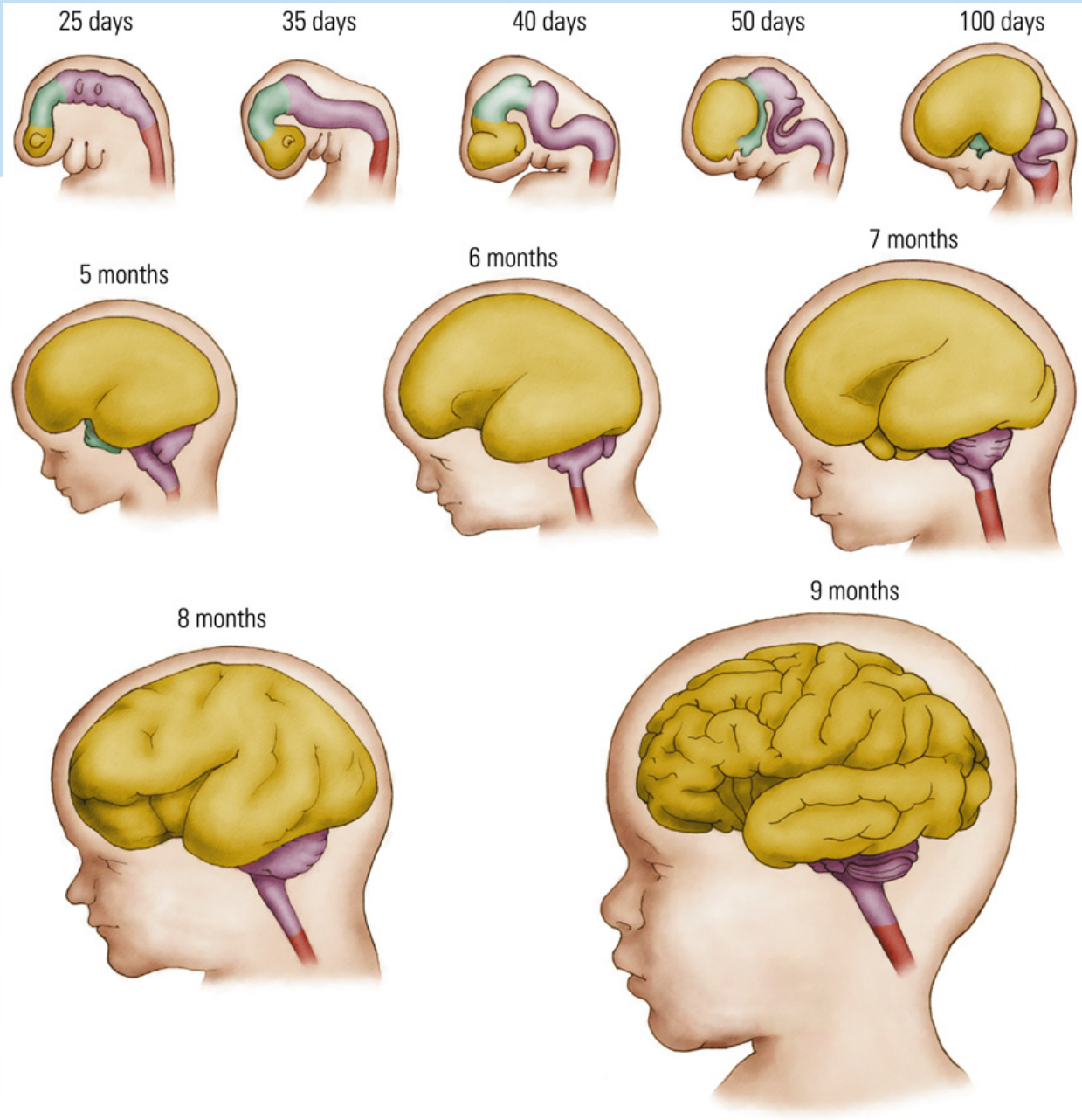



Then they are sculpted actively for 20+ yrs

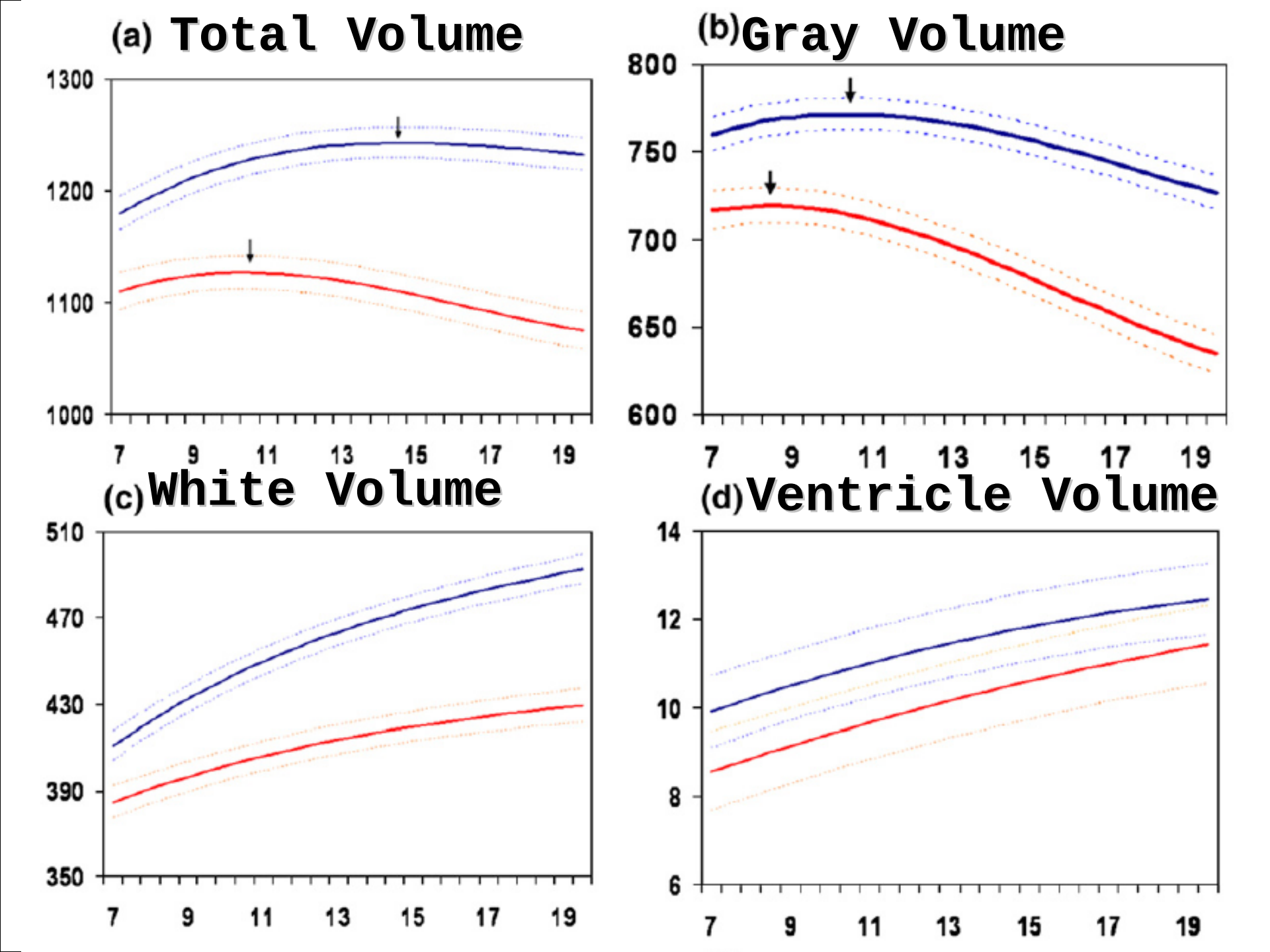
# Cell Death and Synaptic Pruning

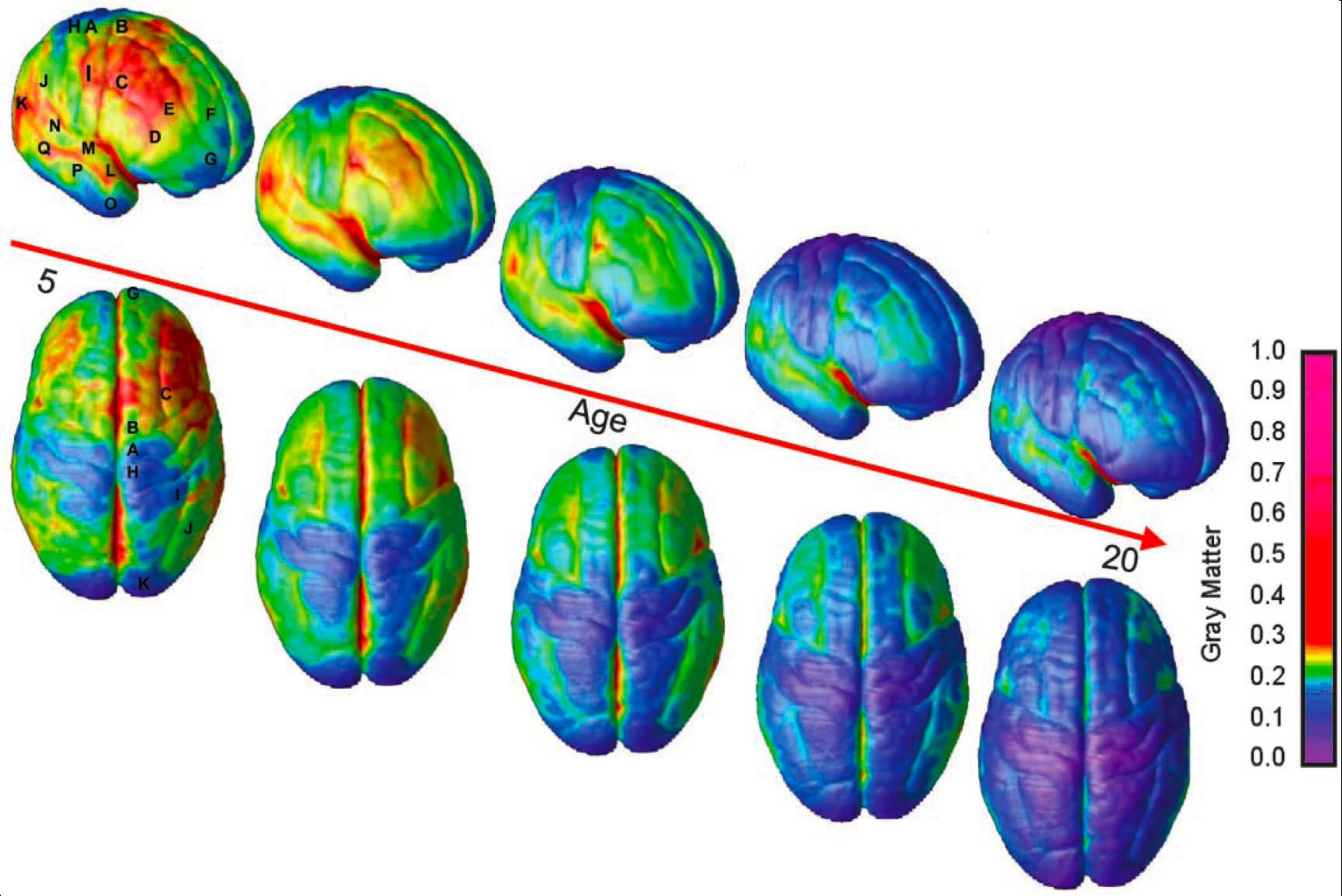


# Development does not end at birth




It continues for at least 20-25 more years


(a) Total Volume
1300
1200
1100
1000
7
9
11
13
15
17
19
(b)Gray Volume
800
750
700
650
600
7
9
11
13
15
17
19
(c)White Volume
510
470
430
390
350
7
9
11
13
15
17
19
(d)Ventricle Volume
14
12
10
8
6
7
9
11
13
15
17
19



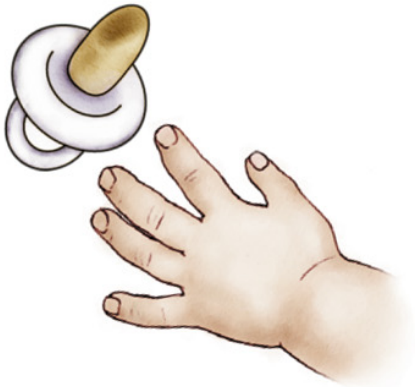

**Cortical thickness drops with development**

# Inferring Neural Development from Behavior

As behaviors emerge we can make inferences about what changes must be happening in the nervous system.

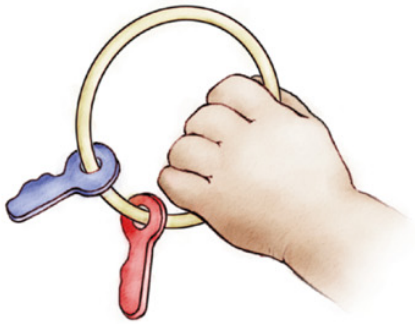
# Behaviours emerge as the brain develops

2 months



Orients hand toward an object and gropes to hold it.

4 months



Grasps appropriately shaped object with entire hand.

10 months

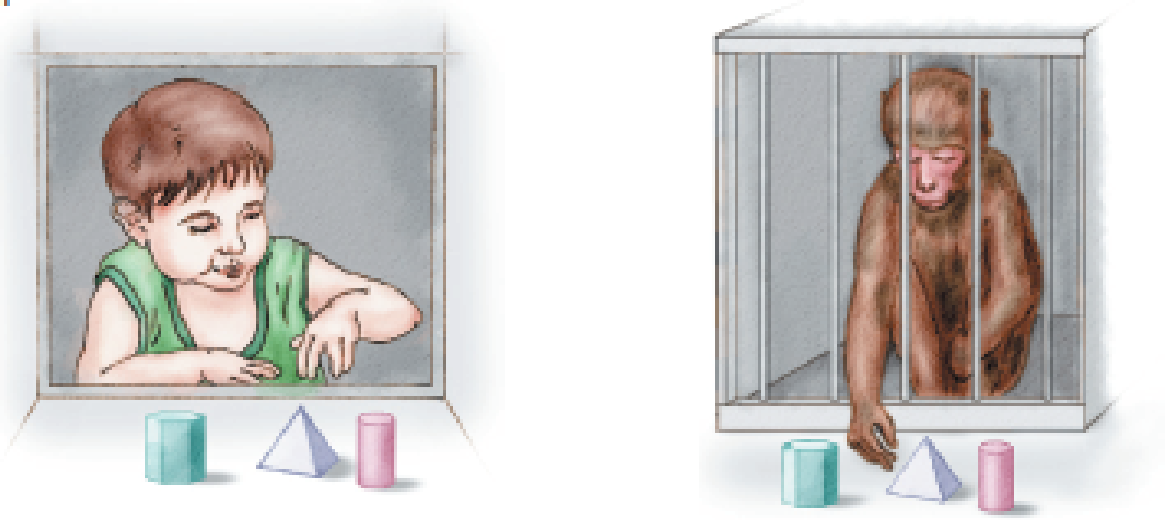
Uses pincer grasp with thumb and index finger opposed.

Behaviours cannot emerge before necessary brain is mature enough…

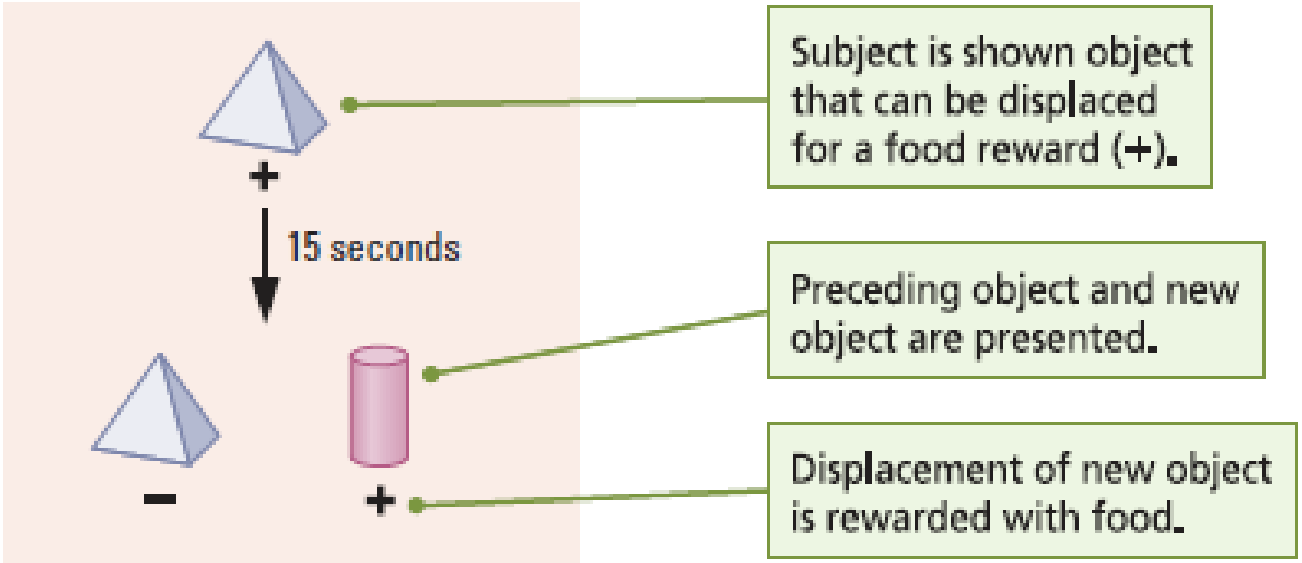
## Question: In what sequence do the forebrain structures required for learning and memory mature?

**Procedure**

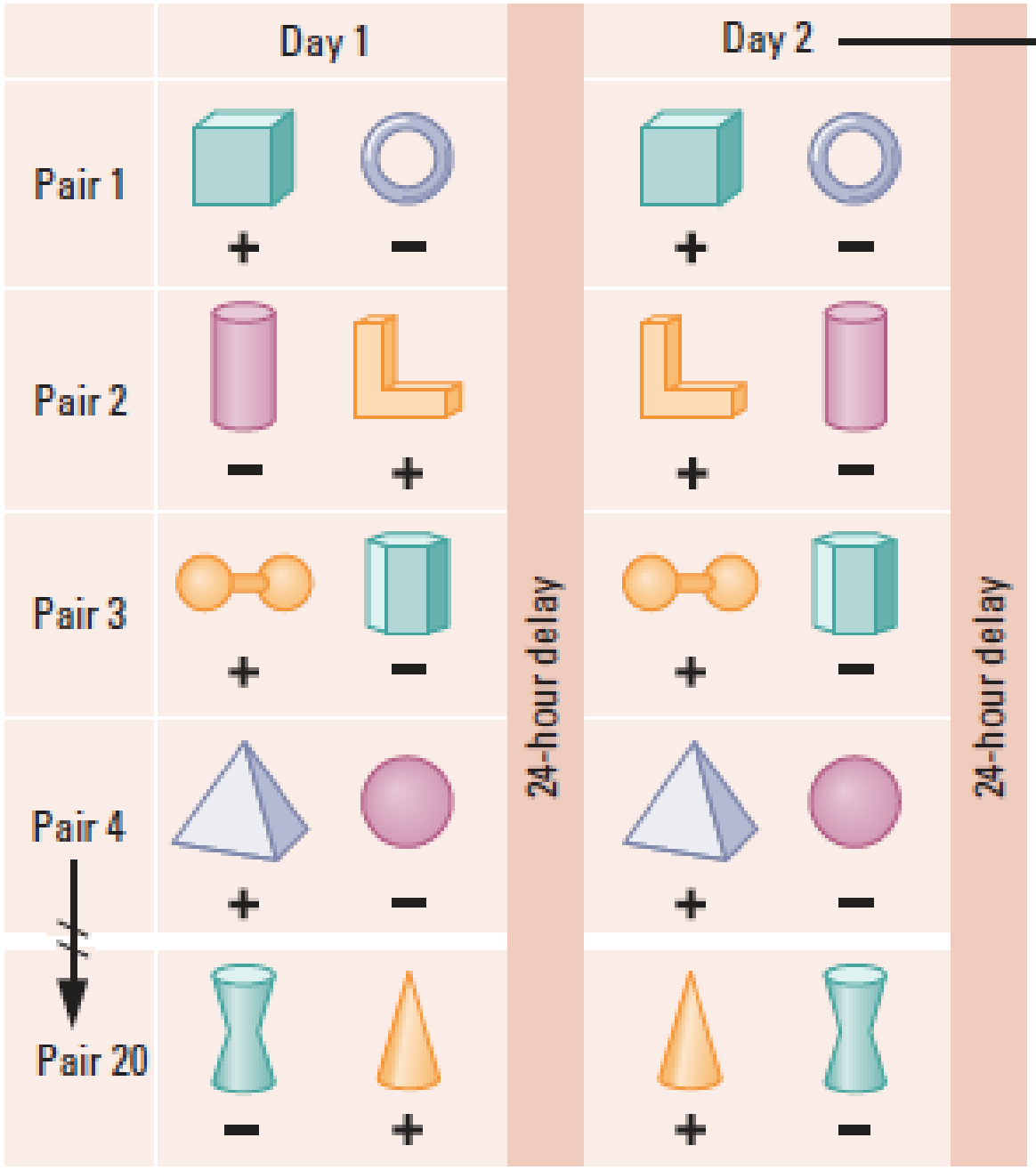
I. Displacement task



II. Nonmatching-to-sample learning task



## III. Concurrent-discrimination learning task



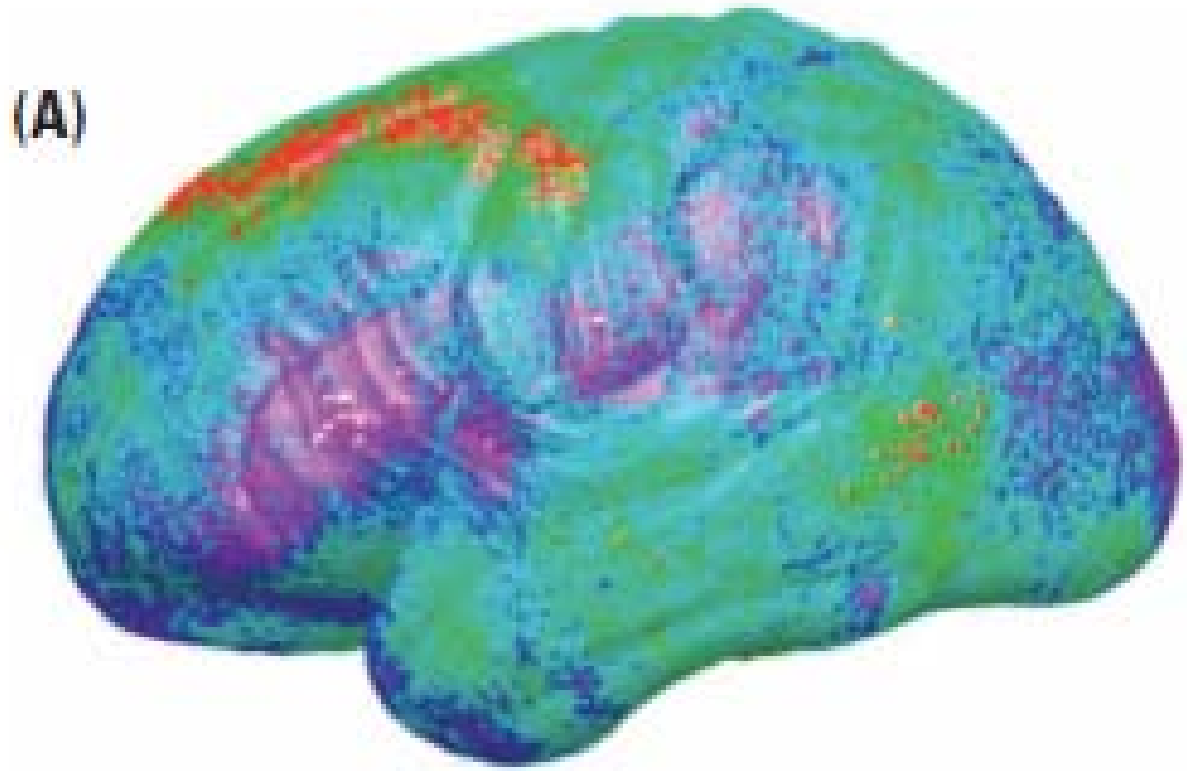

By trial and error, subjects must determine which object in each of 20 pairs should be displaced for a reward of food.

In later trials, the same subjects were presented with the 20 pairs from Day 1 in order to learn and remember which object in each pair should be displaced for the food reward.

# The results reflect differential brain maturation

Both infant humans and monkeys can learn the concurrent discrimination sooner that the seemingly easier matching task

The former task is dependent on the basal ganglia (a habit task) whereas the later task is cortical

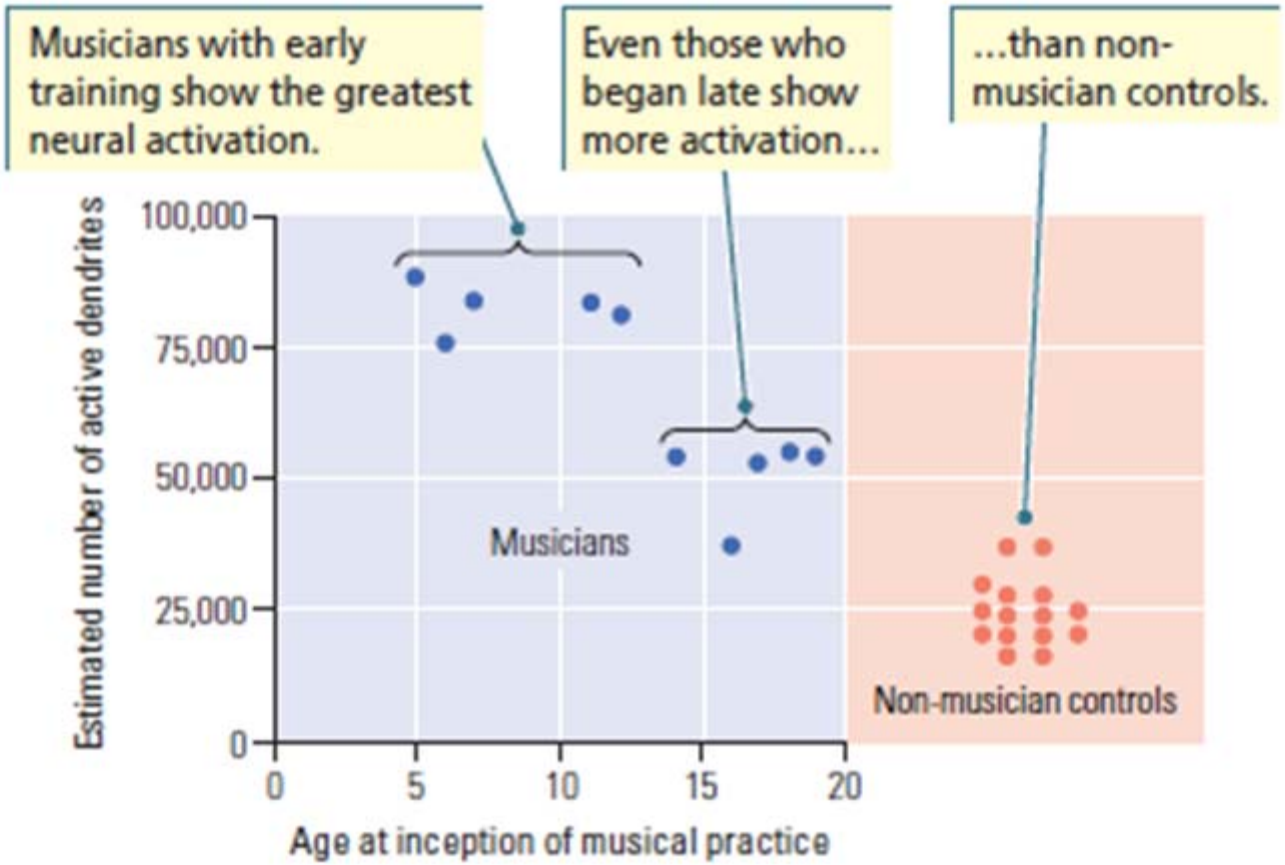



Correlations in brain and behaviour can be counter intuitive:

This shows the correlation between decreasing cortical thickness and improving motor skills. Red dots show regions of cortical *thinning*.


Similarly, this shows the correlation between decreasing cortical thickness and improving vocabulary skills.  Red dots show thinning.

# Ability is related to synapse number



# Factors Affecting brain development

The developing cortex is altered by many pre- and postnatal events.

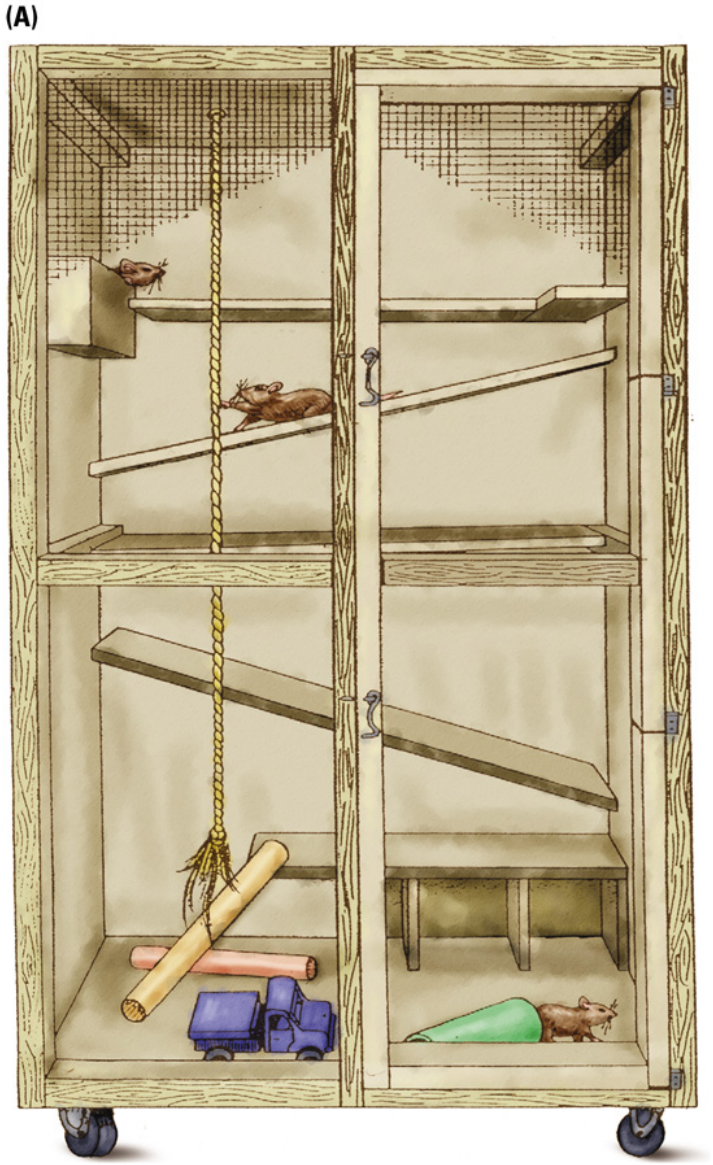
Most of this research is done on lab animals

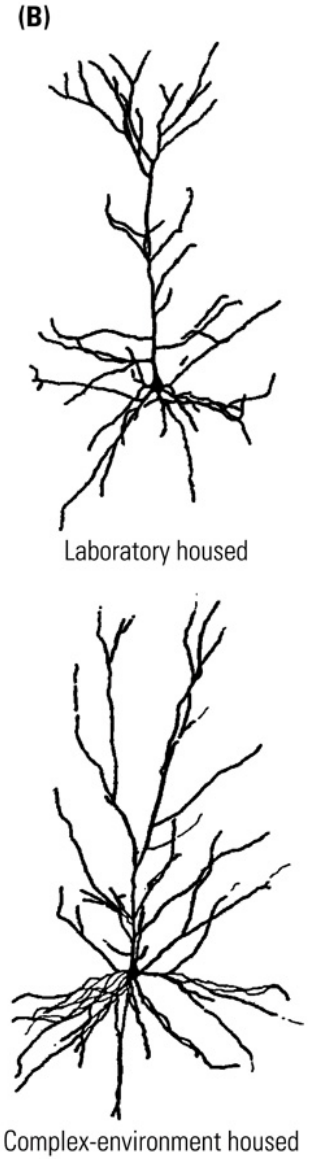
# The principles of brain organization and development are similar for all mammals

# Factors influencing brain development

1. sensory & motor experience

# Shaping Brain Development




Complex Housing
Postnatal

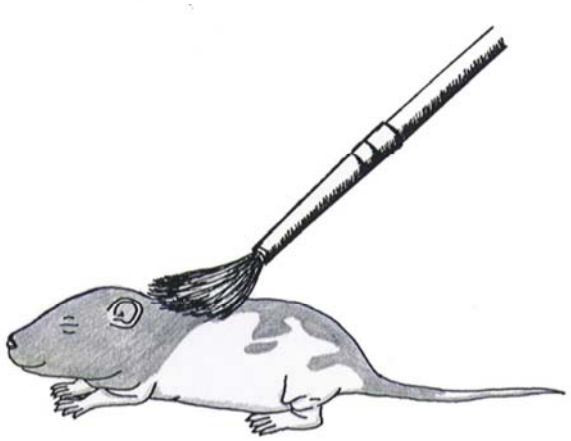
**Prenatal (even dads…)**

Brains are larger,
have more connections

The animals have
enhanced cognitive
and motor behaviour

# Getting to the brain via the skin

Postnatal Infant



Prenatal

Also can use a broad spectrum light…

# What is the effect of the tactile stimulation?

-Larger brain
-More connections
-Enhanced cognitive & motor performance
-Changes in the genes turned ‘on’ and ‘off’

Conclusion:
Experience can alter the production
of proteins in the skin, which in turn
can alter the brain through effects on genes.

# And the point is?

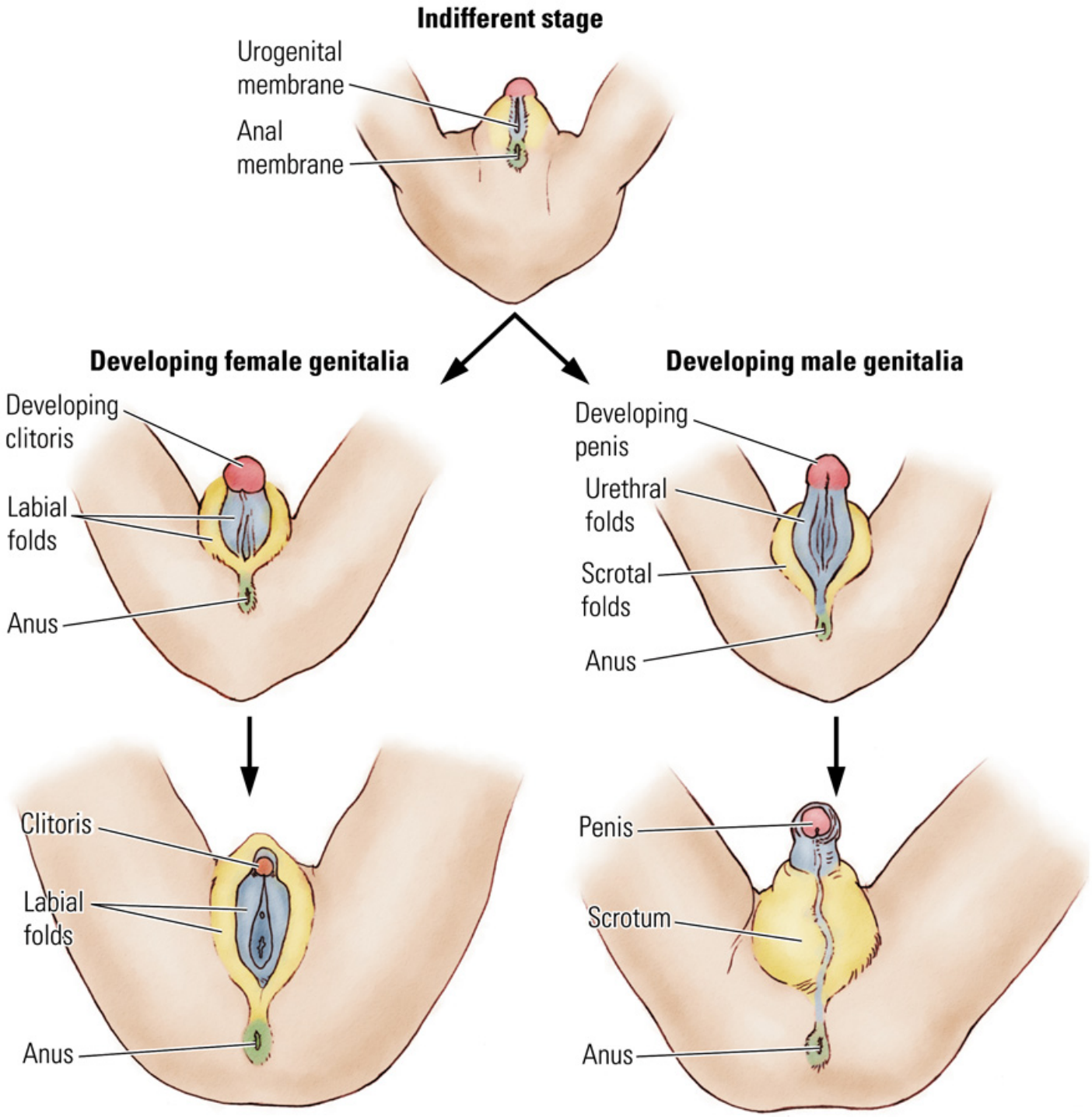
Think about parent-infant interactions. At 6 weeks there is a difference of 6+ hours/day at the two ends of the human parenting spectrum.

But it is not just about time, it is about quality too.

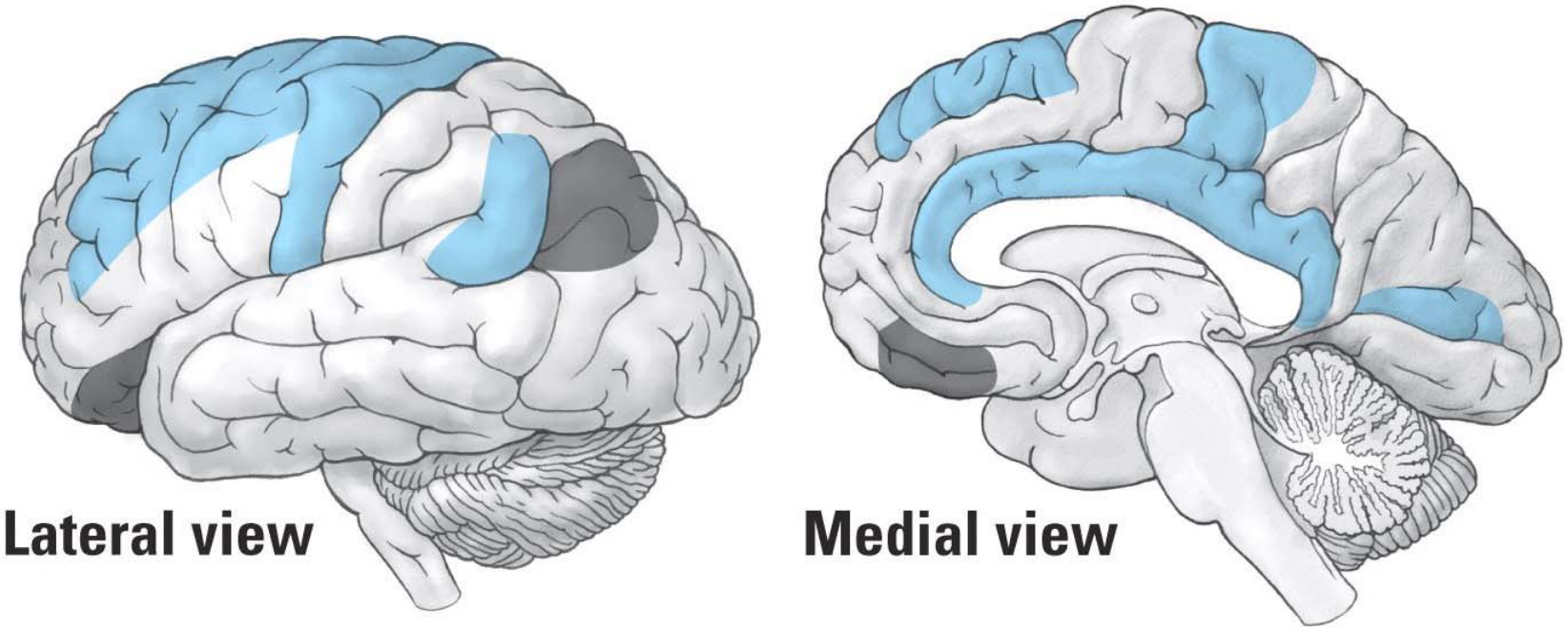
We will return to this…

# Factors influencing brain development

1. **sensory & motor experience**
2. **gonadal hormones**


Indifferent stage
Urogenital membrane
Anal membrane
Developing female genitalia
Developing male genitalia
Developing clitoris
Labial folds
Anus
Developing penis
Urethral folds
Scrotal folds
Anus
Clitoris
Labial folds
Anus
Penis
Scrotum
Anus

# Gonadal hormones change more than the genitals…

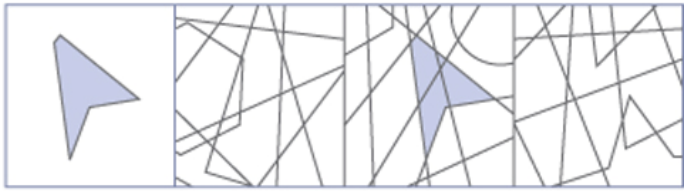
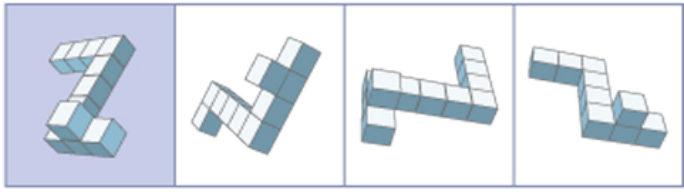
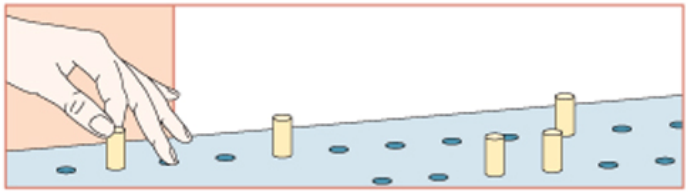
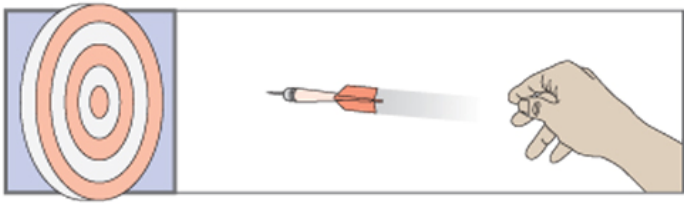
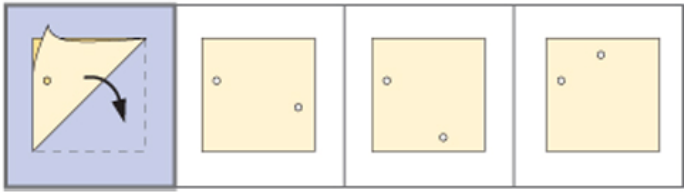



Relative volume of cortical regions in women and men

This means that females and males *should* behave differently!

# How does this relate to sex differences in behaviour?

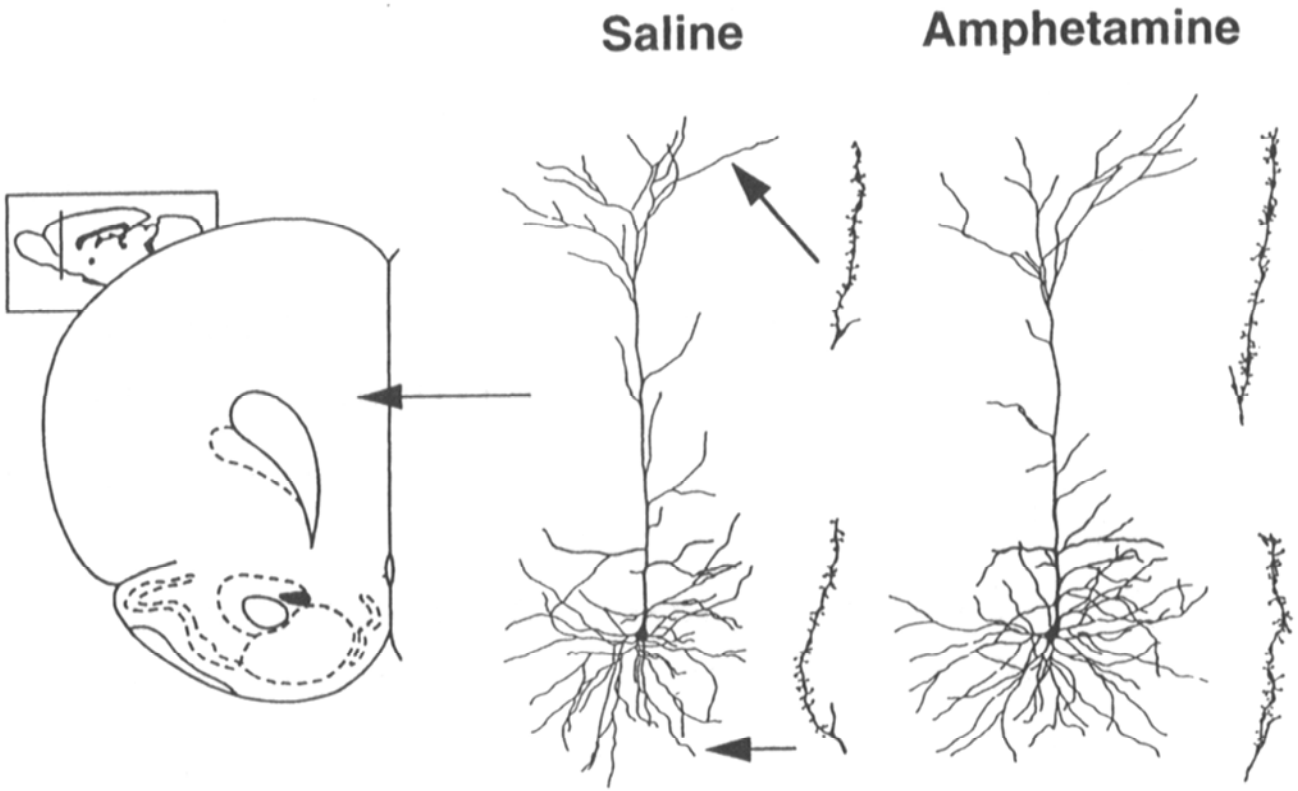
# Sex differences in behaviour

| | Tasks favoring women | Tasks favoring men |
|---|---|---|
| Mathematical calculation | 65: $13 \times 4 - 21 + 34$<br>73: $2(13 + 17) + 18 - \frac{20}{4}$ | |
| Tests of mathematical reasoning | | 1650: If only 40% of seedlings will survive, how many must be planted to obtain 660 trees? |
| Recall of a story, a paragraph, or unrelated words | Story… Run, flower, casserole, water, explosion, pencil, horse, newspaper, book, pliers, bath, dancer… | |
| Mentally finding a geometric form in a complex picture | |  |
| Remembering displaced objects |  | |
| Mentally rotating a solid object | |  |
| Precision, fine motor coordination |  | |
| Target-directed motor skills | |  |
| Rapidly matching items in perceptual tests |  | |
| Visualizing where holes punched in a folded paper will fall | |  |

# Factors influencing brain development

1. sensory & motor experience
2. hormones (gonadal and stress)
3. psychoactive drugs

# Psychoactive Drugs Leave a Footprint in the Brain




**Drugs include:**
nicotine
caffeine
cocaine
antidepressants
valium
marijuana
morphine
antipsychotics
and more…

Changes are areal dependent and in the prefrontal cortex they are usually opposite

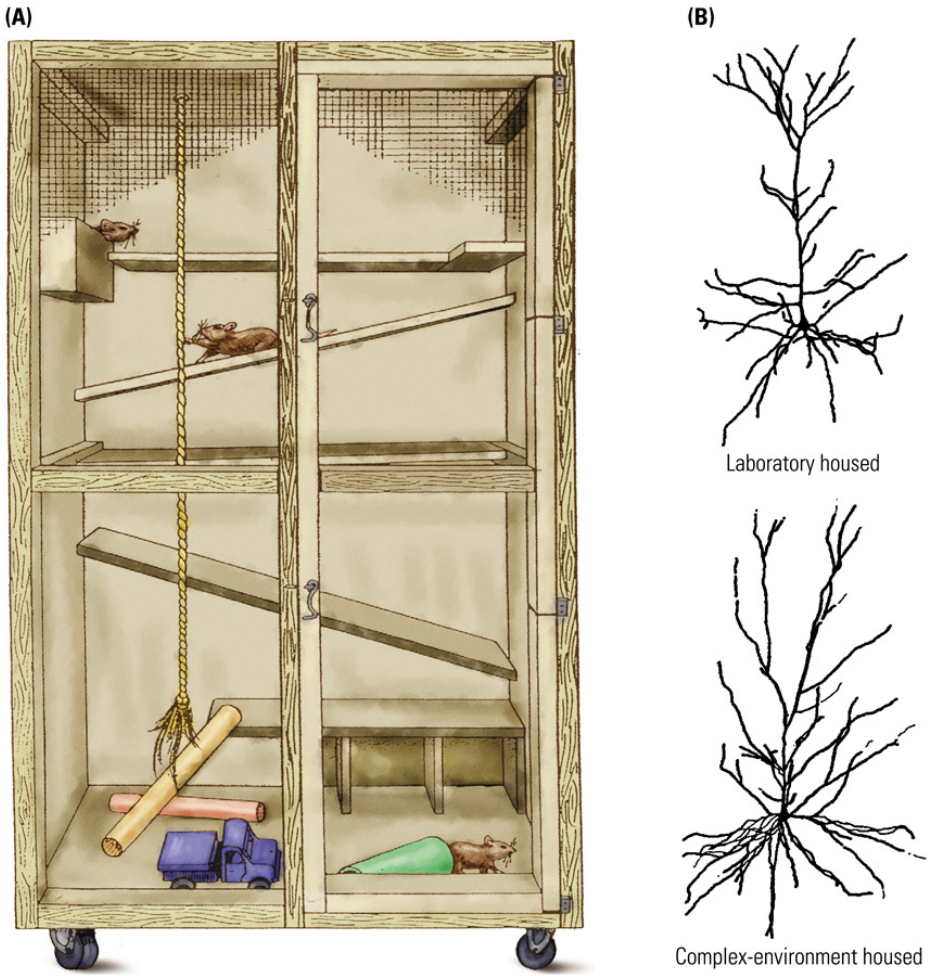
# Drugs with chronic effects in infants & juveniles

**Amphetamine**
**Nicotine**[+]
**Caffeine**[+]
**Morphine**
**Antidepressants** [+]
**Methylphenidate**
**Alcohol**[+]
**Antipsychotics**[+]
**Anxiolytics**[+]

+and prenatally

**Consider: 1) the interaction with sex differences…**
**2) these drugs alter brain development**
**20% of pregnant women are on 'heavy' drugs; 99% on caffeine**

# Drugs also can alter later plasticity




Exposure to stimulants during the juvenile years can alter later response to sensory experiences and alter later learning and memory…

# BUT, early experience can attenuate drug effects and cognitive functions

1. Pre- & postnatal tactile stimulation
2. Early complex housing
3. Pre- & postnatal stress

# Factors influencing brain development

1. sensory & motor experience
2. gonadal hormones
3. psychoactive
4. parent-child relationships

# Parent-infant interactions change the brain

# Consequences?

The caregiver's behaviour affects the lifelong health of the infants via later stress reactivity.

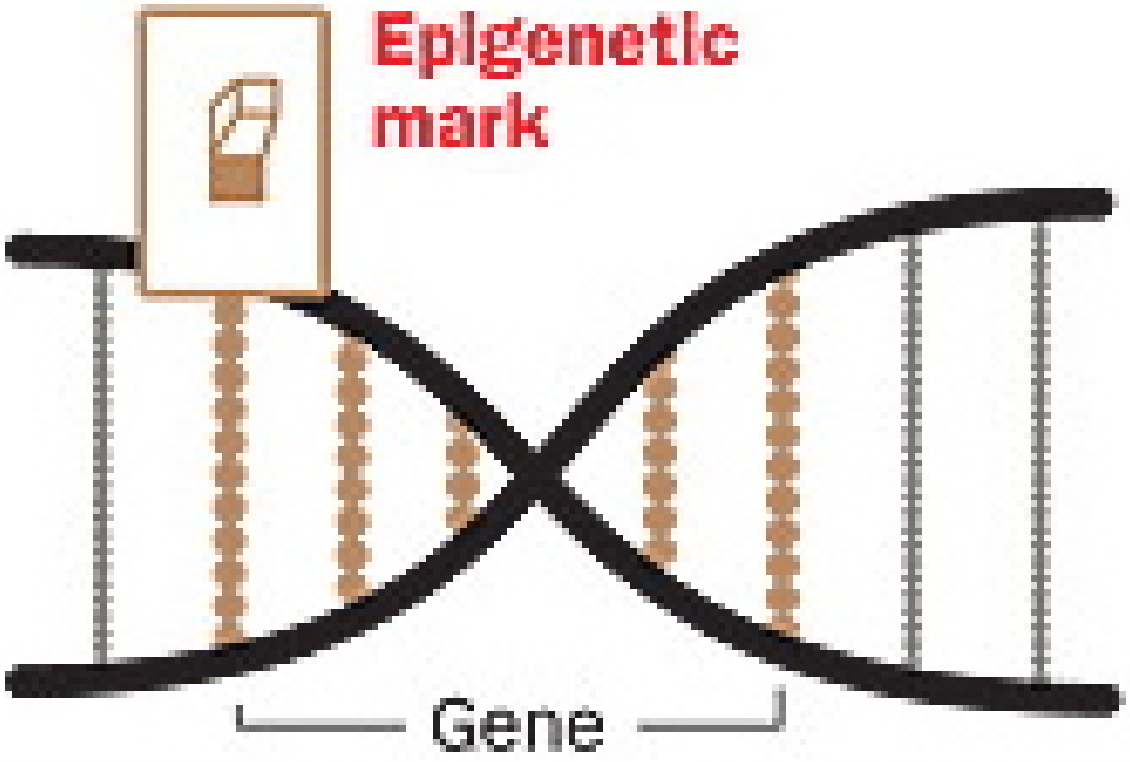
The mom's behaviour is transferred to the pups through changes in gene expression.

# Epigenetics and the Brain


All cells carry the same DNA but different cell types (brain vs bone) are very different

This is because of gene expression differences

# Genes can be switched on and off

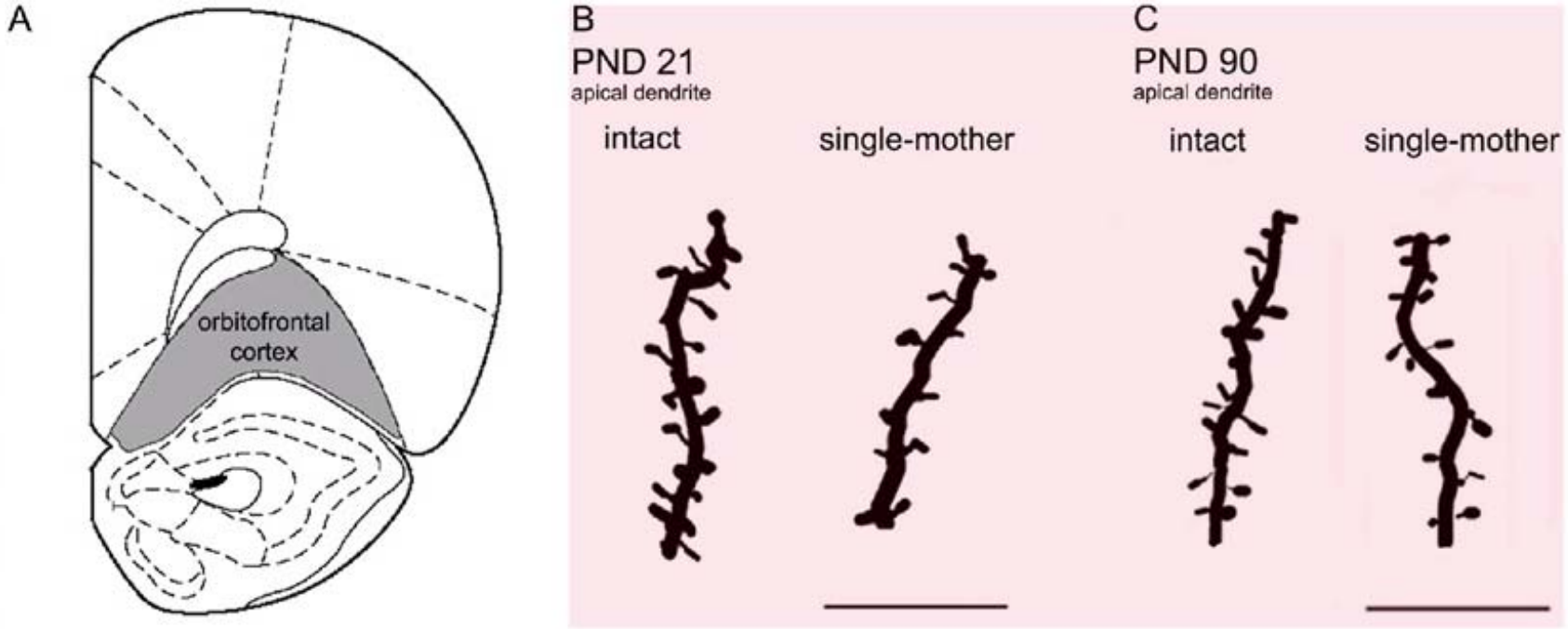


# Animal models of parental care

- Degus have biparental care

# Single parenting alters the frontal lobe in degus

**Helmeke et al., Neuroscience** 163 (2009) 790–798.



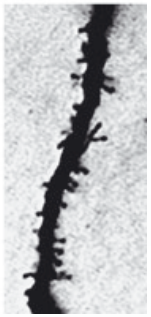
# Factors influencing brain development

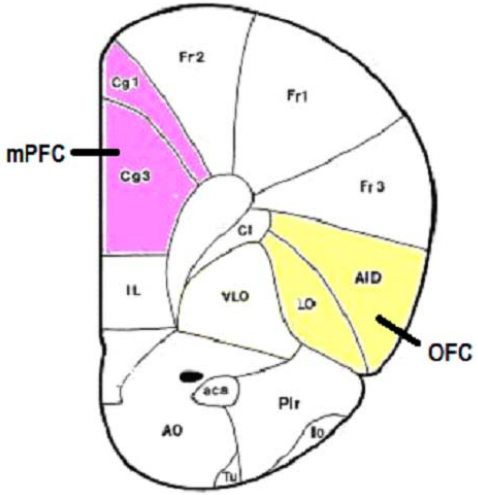
1. sensory & motor experience
2. gonadal hormones
3. psychoactive drugs
4. parent-child relationships
5. stress

# Prenatal Stress

1. Smaller brains

2. Altered frontal lobe development
   =abnormal social behaviour
   =cognitive impairments

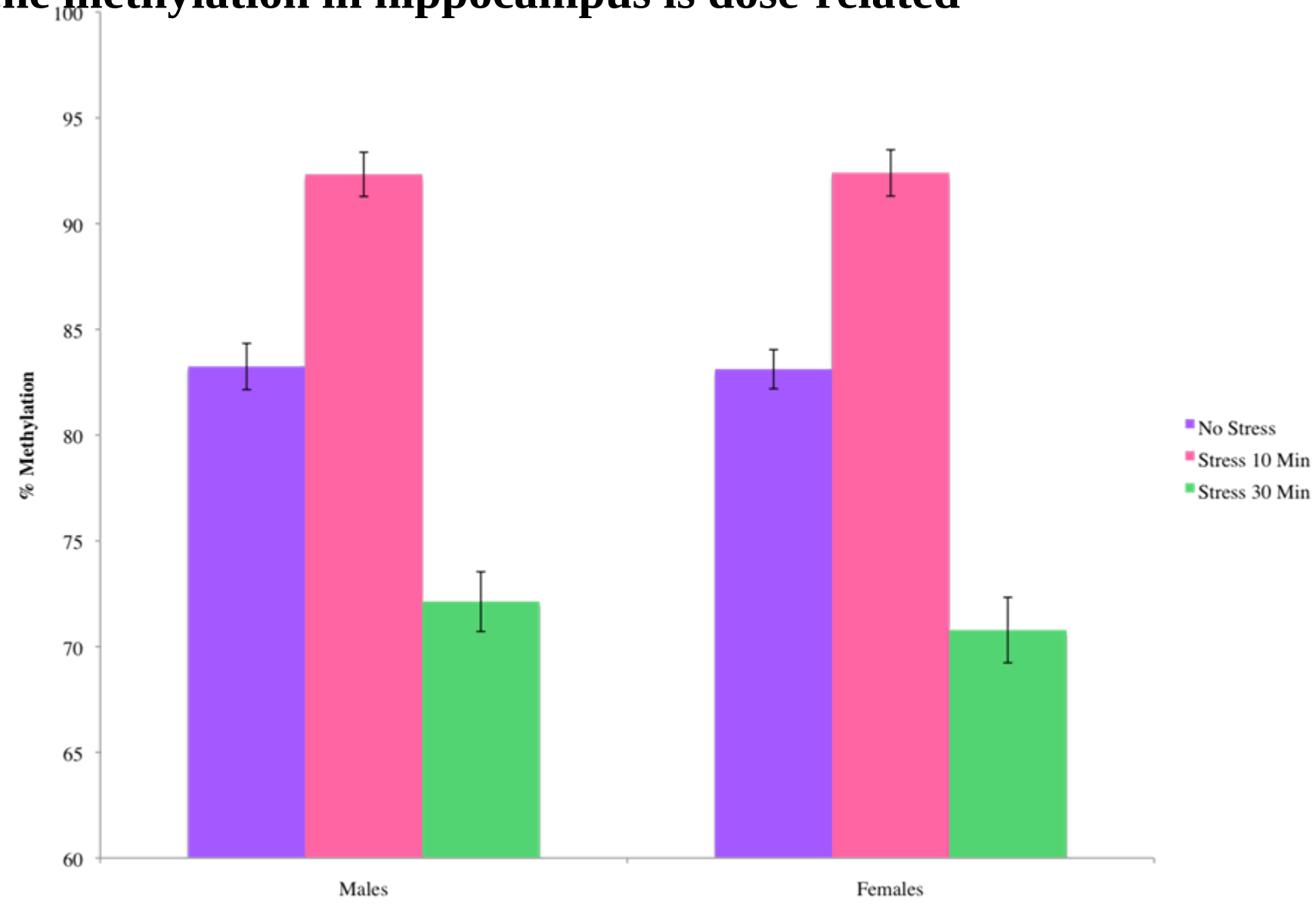





# But there is stress and there is stress

Mild and More Extreme Stress have different effects…

# Gene methylation in hippocampus is dose-related




There are similar results in the prefrontal cortex

# Stress Effects Can be Indirect

Bystander Stress Story

(Mychasiuk, Schmold, Kolb & Gibb, 2010)

# How? – Changed Gene Expression

**27,342**

# of genes in rat genome

**1,181**

# of genes with changed expression

**74**

Correction for # of comparisons

**GRIK 2**

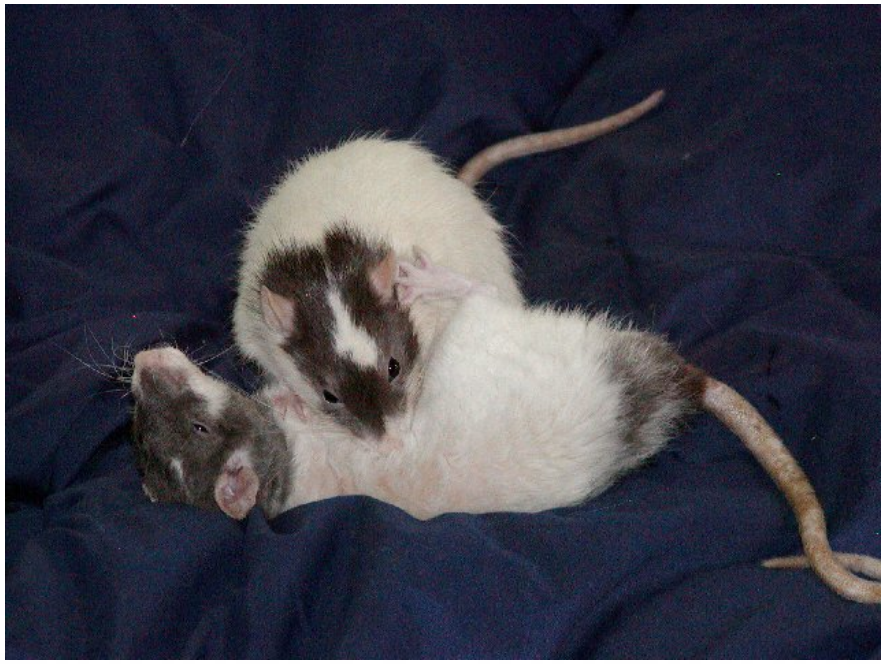
Example: related to glutamate receptor

Mychasiak, Gibb & Kolb, 2010

# Factors influencing brain development

1. sensory & motor experience
2. gonadal hormones
3. psychoactive drugs
4. parent-child relationship
5. stress
6. peer relationships

# All mammals have play behaviour with rules



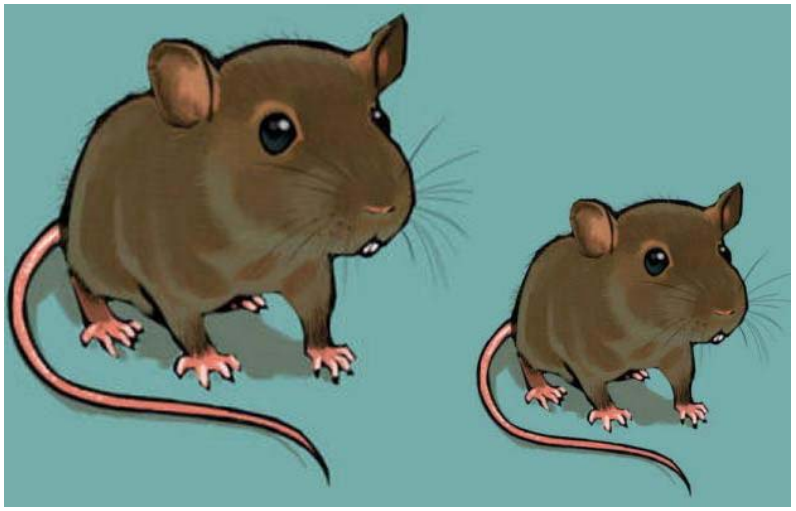
***There are species differences in adult social behaviour that can be seen in trajectories of the development of play behaviour & reflect genetic effects…***

*Macaca fuscata*

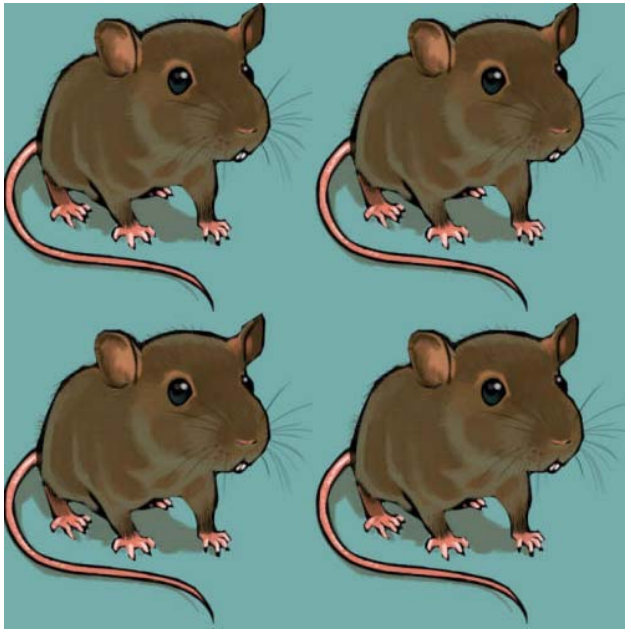
*Macaca tonkeana*

***Tonkeans are more placid and have much more active play behaviour***

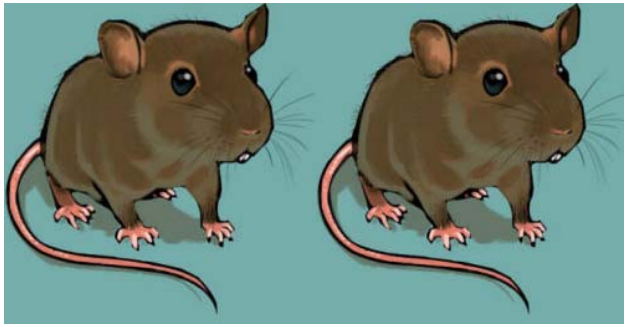
***Rheinhart & Pellis, in progress***



Little Play:  Adult + Juvenile

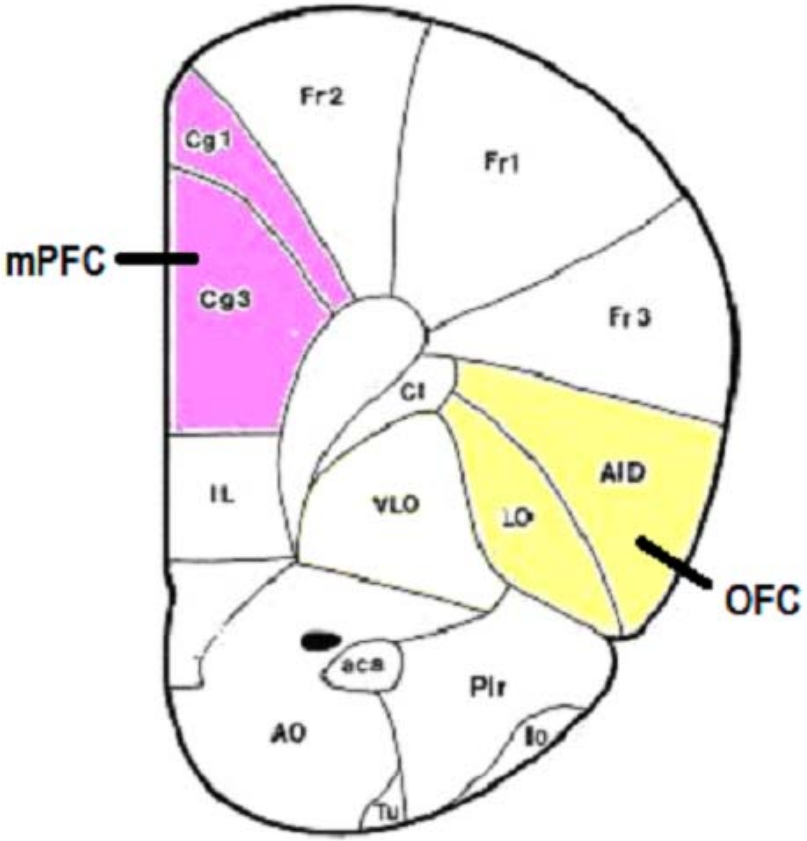


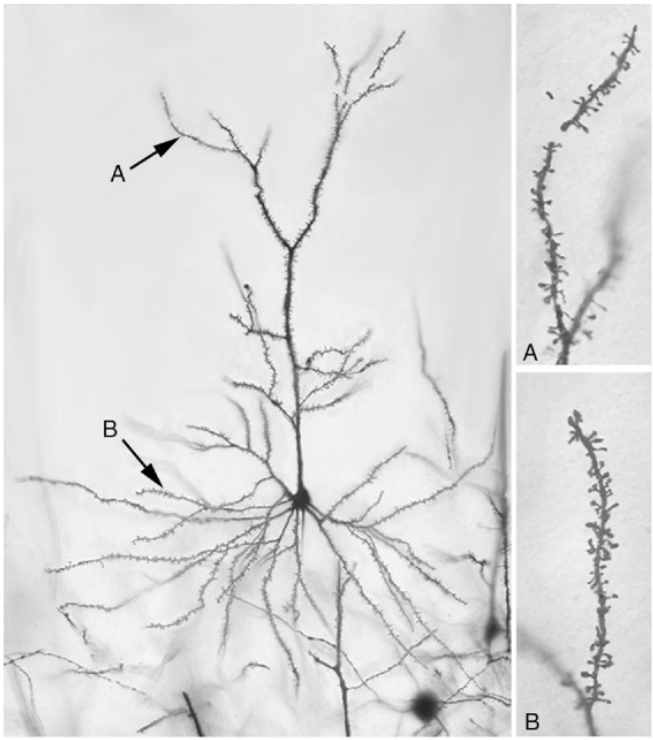
Enriched Play: 4 Juveniles



Limited Play: 2 Juveniles

**Bell, Pellis & Kolb, 2009**



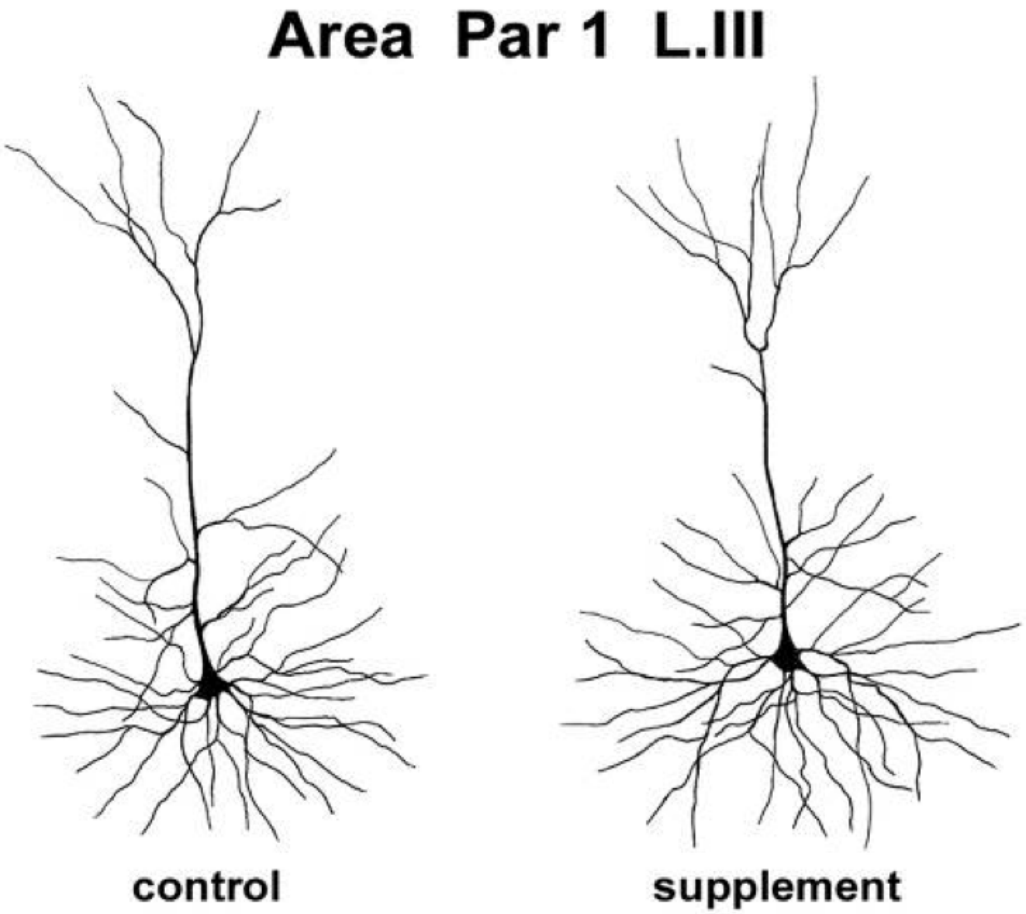




Sibling play = more complex mPFC

Conspecific number = more complex OFC

# Factors influencing brain development

1. sensory & motor experience
2. psychoactive drugs (e.g., nicotine, caffeine, antidepressants and more…)
3. hormones (gonadal and stress)
4. parent-child relationship
5. stress
6. peer relationships
7. diet




Empower Plus given to pregnant moms increases dendritic length and spine density in cortex and hippocampus

This is correlated with motor & cognitive enhancement

# Factors influencing brain development

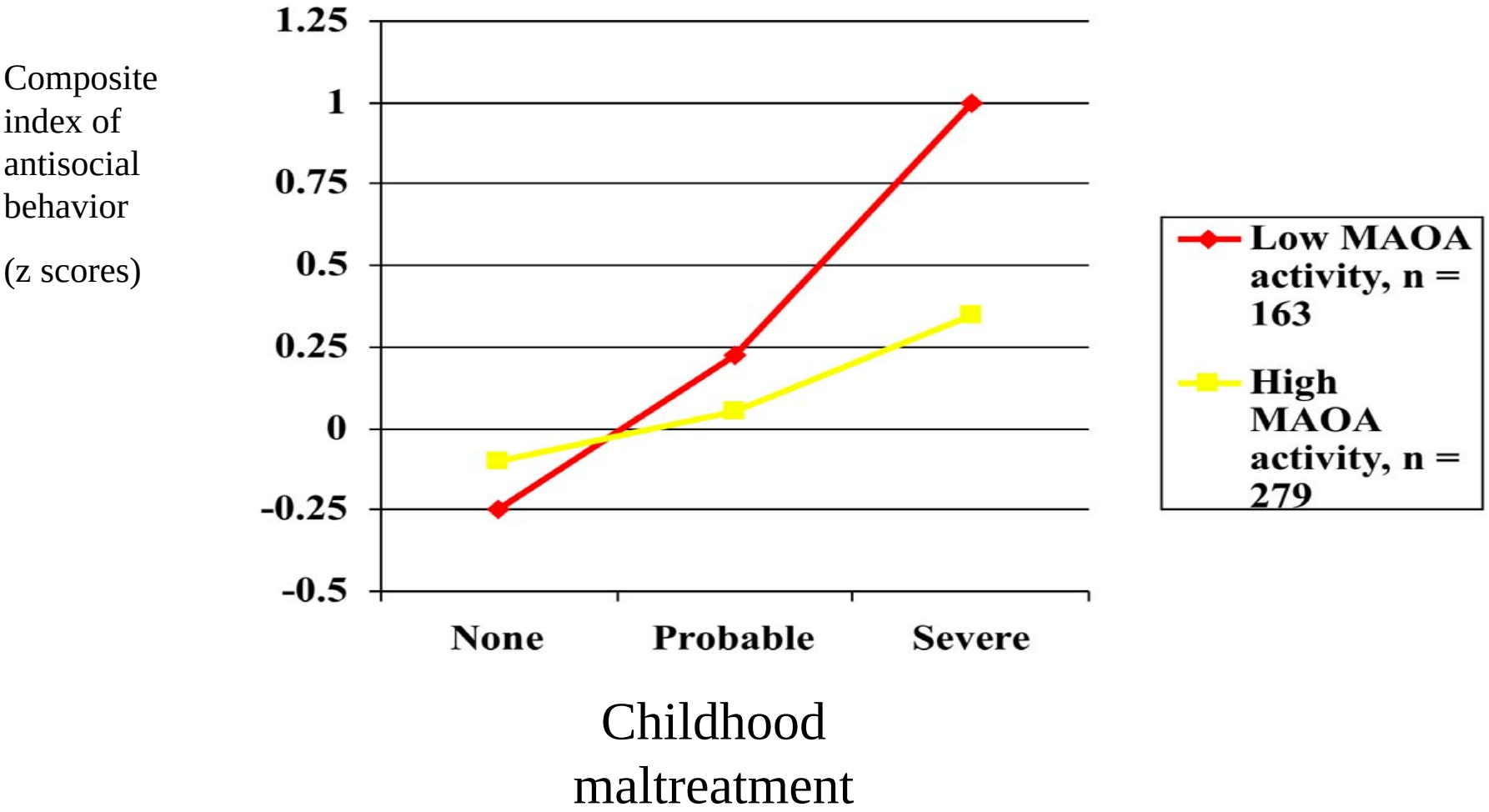
1. sensory & motor experience
2. gonadal hormones
3. psychoactive drugs
4. parent-child relationship
5. stress
6. peer relationships
7. diet
8. gene X experience X brain interactions

# Gene-Experience Interactions

Early experiences influence the expression of genes related to disorders such as antisocial behaviour and depression.

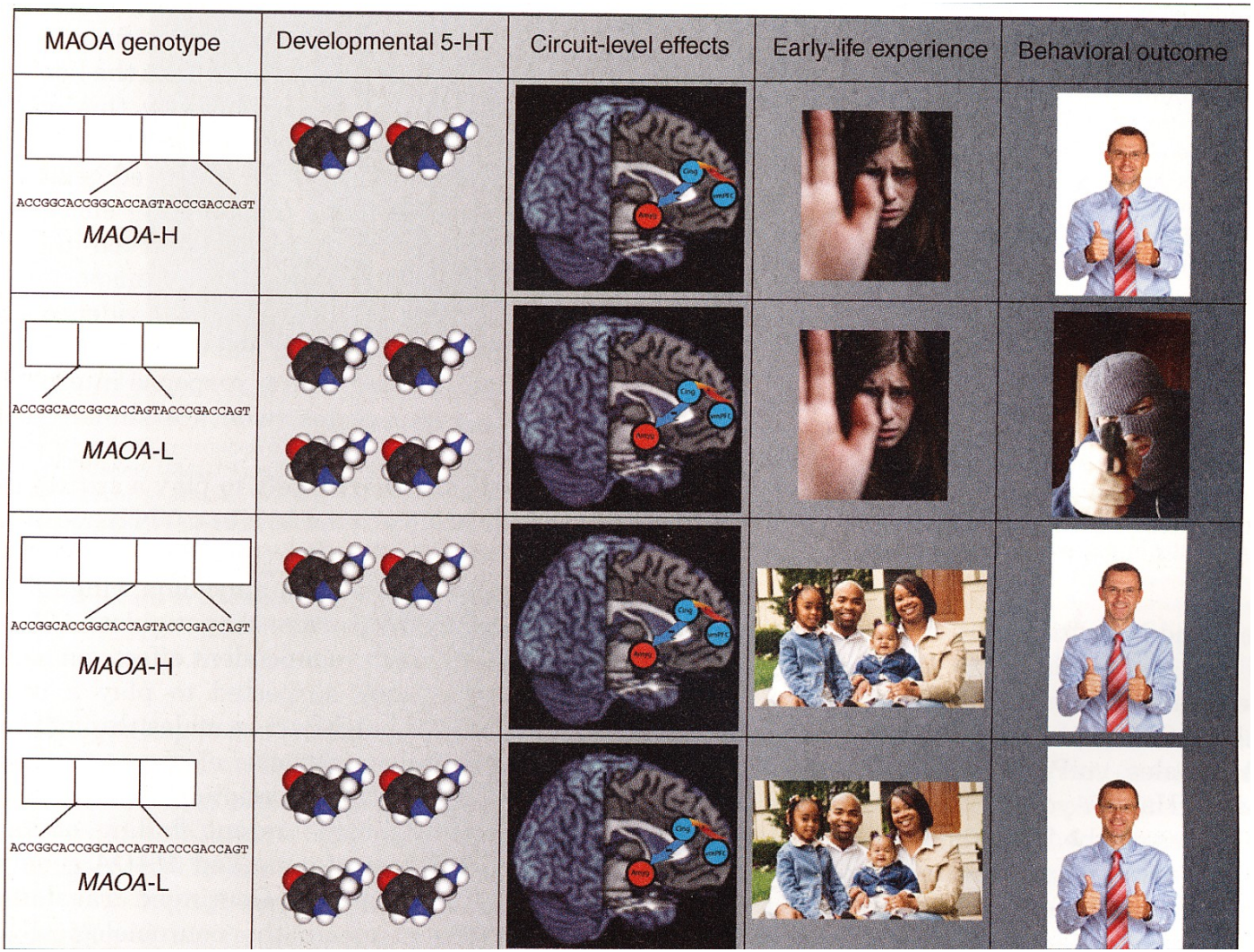
And, altering gene expression alters the brain.

# ANTISOCIAL BEHAVIOR AS A FUNCTION OF MAO-A ACTIVITY AND A CHILDHOOD HISTORY OF MALTREATMENT (from Caspi et al., 2002)

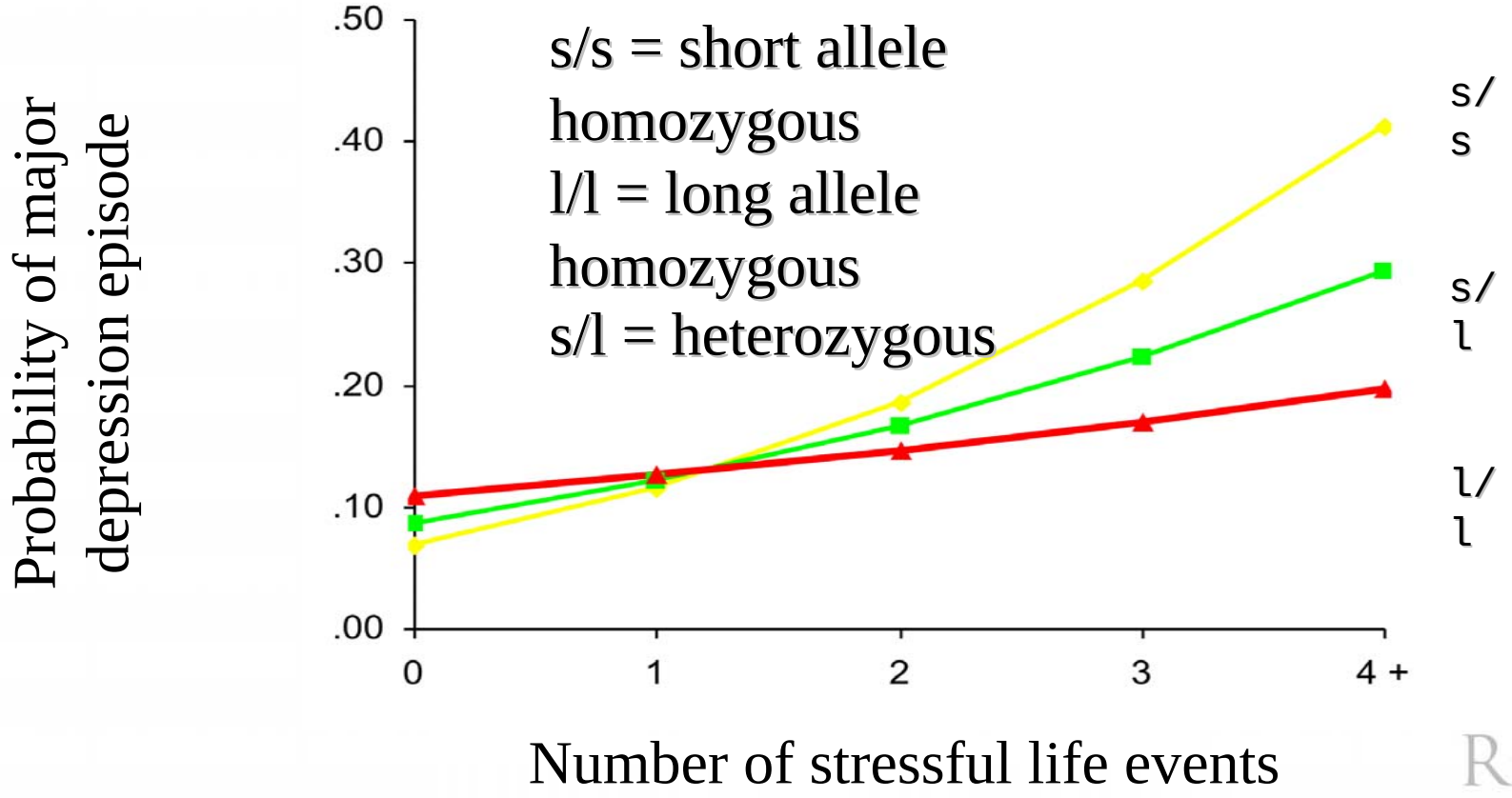


# Human aggression and the MAO-A gene Buckholtz & Meyer Lindenberg, 2008

Nature Nuture



# EFFECT OF LIFE STRESS ON DEPRESSION MODERATED BY 5-HTT GENE (from Caspi et al., 2003)



# Conclusions

1. Brain & cognitive development is prolonged and influenced by a wide range of factors.
2. Perinatal events can have important implications for understanding adult brain and behaviour relationships.
3. Epigenetic changes are just beginning to be understood related to brain plasticity.
4. Understanding the issues around brain plasticity and behaviour have important implications for public policy.