

# Brain in transition

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Stramehs, Venice, 16 December 2014

Building bridges

CAMHS

Transitional Psychiatry

AMHS

NL government prevents building bridges 1-1-2015

Create awareness

# Transitiepsychiatrie anno 2015

-naareengeïntegreerdeaanpakvoor 15  
tot 24 jarigen-



# CAMH – AMH 18y gap

■ Organizational Dutch transition Vaessen et al, 16/12

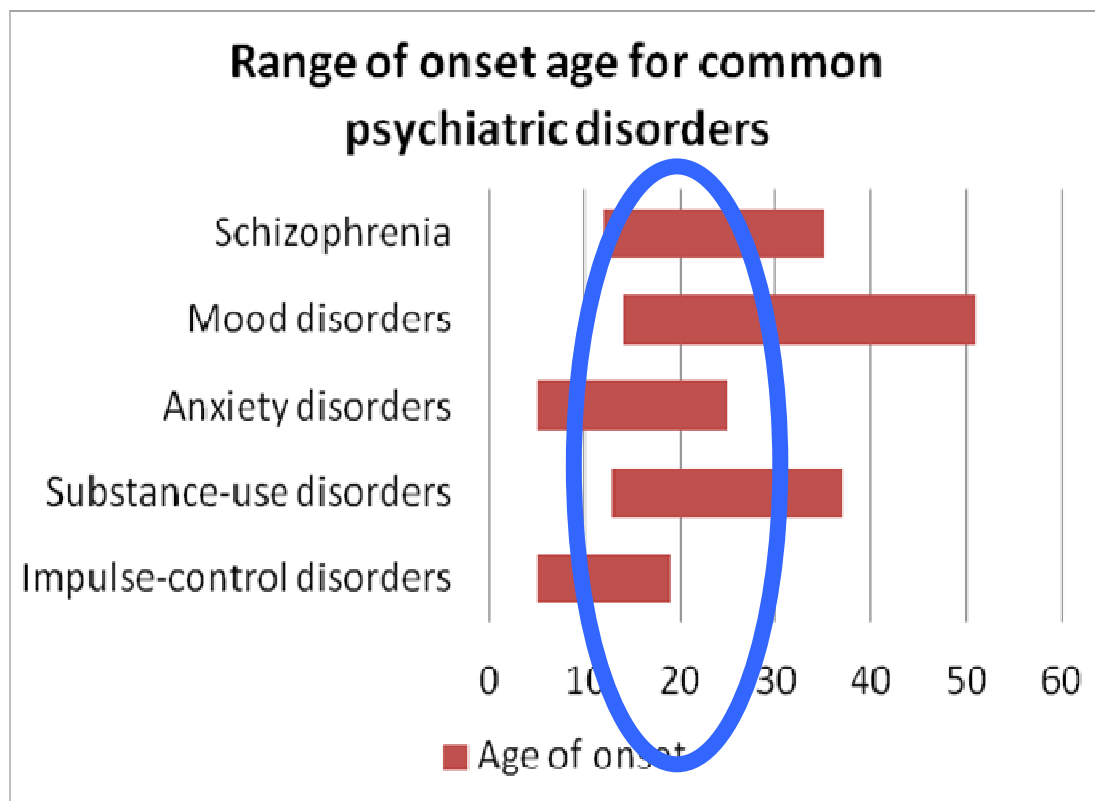
■ Clinical (knowledge)

■ Scientific

## **Scientific gap around 18**

- pharmacology – clinical trials
- MR imaging - mechanistic
- PET/SPECT – mechanistic /drugs
- epidemiology – cohorts e.g. NEMESIS

# Age of Onset (AOO)



75% emerge before age 24

Kessler et al, 2005

# Gap around age 18 - science

## Need for continuity

High prevalence  
Psychiatric problems



Lack of knowledge

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OPINION

# Why do many psychiatric disorders emerge during adolescence?

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*Tomáš Paus, Matcheri Keshavan and Jay N. Giedd*

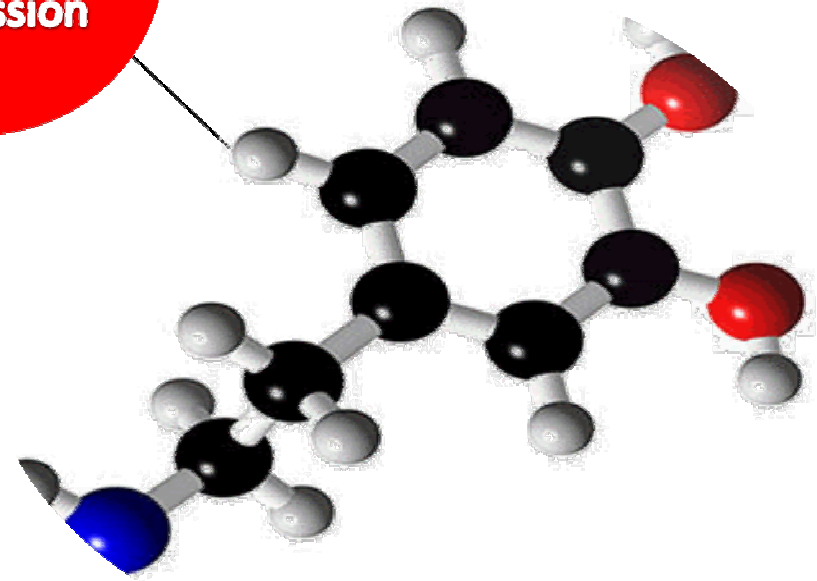
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## Brain



# Neurotransmitters



**Psychosis**  
**Anxiety**  
**Depression**

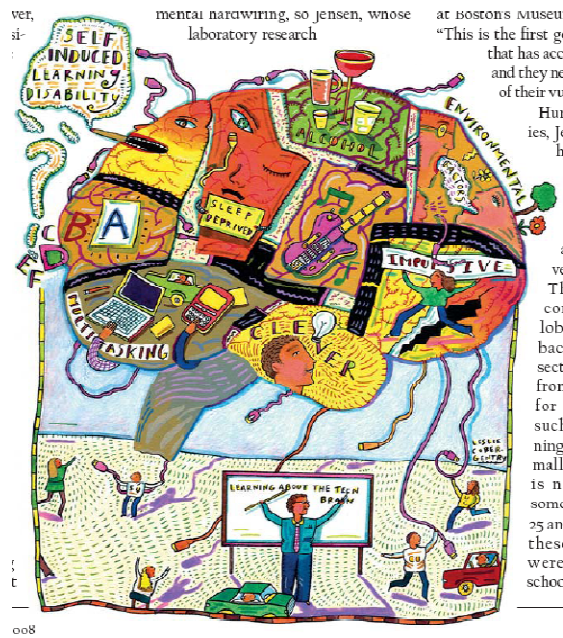
# Risky period



# Adolescence

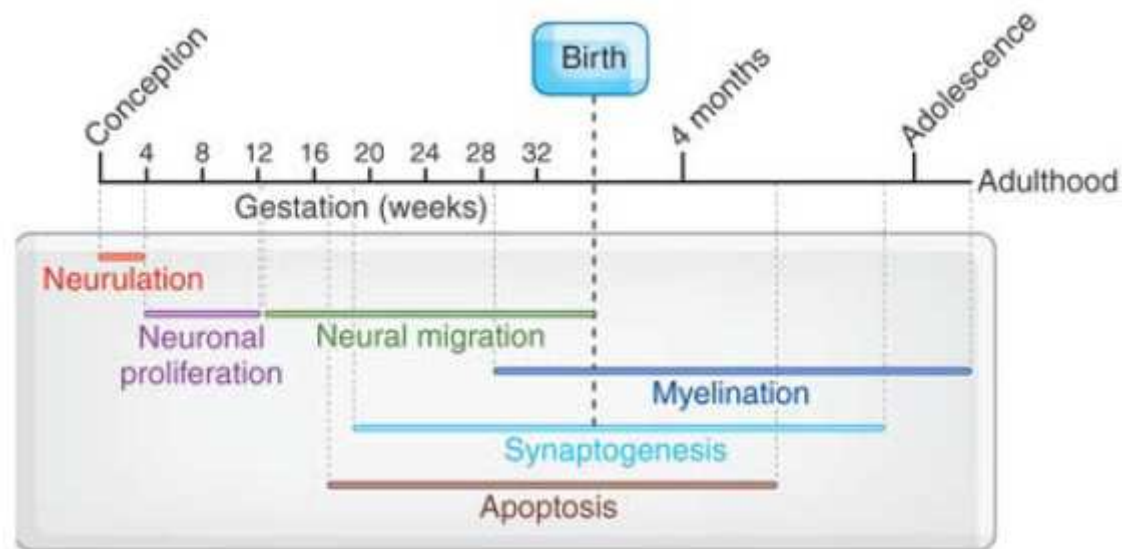
- Peak of physical robustness
- Elevated risk of death & injury
- Alcohol/drugs/suicide major cause of death youth

- Relation brain development and behavioral change
- Unknown by most people (Dutch survey amongst parents)
- More awareness necessary, education



## = Brain in transition:

- structural:
  - grey matter pruning
  - white matter myelination
- functional:
  - connectivity
  - neurotransmitters



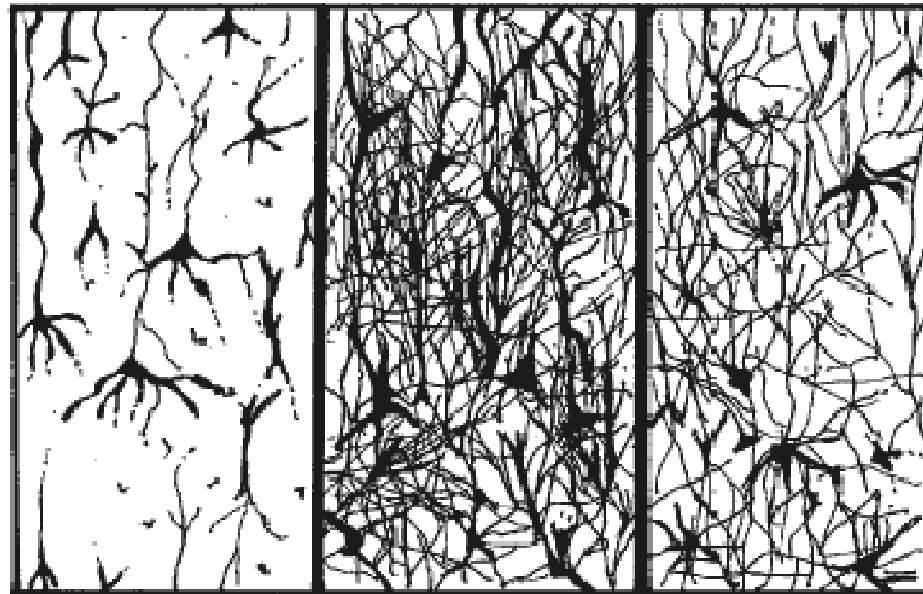
Migration – preprogrammed, until birth

Synaptogenesis – peak 1.8 million synapses/sec

50% reduction age 16 years

adolescence - loss 20 billion synapses/day

# Grey matter pruning



at a child's birth

at 7 years of age

at 15 years of age

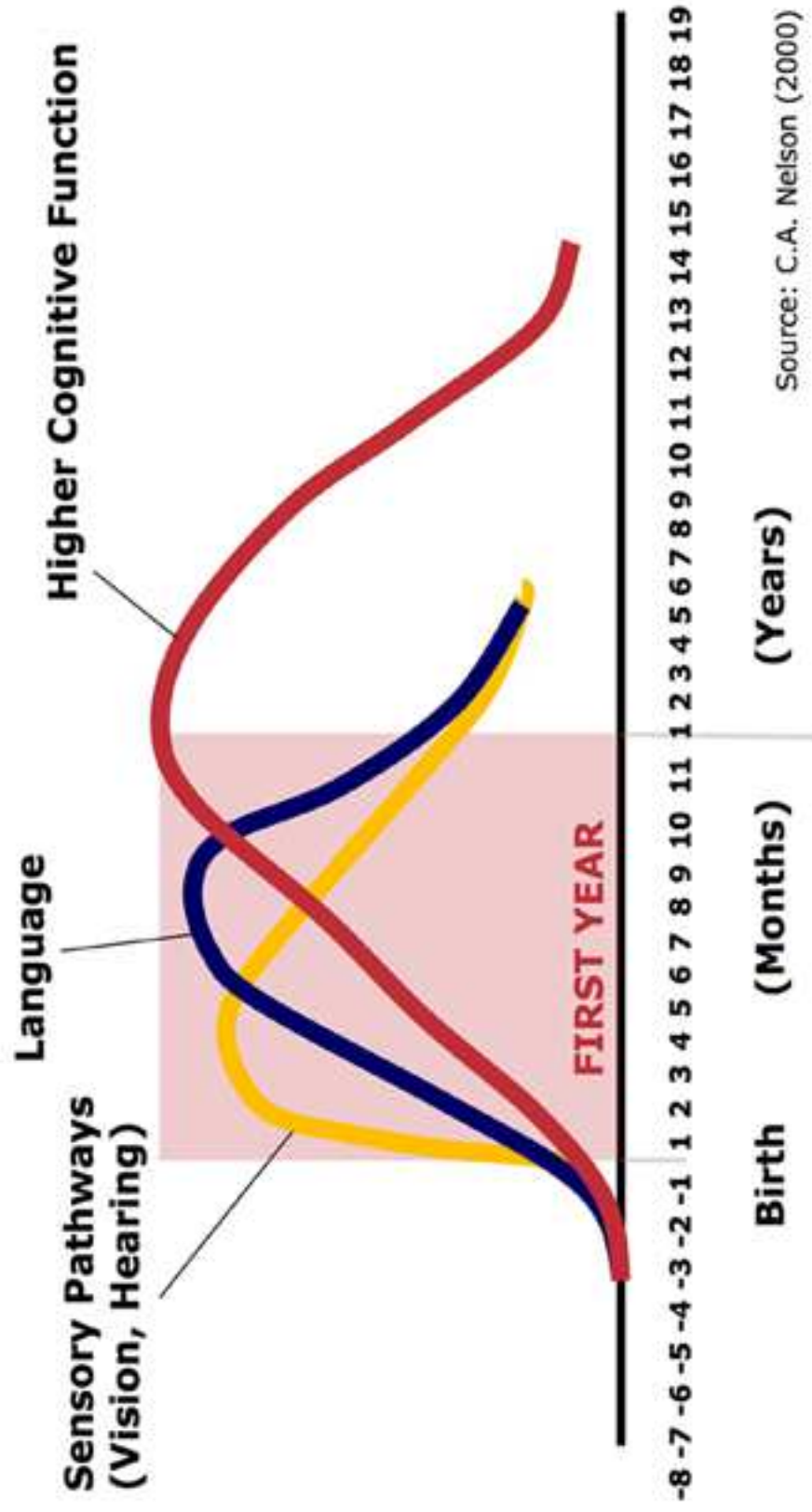




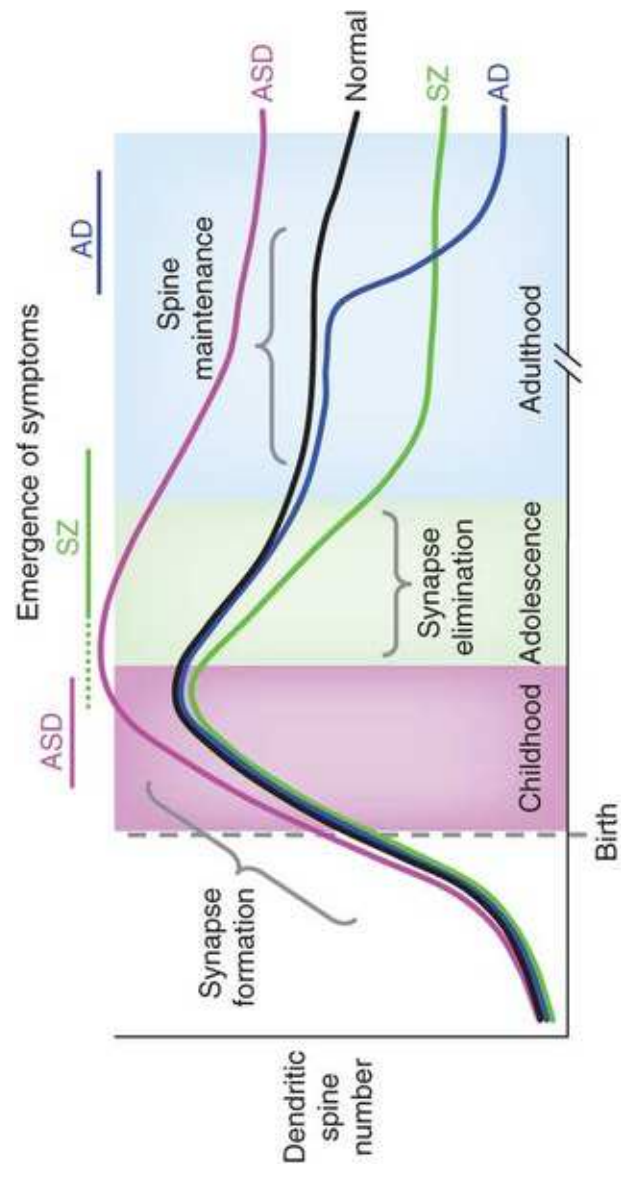
Center on the Developing Child  
HARVARD UNIVERSITY

## Human Brain Development

### Neural Connections for Different Functions Develop Sequentially







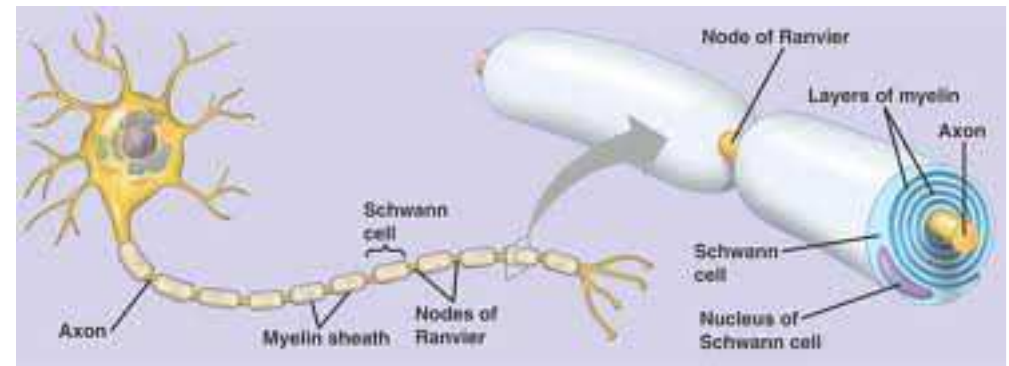
## Transition in brain



- ~15% grey matter volume

pruning

Use it or lose it!



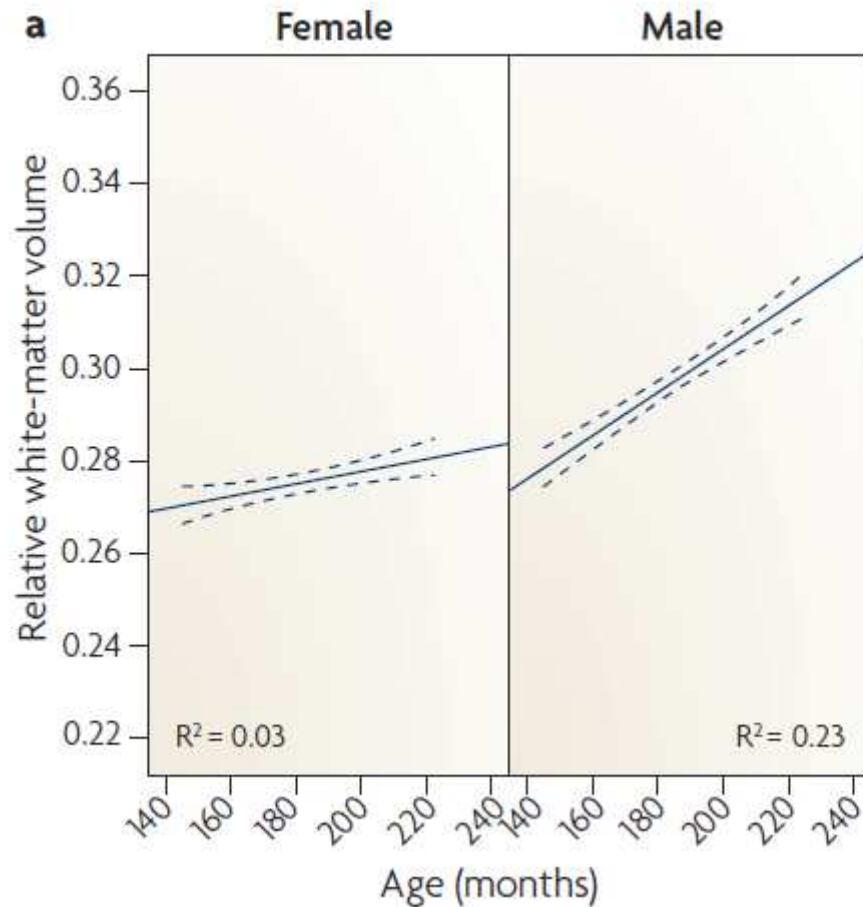
+ ~15% white matter volume

white matter, myelination

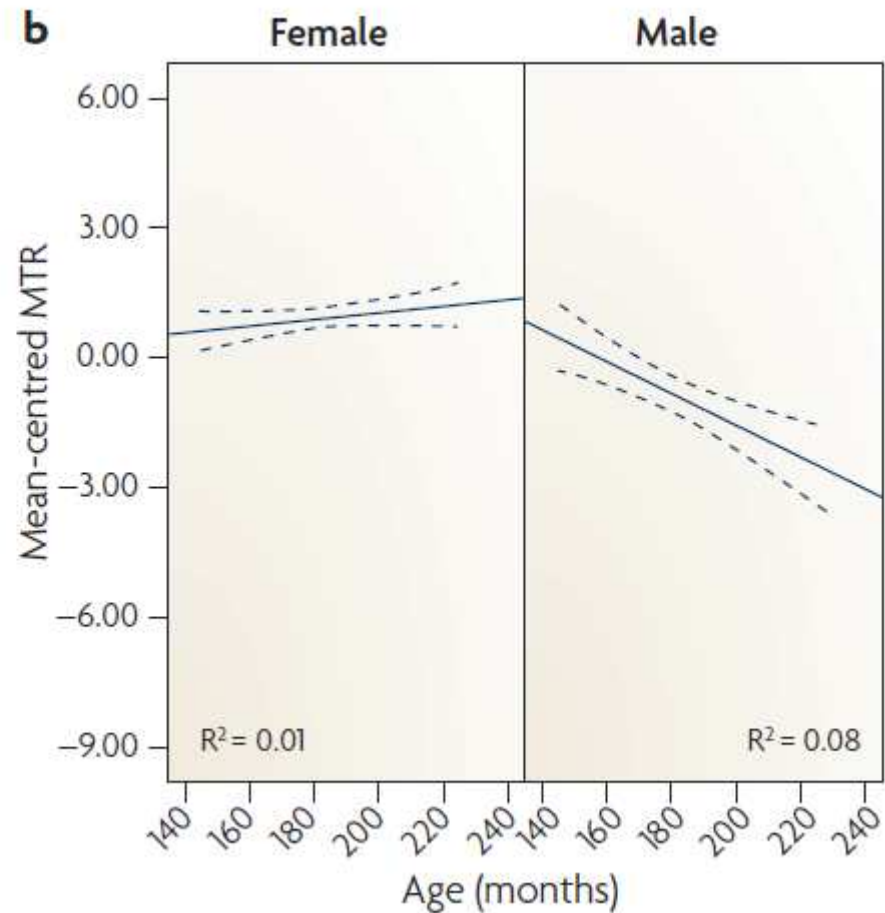
Increasing efficiency

# Gender differences!

## White matter volume



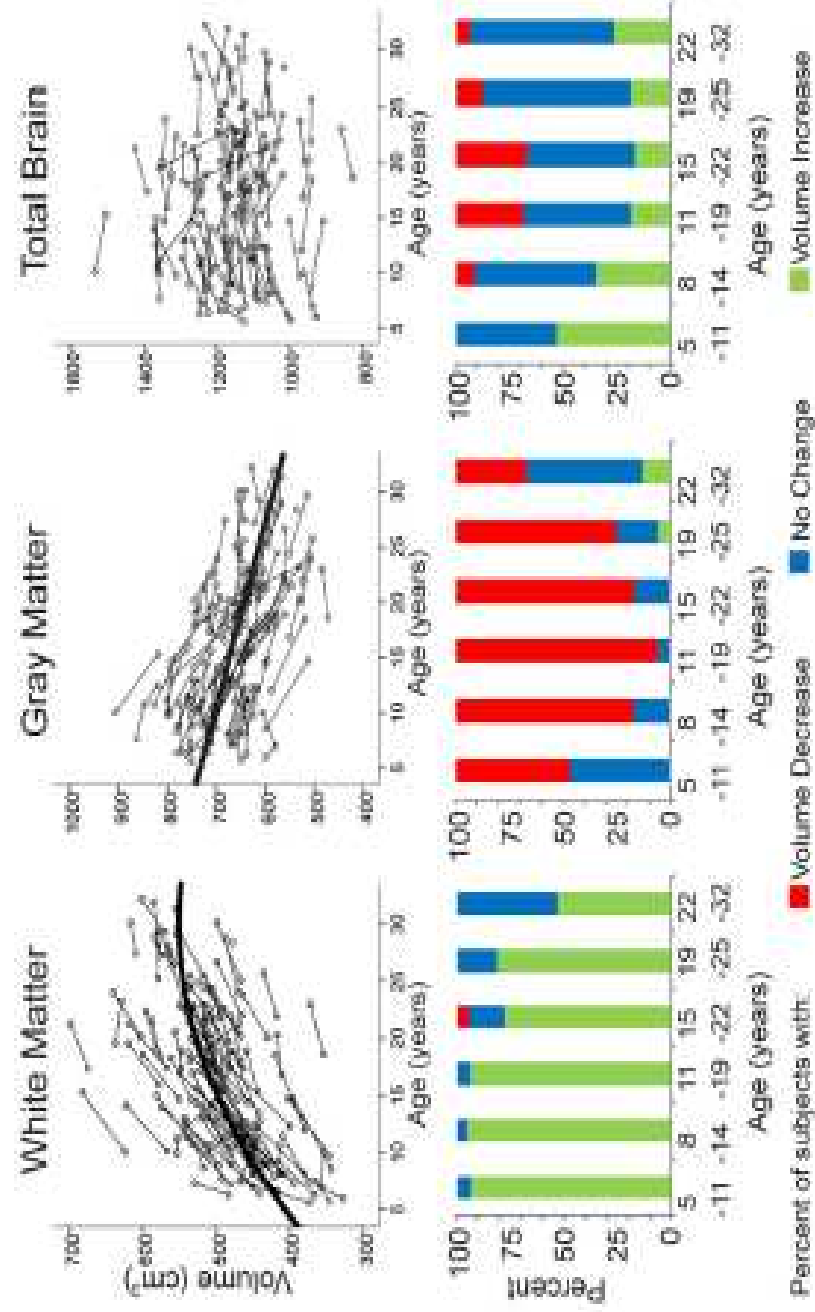
## Myelin fraction



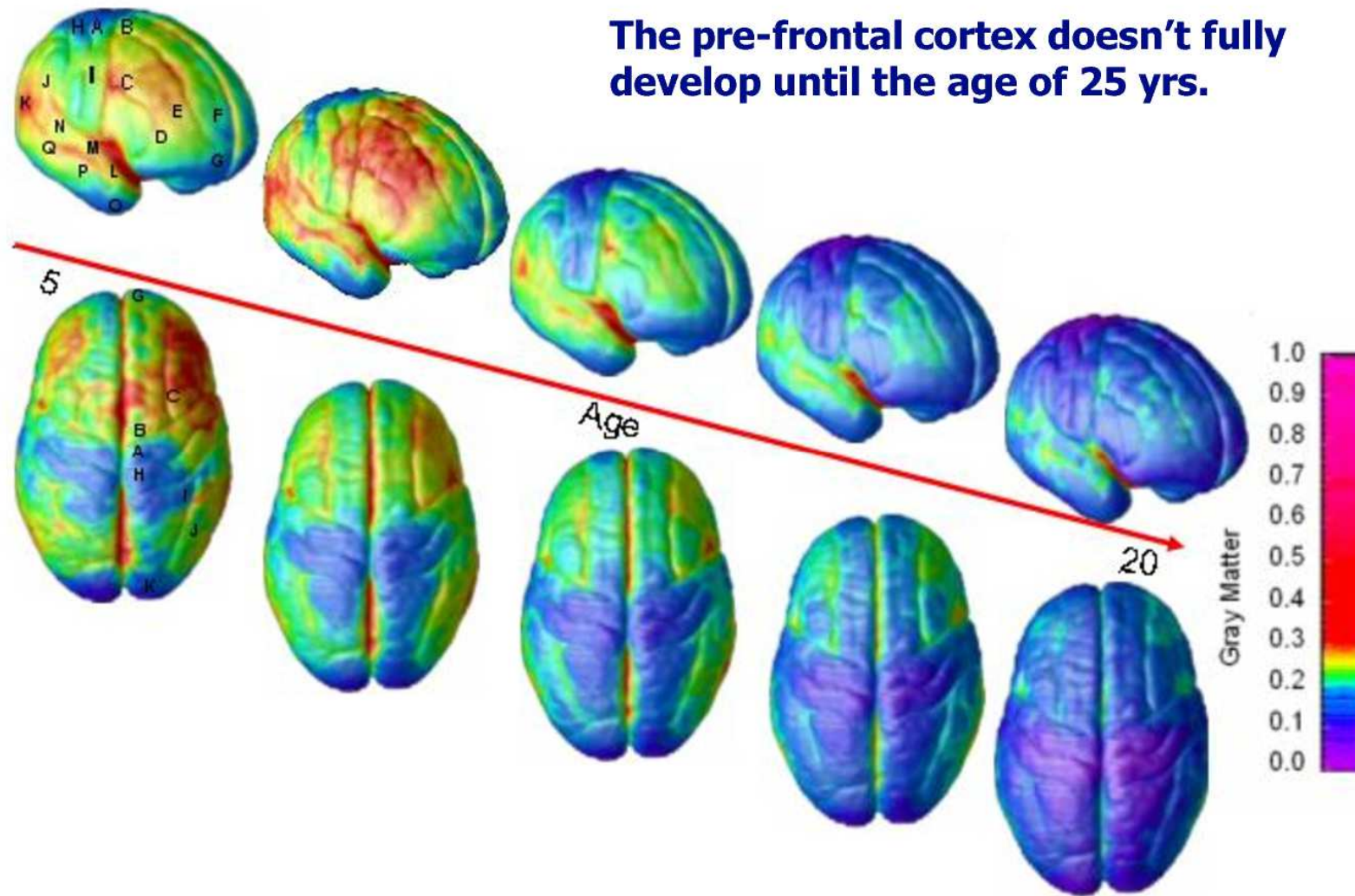
# Longitudinal Development of Human Brain Wiring Continues from Childhood into Adulthood

Catherine Lebel and Christian Beaulieu

Department of Biomedical Engineering, University of Alberta, Edmonton, Alberta T6G 2V2, Canada



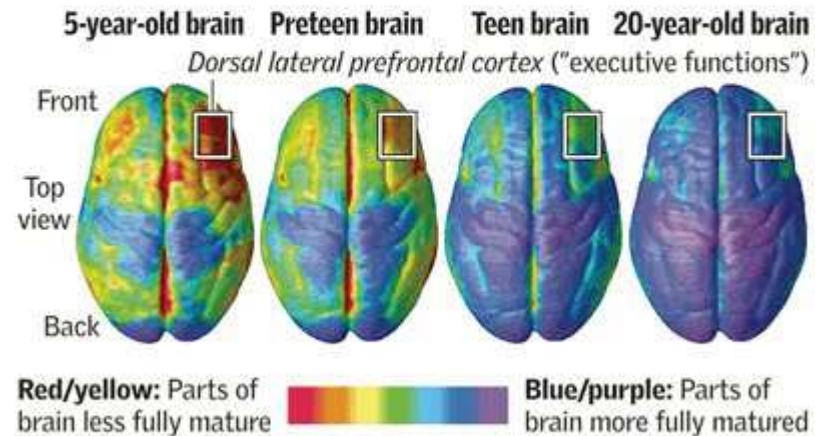
**The pre-frontal cortex doesn't fully develop until the age of 25 yrs.**



# Frontal lobe = CEO

## Judgment last to develop

The area of the brain that controls "executive functions" — including weighing long-term consequences and controlling impulses — is among the last to fully mature. Brain development from childhood to adulthood:

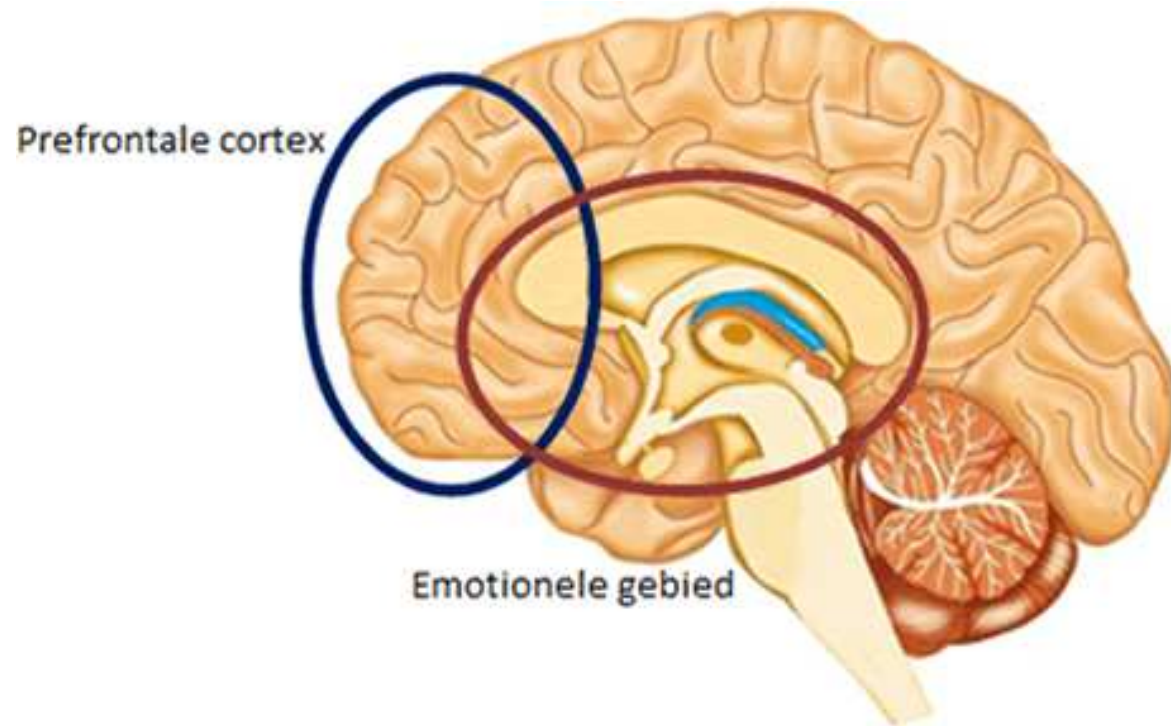
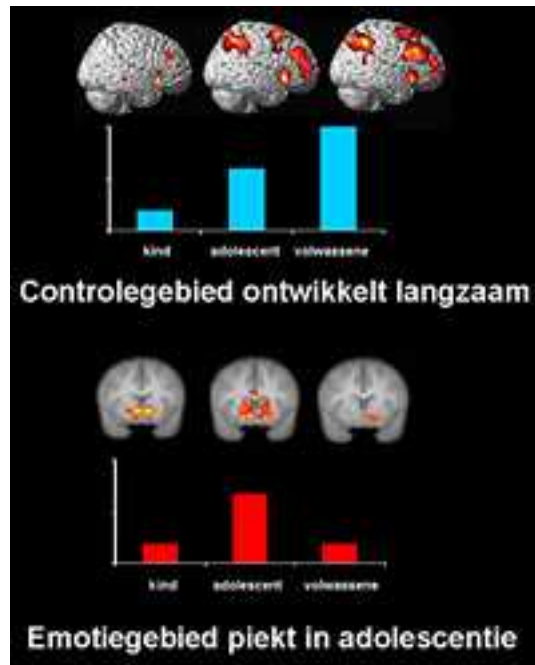


Sources: National Institute of Mental Health;  
Paul Thompson, Ph.D., UCLA Laboratory of  
Neuro Imaging

Thomas McKay | The Denver Post

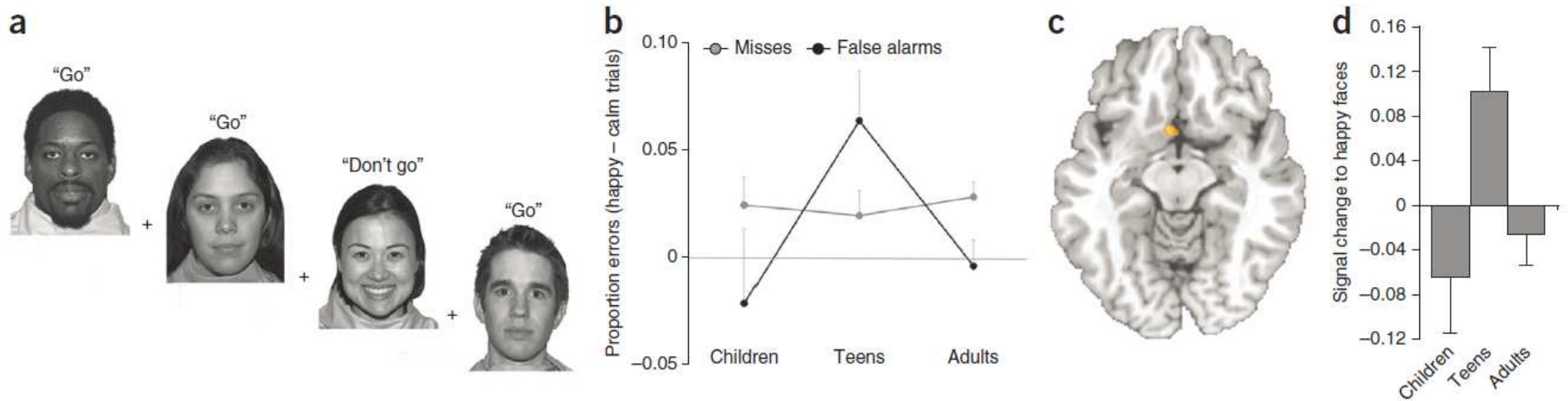


# Insufficient impulse control



**Sensitivity for immediate reward, emotional stimuli**

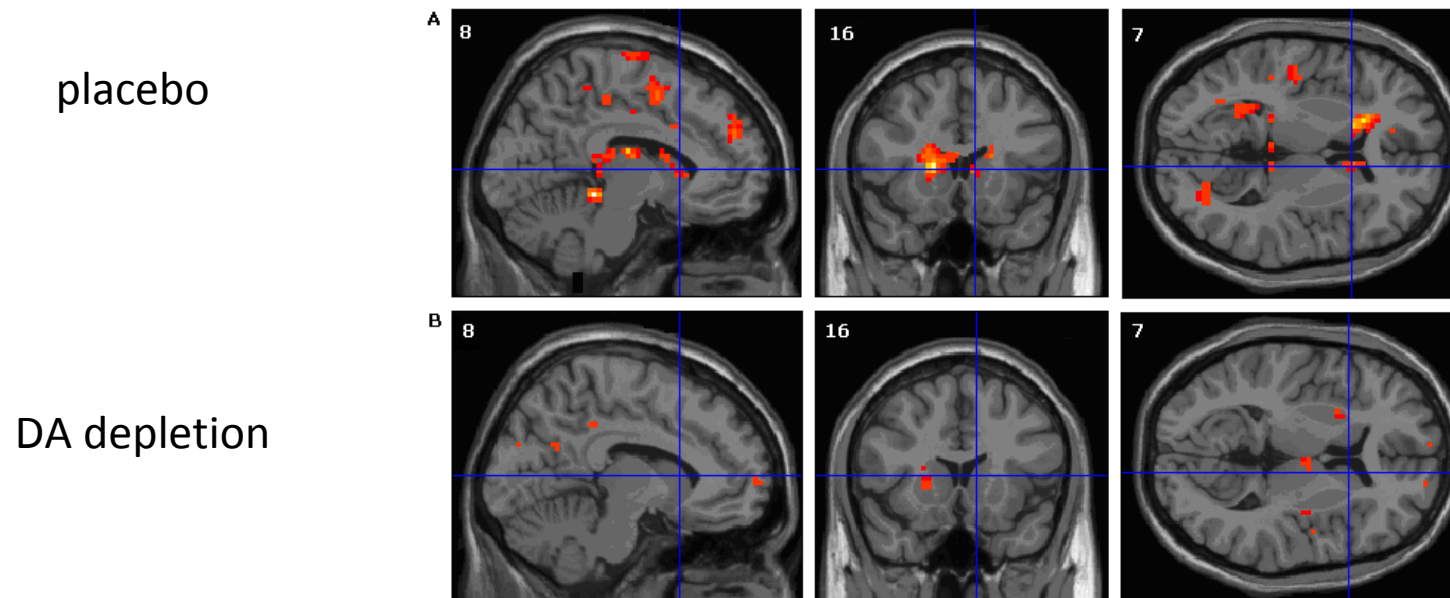
# Inability to resist emotional stimuli



Blakemore & Robbins, 2012



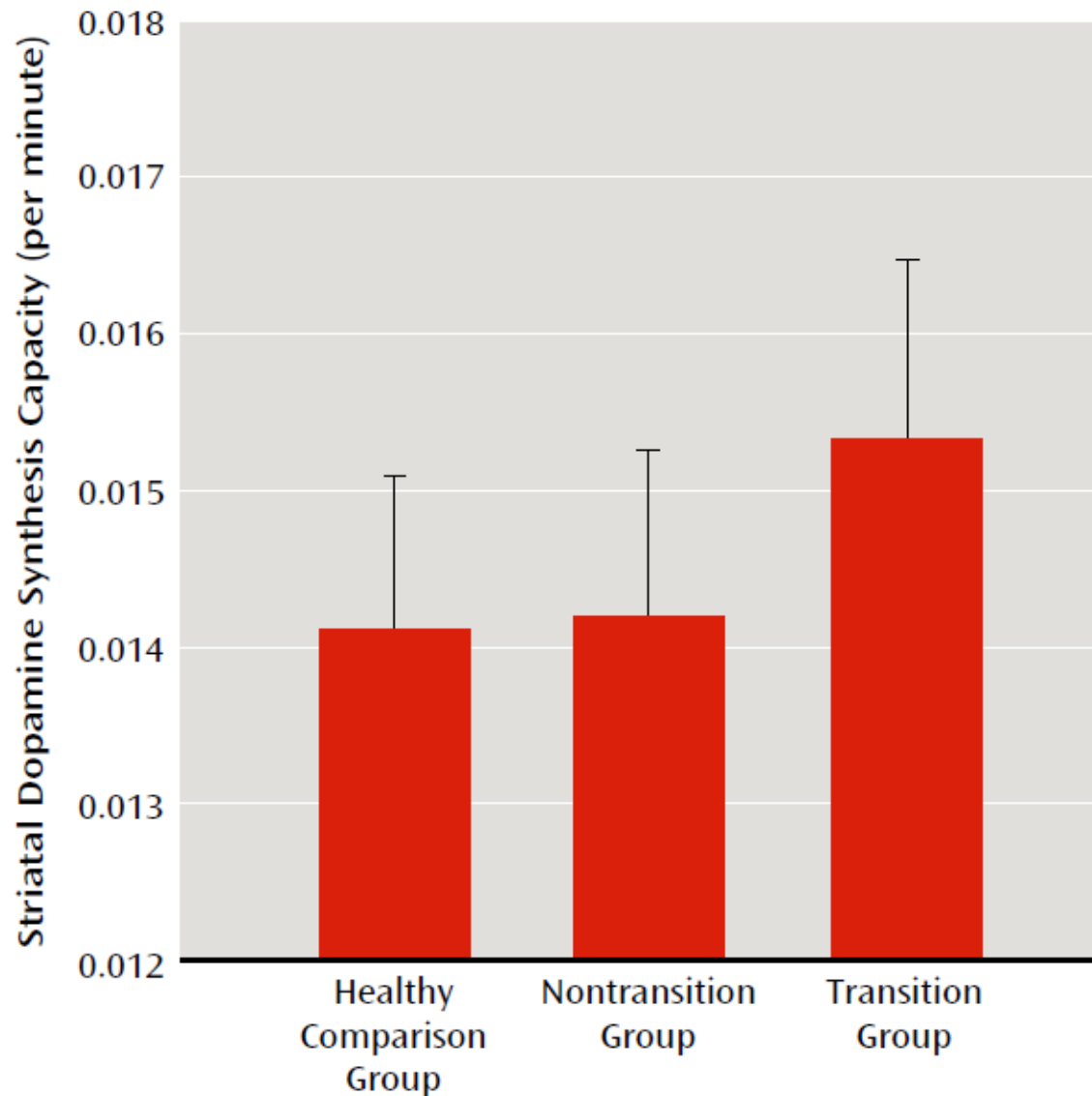
# Reward processing modulated by dopamine



(A) PLA condition significant BOLD activation of the caudate body

(B) reduced BOLD activation during AMPT condition.

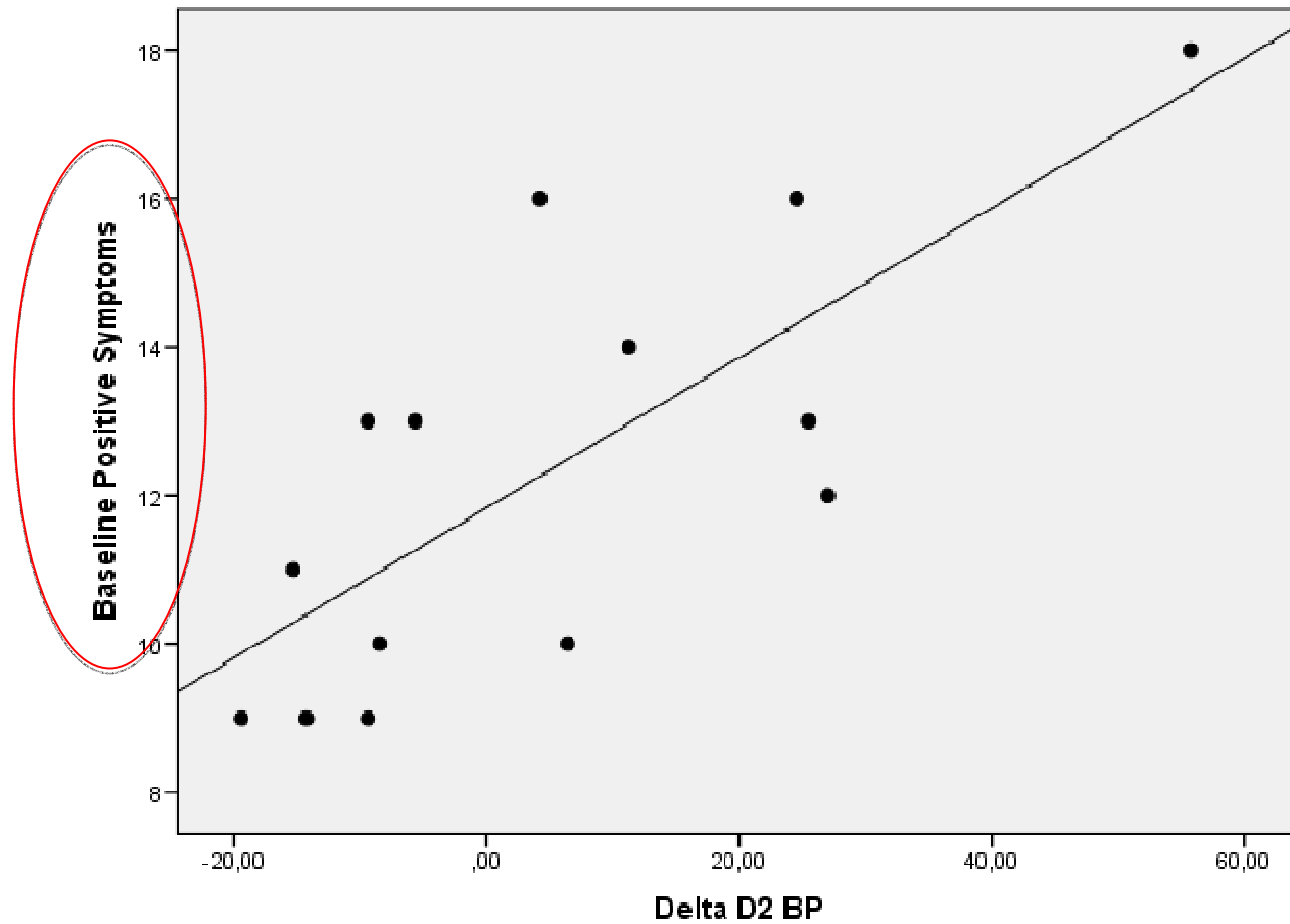
# striatal DA in ARMS youth



High risk patients

Howes et al 2011

# Striatal DA in ARMS youth



# Worth the wait: effects of age of onset of marijuana use on white matter and impulsivity



Staci A. Gruber • Mary Kathryn Dahlgren •  
Kelly A. Sagar • Atilla Gönenç • Scott E. Lukas

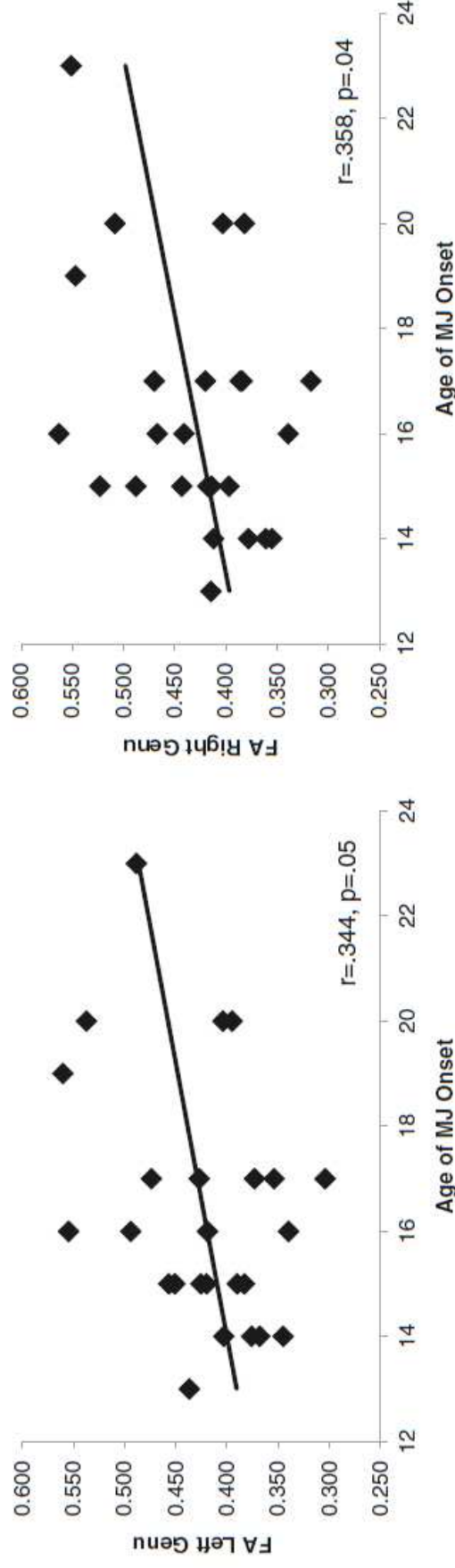
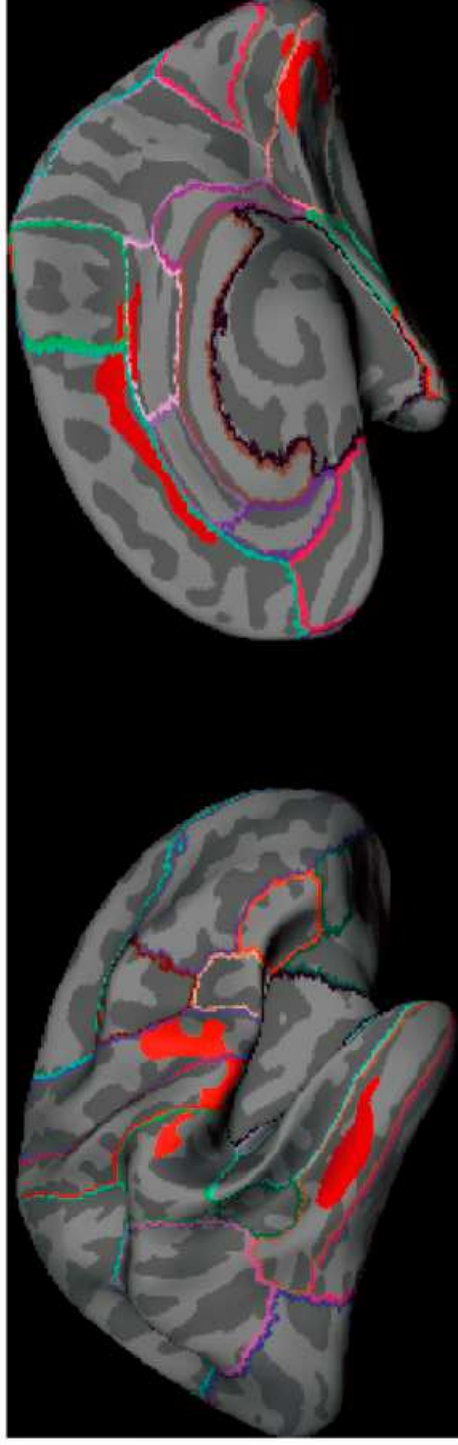


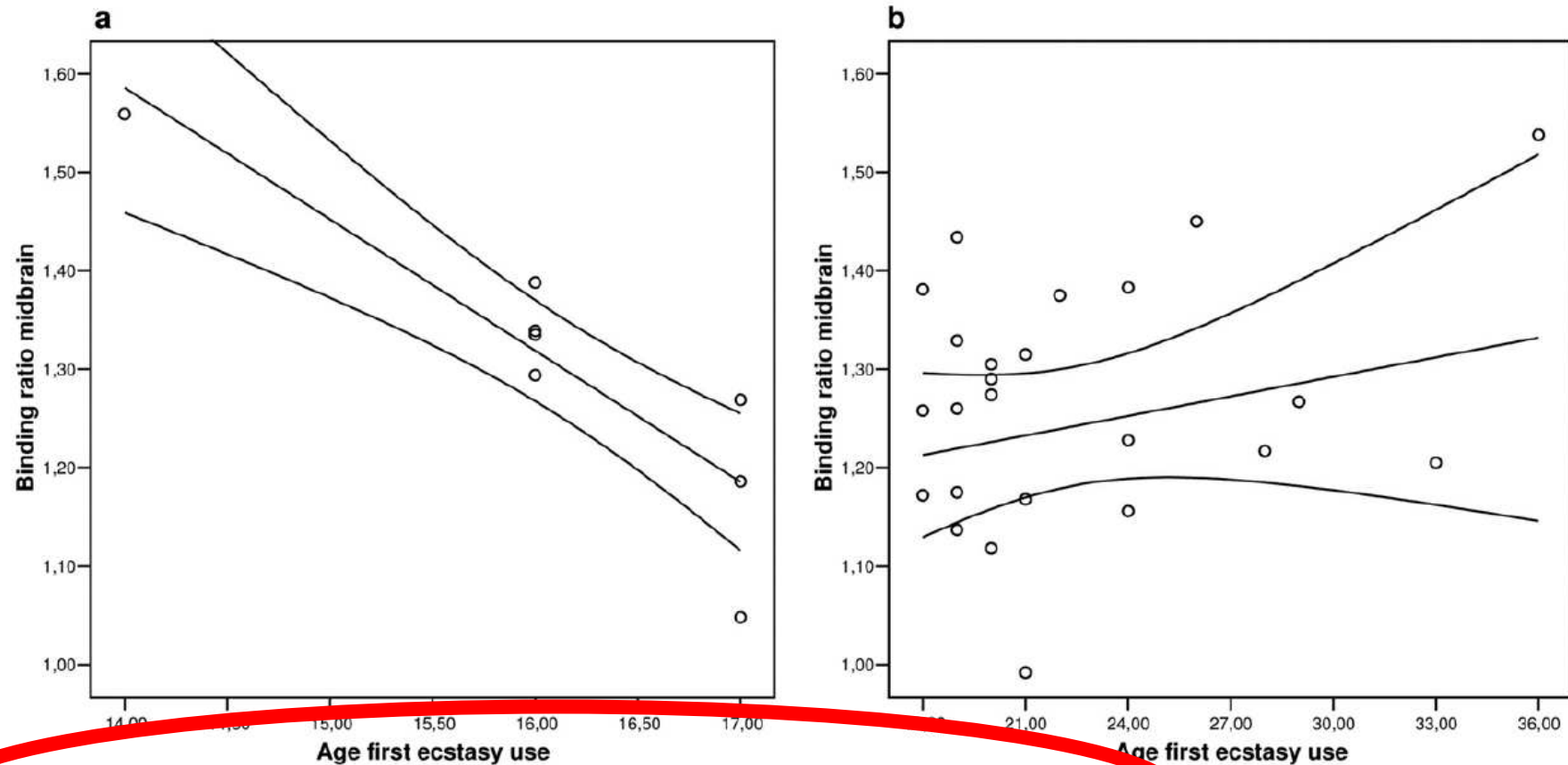
Fig. 1 Correlational analyses of age of onset of MJ use and left and right genu FA

# Effects of alcohol use initiation on brain structure in typically developing adolescents

Monica Luciana, PhD<sup>1</sup>, Paul F. Collins, PhD<sup>1</sup>, Ryan L. Muetzel, BA<sup>2</sup>, and Kelvin O. Lim, MD<sup>3</sup>

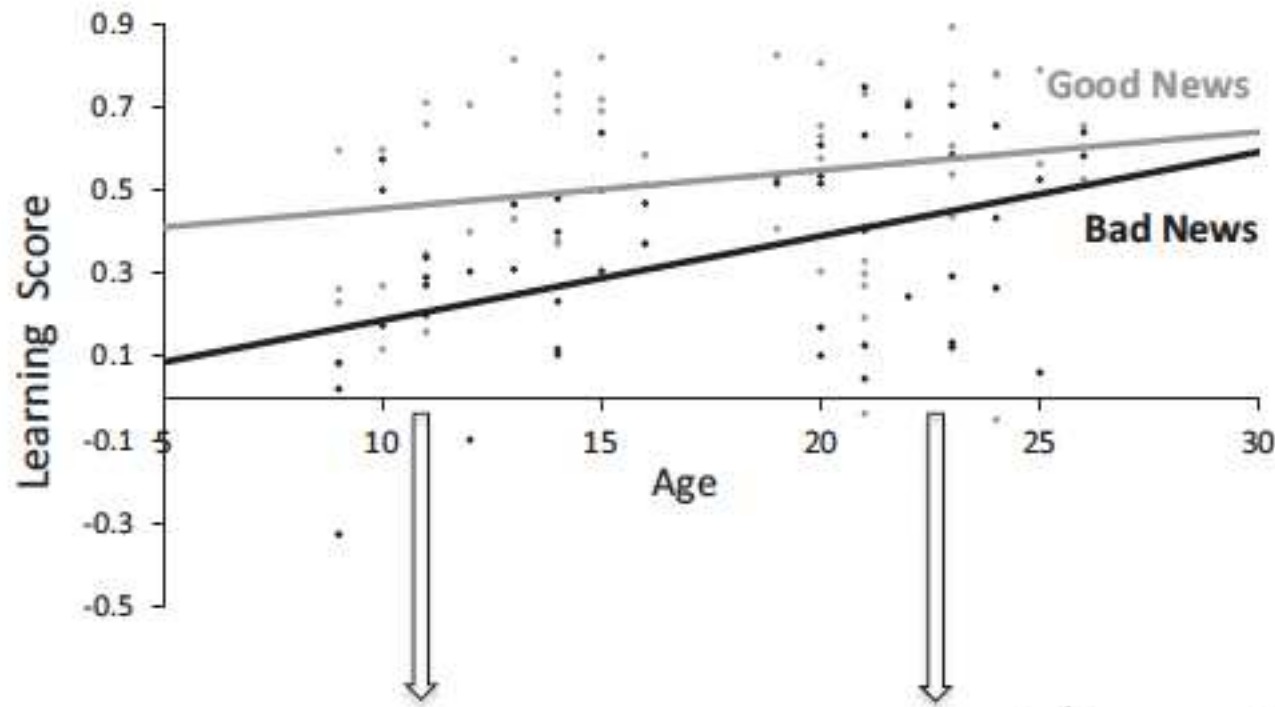


# Effects of XTC on 5-HT in brain depends on age of first exposure



**Figure 1. Early age of ecstasy use predicts higher SERT density in the developing brain.** Midbrain SERT binding ratio plotted against age-at-first-ecstasy exposure during a) brain development (first ecstasy use before 18 years;  $r^2 = 0.789$ ,  $r = -0.888$ ,  $p = 0.003$ ) and in b) in the mature brain (first ecstasy use 18 years or older;  $r^2 = 0.032$ ,  $r = 0.179$ ,  $p = 0.393$ ). 95% confidence limits are included with the regression line.  
doi:10.1371/journal.pone.0047524.g001

# Adolescents don't learn from bad news



Explains why campaigns against drugs, alcohol etc have limited impact?

Should we change strategy: emphasize benefits from stopping smoking instead of Emphasizing harmful effects of smoking?



# Conclusion

- brain development dynamic process
- maturation continues until at least 25 years
- gender differences
- adolescent brain vulnerable for external influences

## Mental illness or adolescent turmoil?



More research of adolescent (brain) needed!

