Genetic modelling of cognitive brain maturation in pre-adolescence: a longitudinal study in healthy twins.

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Background

Puberty is a critical period in human development. Physical growth takes place, large amounts of gonadal hormones are secreted and in the brain, gray matter volume starts to decrease, whereas white matter continues to increase into adulthood (figure 2)[1].These changes may be essential for optimal adult functioning. It is unknown what factor(s) mediate(s) the change in gray matter growth or to what extent they are influenced by the same or different genetic and environmental factors. In this multicenter study we aim to elucidate the mechanisms of the developmental changes in early adolescence.

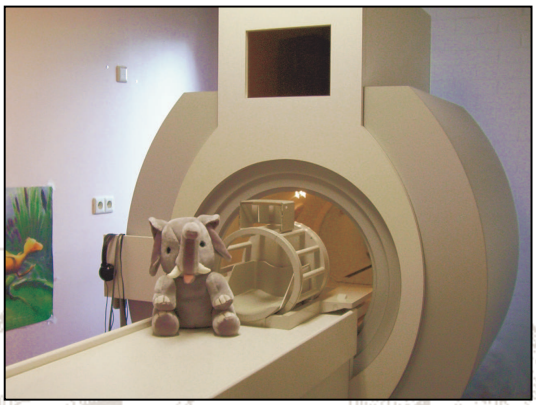

Fig 1: Dummy scanner in the UMC

Data acquisition UMCU

- All subjects practice in a dummy scanner, to get used to the equipment and sounds (fig 1).
- **Scanning:**
  - volumetric MRI: to measure brain volumes and density.
  - Diffusion Tensor Imaging (DTI): to visualize white matter tracts (see figure 3).
  - Magnetization Transfer Ratio (MTR): to quantify myelinization.
- **Other**: a Tanner-stage questionnaire is administered to assess body development.
- Data on **cognition and gonadal hormones** will be collected at the VU Amsterdam.

Objectives

- What focal areas in the brain are associated with cognitive functioning and what is the influence of genes in this relation?
- To what extent is connectivity between frontal and occipital areas influenced by genes?
- What is the influence of endogenous sex steroids on brain morphology at the start of puberty?

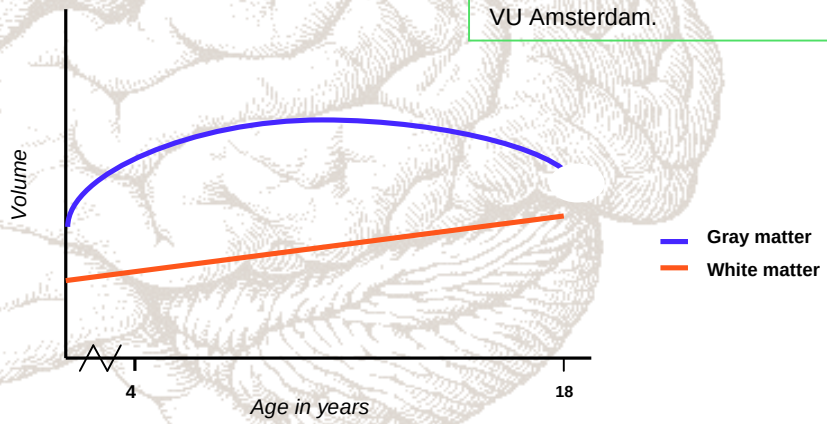

Figure 2: Gray and white matter development (based on Giedd et al (1999)[1].

Subjects

- N=300 subjects coming from 100 families (power analysis). Composed of:
- Healthy DZ and MZ twin pairs (all 9 y) and full siblings (9-14 y). Recruited from:
- Netherlands Twin Registry
- Follow-up: two years later (i.e. when the twins are 11 years old) to investigate developmental changes in this period.
- Subjects with neurological or psychiatric disorders are excluded.

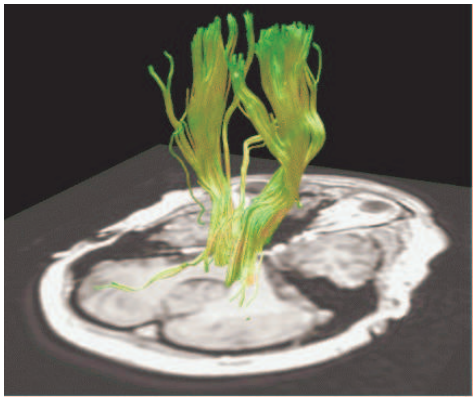

Figure 3: Fiber tracking with DTI

UMCU update & Planning

- Until now 46 children are scanned, coming from 17 families. Furthermore, 50 families have agreed to participate in the study.
- Planning of the measurements:
  - Now-09/2005: finishing of T1
  - 09/2005-09-2006: Data processing and analysis T1
  - 09-2006-09-2007: Follow-up (T2) and data analysis T2

1. Giedd, J.N. et al. (1999). Brain development during childhood and adolescence: a longitudinal MRI study. *Nat. Neurosci* 2 (10): 861-2.