Heritability of pre-adolescent brain development

a longitudinal structural MRI twin study on brain changes in volumetric measures and cortical thickness

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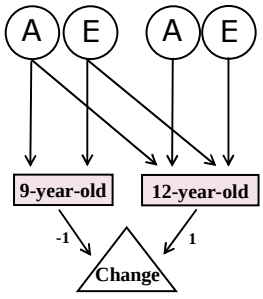
Background and Aim

Understanding the influences on the dynamic process of healthy brain development is of great importance. Several studies have illustrated that psychopathologies show a deviation from normal developmental trajectories. In the present longitudinal study, twins were scanned with a narrow age range at 9 and at 12 years old. Using this longitudinal genetic informative sample, we were able to disentangle different genetic mechanisms that underlie individual differences in developmental brain changes over time.; Are there age-specific genetic factors, or do the same genetic factors act at both ages?

Methods

At baseline 190 monozygotic and dizygotic twins were included with mean age of 9.2 (0.1) years old, and at follow-up 125 twins with mean age of 12.1 (0.3) years old. Mean interval was 2.9 (0.2) years. The scan protocol included a T1-weighted structural MRI scan on a 1.5T scanner. Volumes were assessed of total brain, cerebellar, total cerebral and cerebral gray and white matter[1]. Cortical thickness was calculated for 81.924 points on the cortex[2].



Genetic structural equation modeling was used to decompose the variance in brain volumes and local cortical thickness into genetic (A) and environmental components (E), and the genetic and environmental covariance between baseline and follow-up measures. All analyses were corrected for age at moment of scan, sex and handedness. Through the longitudinal sample, it was possible to calculate the heritability (i.e. proportion of total variance that is attributed to genetic variance) of developmental changes between 9 and 12 years old (fig.1).

Figure 1. *Longitudinal genetic model*

Results

Total brain, cerebellar, cerebral, and cerebral white matter volumes increased ($p<.01$). Cerebral gray matter showed a decrease in volume ($p<.01$), in combination with local cortical thinning, most profound in areas of occipital, frontal and parietal regions (fig. 2; max. 0.08 mm/y). Heritability of volumetric measures was high at age 9 (88%-94%) and at age 12 (88%-96%). Significant heritability of volumetric change was found for total brain (19%), cerebral (20%), and cerebellar volume (54%) and was completely driven by amplification of the genetic factor already present at age 9.

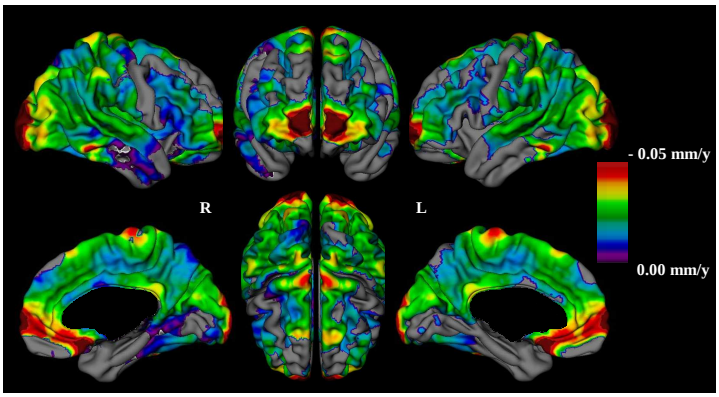


Figure 2. *Significant cortical thinning of between 9 and 12 years old (FDR corrected; $\alpha = 0.05$).*

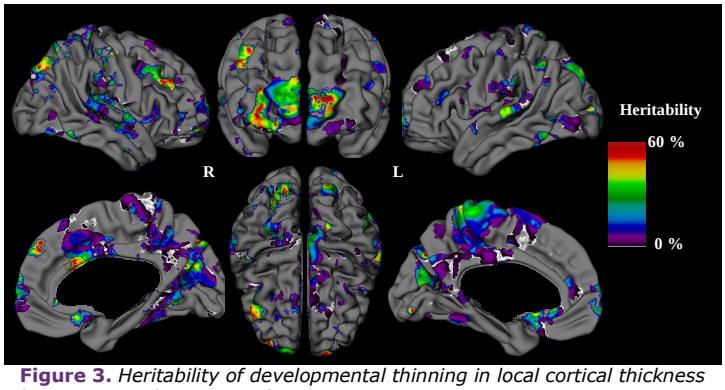


Figure 3. *Heritability of developmental thinning in local cortical thickness between 9 and 12 years of age.*

Significant heritability for local thickness at age 9 reached up to 78%, and at age 12 up to 91%. Heritability of the extend of cortical thinning was observed in several regions (max. 79%, fig. 3). This was partly driven by gradual changes of the same genetic factor (i.e. (de-)amplification), as well as age-specific genetic factors between 9 and 12 (fig. 4).

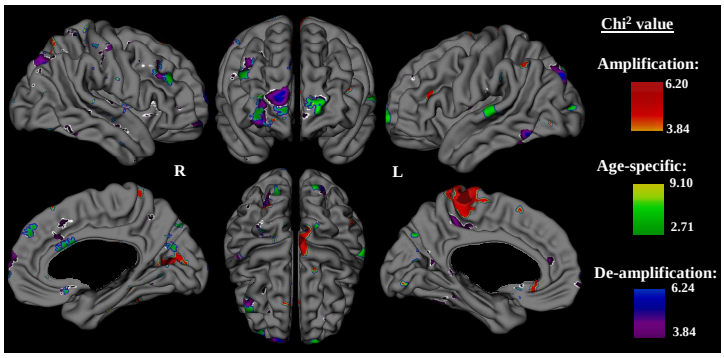


Figure 4. *Areas where significant age-specific genetic factors (green), and significant amplification (red) or de-amplification (blue) were found.*

Conclusions

We now show for the first time how genetic mechanisms influence brain changes during pre-adolescence. We found that common stable genetic factors increase their influence on individual differences in volumetric measures with increasing age. More importantly, besides gradual differences in contribution, we find a shift to other gene pools influencing maturation process of cortical thinning, at the brink of puberty.

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[1]Brouwer, et al., 2010; [2] Kim et al., 2005