

Background

Previous studies showed cortical thickness to be negatively correlated with age (figure 1). In addition, regionally specific cortical thinning was found to be associated with Alzheimer's disease (AD) (figure 2). Studying cortical thickness in cognitively healthy, identical twins can be a useful approach to understand how genetic and environmental risks contribute to this trait. Previous twin studies (age range 5-59 years) showed that heritability for cortical thickness varies greatly across the cortex with the highest value (.76) for frontal regions (Blokland 2012). Further, a family-based study, showed heritability estimates to be stable between 18-70 years, but suggested that these estimates might change after 70 years of age (Chouinard-Decorte 2014). This is the first study assessing correlations for cortical thickness in a sample of 60-90 year old cognitively healthy twins.

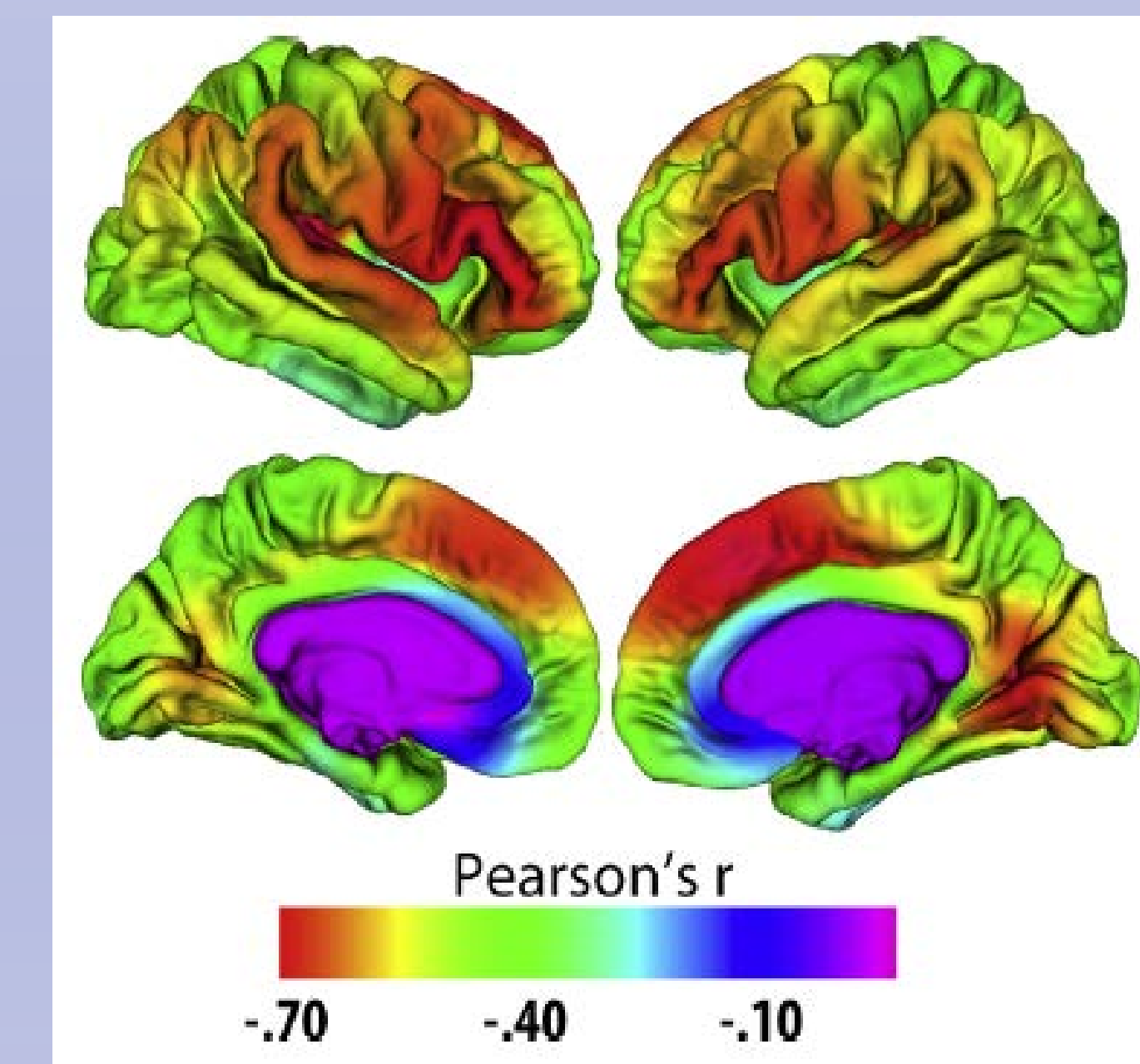


Figure 1. Age-thickness correlations (Fjell 2014)

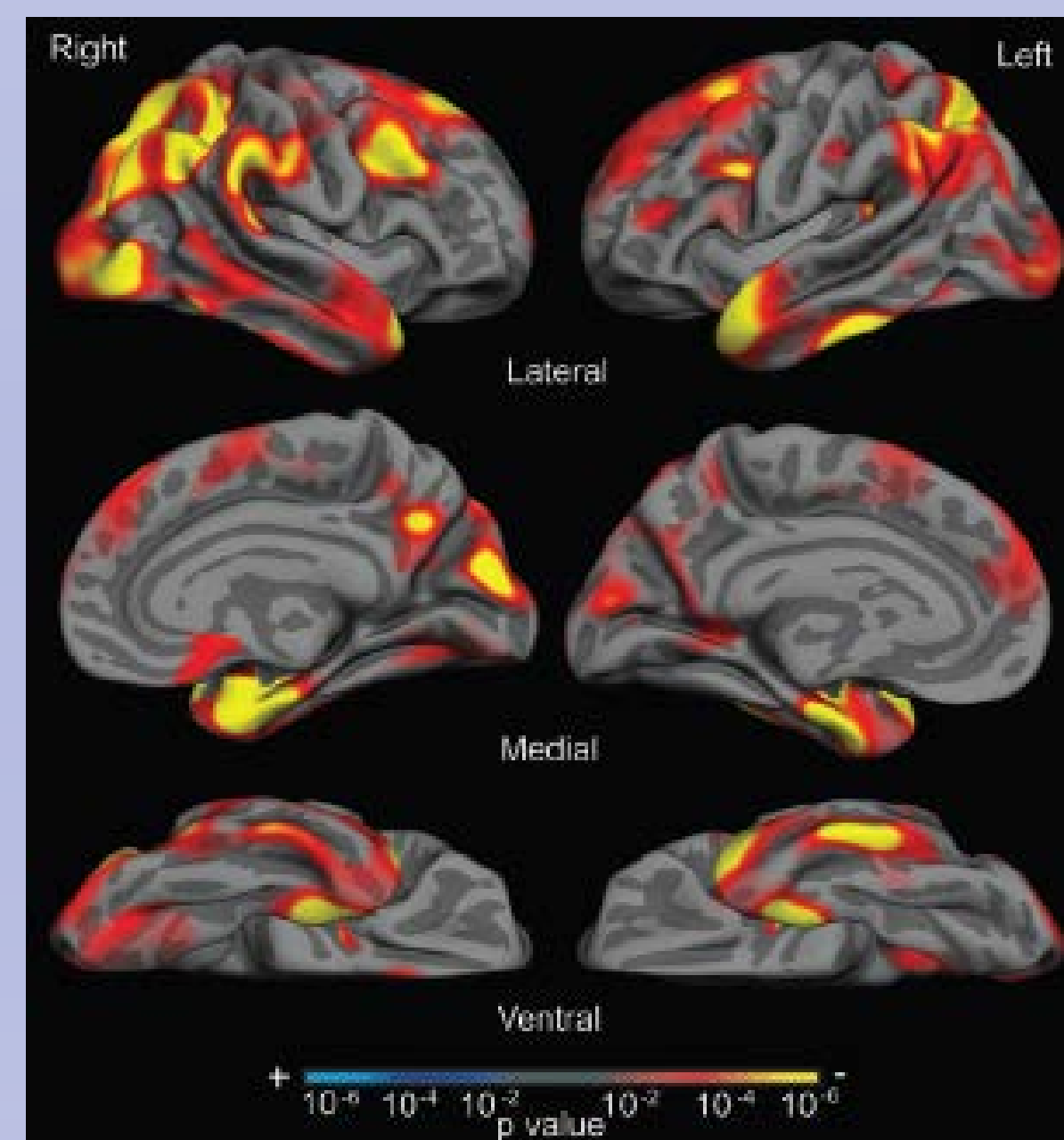


Figure 2. Regions showing significant cortical thinning in AD patient compared to older controls (Dickerson 2009)

Aim

1. Determine the contribution of genetic and environmental influences on cortical thickness.
2. Investigate whether the contribution of genes and environment changes after the age of 70.

Subject characteristics	
N (pairs)	144 (72)
Female (n,%)	82 (56.9%)
Age, years, mean (SD)	69.2 (7.4)
Education, years, mean (SD)	15.3 (4)
MMSE, median (IQR)	29 (28-30)



Methods

Monozygotic twins were selected from the Netherlands Twin Register

Inclusion criteria:

- Age ≥ 60 years
- CERAD 10 word list > -1.5 SD; TICS-m ≥ 23; GDS < 10; CDR 0

MRI:

- 3D T1-weighted structural MRI scans (3.0T Philips Achieva)
- Cortical thickness estimated automatically using Freesurfer (figure 3)

Statistical analysis:

- Monozygotic (MZ) twin correlations calculated in SPSS

Results

- MZ twin correlation for cortical thickness ranged from .47 (bankssts) to .83 (rostral middle frontal), with an average correlation of .67

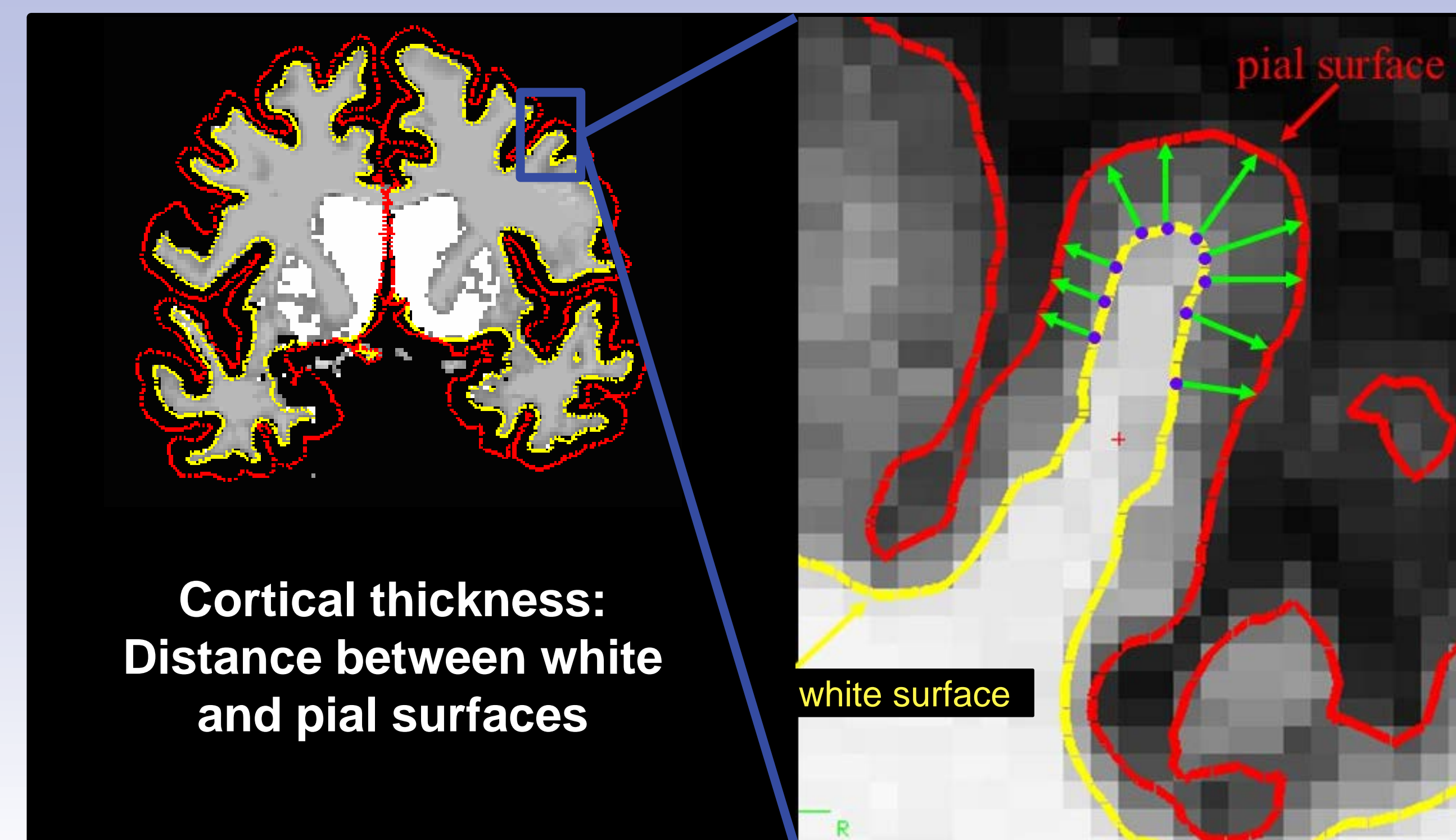


Figure 3. Cortical thickness as estimated using Freesurfer software

- Correlations did not significantly differ between left and right hemispheres, MZ twins <70 and ≥70 years (average correlation .66 and .65, respectively), and AD versus non-AD associated brain regions (average correlation .67 for both) (figure 4)
- Correlations assessed in randomly paired subjects were lower (<.2) and not significant

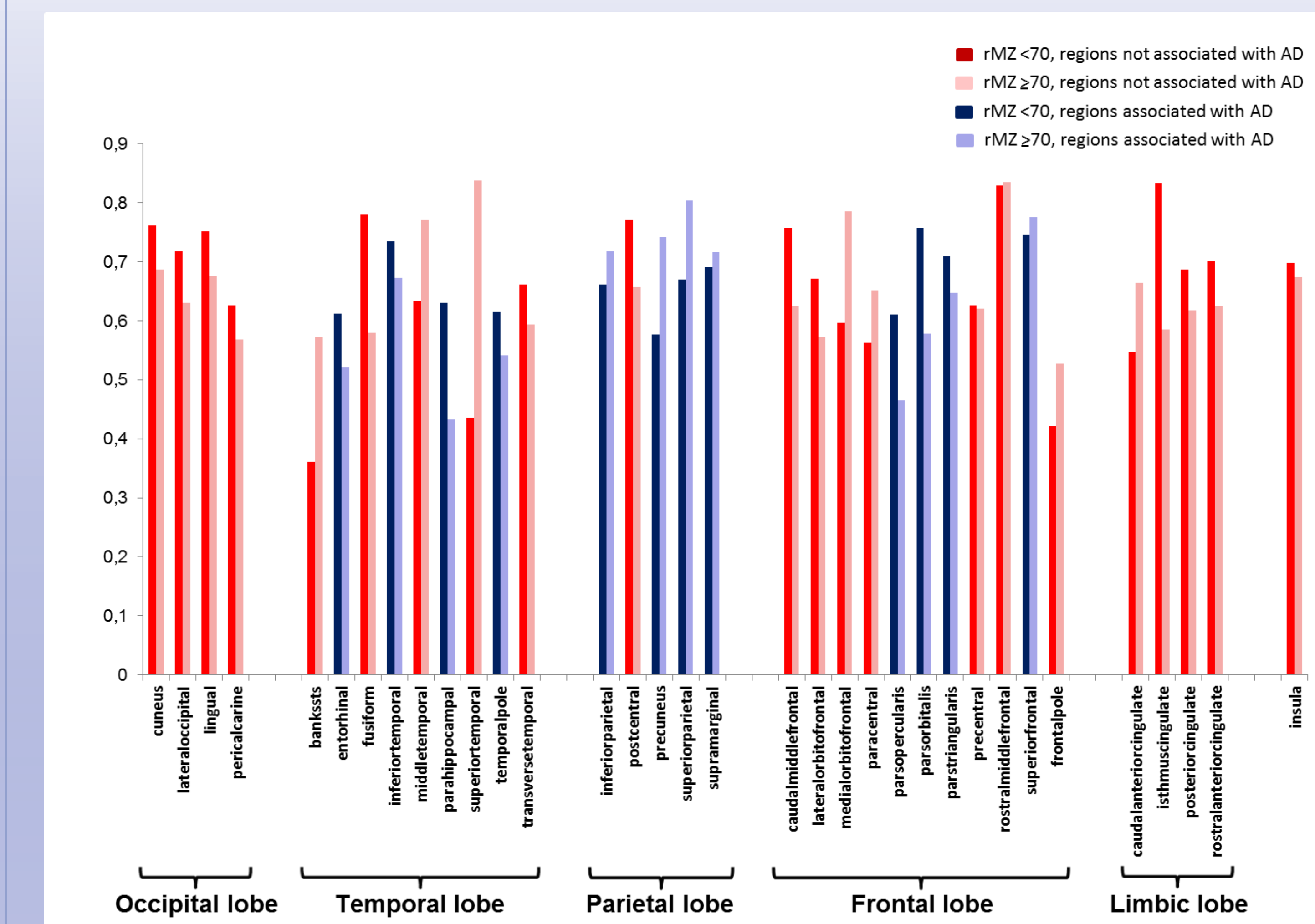


Figure 4. MZ twin correlation for cortical thickness in 34 brain regions

Conclusions & future directions

1. Besides a strong involvement of genetic factors also non-genetic factors substantially influence cortical thickness in elderly subjects
2. These effects do not change after the age of 70 years

Future studies should focus on identifying modifiable risk factors associated with MZ twin discordance for cortical thickness, which might eventually lead to the discovery of early treatment targets for AD.