Rates of brain tissue changes in the general population of elderly - The AGES-Reykjavik Study

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Introduction

Estimations on age-related rate of changes of brain tissue volumes have mostly been gathered from cross-sectional magnetic resonance imaging (MRI) studies. A limitation of cross-sectional design is the inability to directly assess intra-individual change and rely on group averages. A truer estimate can be obtained with a longitudinal design where change is assessed directly over repeated assessments within an individual. Direct measurements of the various brain tissue volumes from longitudinal studies on large population cohorts are lacking.

Objectives

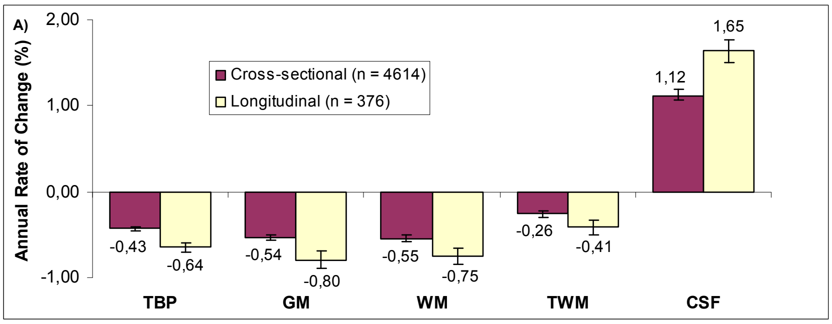
To compare estimated rates of cross-sectional and longitudinal changes with age in brain tissue volumes in a well-characterized population-based cohort of older persons with a high mean age.

Methods

The study population comprised participants from the Age, Gene/Environment Susceptibility (AGES)-Reykjavik Study. The sample with available MRI data consisted of 4614 subjects (1934 men (42%) and 2680 women (58%)), mean age 76±6, including 376 subjects (156 men (41%) and 220 women (59%), mean age 76±6 years), who participated in additional MRI examination a mean 2.5±0.2 years after the baseline exam. MR images including T1-, PD-, T2-weighted and FLAIR images were acquired on a 1.5T system. Brain tissue volumes, including grey matter (GM), white matter (WM), cerebral spinal fluid (CSF) and white matter hyperintensities (WMH) separately, were generated using the multi-spectral MR images and an automatic image analysis pipeline designed for high throughput of a large sample. Total brain parenchymal volume (TBP) was computed as a sum of GM-, WM- and WMH volume. Total WM was computed as the sum of WM- and WMH volume. The intra-cranial (IC) volume was computed as the sum of TBP- and CSF volume. Estimates of the population distribution/rate of change in tissue volumes per year after adjusting for IC volume and sex were assessed and age-sex interactions were examined. Results were presented with 95% confidence intervals (CI).

Results

The percentage estimated annular rates of change in TBP, GM, normal WM, total WM and CSF are presented in figure 1A and WMH in figure 1B for the cross-sectional sample and the longitudinal sub-sample. With increasing age, volumes of TBP decreased and CSF and WMH increased, both according to the cross-sectional estimates and the longitudinal estimates. A reduction in both WM- and GM volume contributed to brain shrinkage. However, the longitudinal data show a substantially higher age-related rate of change in tissue volumes for all tissue types when compared to the cross-sectional estimates. Age-sex interactions for a relative change in volumes for the individual tissue types were not significant in the cross-sectional estimates. However in the longitudinal findings, there was a significant age-sex interaction between men and women in TBP volume and total WM volume ($p<0.001$) with greater rate of change in men.



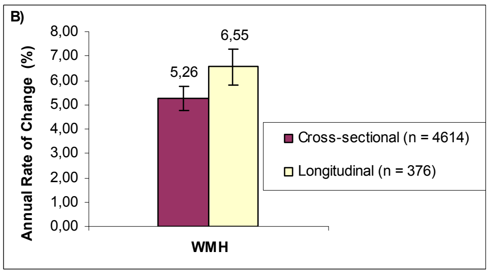


Figure 1. The percentage estimated annular rates of change in TBP, GM, normal WM, total WM and CSF are presented in figure 1A and WMH in figure 1B for the cross-sectional sample and the longitudinal sub-sample.

Conclusions

Our findings show that the cross-sectional data underestimates the rate of change in tissue volumes; the longitudinal data show substantially greater rate of change with age in tissue volumes for all tissue types. The cross-sectional rates of change in tissue volumes reported in previous studies may be underestimated.