Age-related changes in cerebral white and grey matter structures from infancy to adulthood: a voxel-based morphometry study

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Introduction

Quantifying and mapping morphometric changes in the human brain during normal development has long been a challenge to scientists. Post-mortem studies suggest that brain morphology undergoes conspicuous growth during the first years of life. With the advent of magnetic resonance imaging (MRI) it has become possible to visualise this development in vivo. Previous MRI studies provide quantitative evidence of developmental changes during childhood and adulthood (for review see [1]). However, most of those studies focus either on specific regions of interest or on grey matter only, or are limited by a small number or age range of subjects.

We used voxel-based morphometry (VBM) as an objective whole-brain technique for quantifying and localising changes of grey and white matter structures in the brain during normal development. Essentially VBM enables identification of regionally specific differences in structural images on a voxel-by-voxel basis, having removed macroscopic differences through normalisation of images to a template [2]. This study develops and extends previously presented data [3], increasing both the number and age range of subjects, especially in the crucial periods of infancy and childhood.

Methods

3D-FLASH structural brain scans with a voxel size of 0.78x.78x1mm were acquired from 159 healthy subjects, with an age range of 0-30 years. The images were processed using statistical parametric mapping (SPM 2; Wellcome Department of Imaging Neuroscience, London, UK). For the analysis of overall volumes of grey and white matter, all images were first normalised to a template, which had been created from all subjects, and then segmented into grey matter, white matter and CSF segments. A modulation step was included to preserve the total volumes. For the analysis of regional changes of grey and white matter during different stages of development, 3 age-groups were created, covering childhood (1-10 years, n=50), adolescence (11-16 years, n=50) and young adulthood (17-30 years, n=32). In the childhood group only subjects over 15 months of age were included because under this age the grey and white matter MRI signal intensities are very different from all subsequent age ranges. Age-group-specific templates were created from all subjects from within each age-group. The images were smoothed using a 12mm isotropic Gaussian kernel for the statistical analyses. Using both unmodulated and modulated smoothed images, statistical regression analyses were performed within each age group with age as a covariate and gender as nuisance variable in order to localise age-related changes both in tissue concentration and volume. Results were corrected for multiple comparisons using the family-wise error.

Results

Relative to brain size, overall grey matter volume decreases non-linearly over the whole age range, whereas overall white matter volume increases (figure 1). Most significant changes occur in infancy and early childhood. The total volumes of both grey and white matter increase non-linearly over this age range, with a clearly stronger increase of white than grey matter, resulting in an increase of the white to grey matter ratio (figure 1). Females are found to have more grey matter relative to brain size than males, resulting in higher white to grey matter ratios, especially after puberty. A special situation is seen in infants under 1 year of age, where an inverse trend of grey and white matter development is apparent, reflecting the changes in grey to white matter contrast on MR images during early maturation.

In addition, specific brain structures showed regionally specific behaviour; some brain structures were found to diminish in size and others to increase at the same developmental stage. The most significant changes were found to occur during childhood in the cortico-spinal pathway and in association cortices (figure 2). However, regional changes were also found during adolescence and young adulthood; for example an increase in both tissue concentration and volume of frontal commissural pathways was observed during young adulthood.

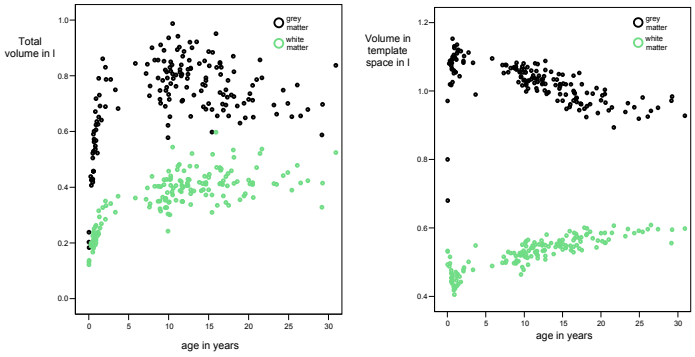

Figure 1. *Left*: Total volumes of grey and white matter. Right: Volumes of grey and white matter in template space, i.e. relative to brain size.

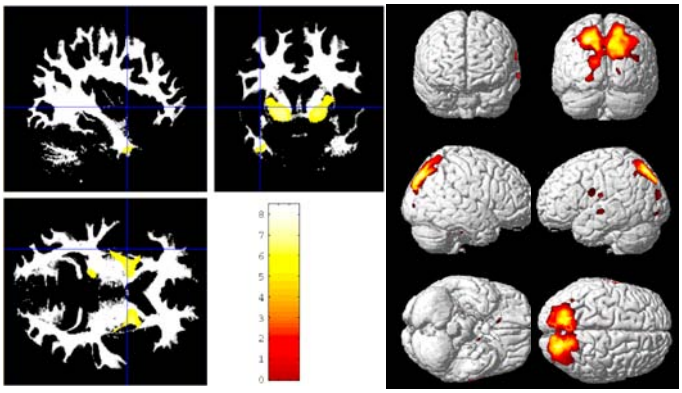

Figure 2. *Left*: White matter volume changes during childhood. Regions of positive correlation with age are superimposed on a normalised white matter image from one of the subjects. The colour bar represents the *T* score. *Right*: Grey matter volume changes during childhood. Regions of negative correlation with age are superimposed on the surface of an example brain.

Discussion

Our results show that age-related changes of overall grey and white matter volumes occur most markedly in infancy and early childhood but continue into adulthood. In addition to these overall changes, regionally specific changes are observed. The process of regional changes of maturation appears to be associated with a decrease of grey matter volume and concentration and an increase of white matter volume and concentration. Our results corroborate and extend results of previous quantitative MRI studies [1]. It appears likely that these findings reflect the functional development of the human brain, in which the underlying physiological processes consist of both progressive (cell proliferation, arborisation, myelination) and regressive phenomena (cell death, synaptic and axonal pruning, apoptotic processes). The reported regionally dependent developmental differences are important to take into account when functional or pathological changes are being investigated.

References

1. Sowell ER, Thompson PM, Toga AW (2004) Mapping changes in the human cortex throughout the span of life. Neuroscientist 10: 372-392.

2. Ashburner J, Friston KJ (2000) Voxel-based morphometry--the methods. Neuroimage 11: 805-821.

3. Groeschel S, Vollmer B, Connelly A (2004) Age-related changes of cerebral white and grey matter structures from childhood to adulthood using voxel-based morphometry. Proceedings of the Workshop of the ISMRM "Advanced MRI of Age-related White Matter Changes in the Brain", Boston, USA.