

Global gray/white matter ratio and gray matter volume reflect abnormal aging neurodevelopment in treatment naive schizophrenics

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Introduction

An “optimal” balance in the amount of gray and white matter is thought to minimize energy consumption and maximize functional efficiency in healthy people (1). A previous study (2) found that global gray matter volume decreased linearly with age, but there was no age-related decline for the white matter volume. Thus the global gray/white matter (G/W) ratio, a parameter indicating global development (3), while not affected by brain size, will also be influenced by age. Schizophrenia is a disease associated with epigenetic and abnormal neurodevelopment which may disrupt the balance of gray and white matter (3). Studies have shown morphological abnormalities of the cerebral gray and white matter in patients with schizophrenia (4, 5). However, to date no studies investigated the changes of G/W ratio and its association with age. We aimed to characterize the G/W ratio in addition to gray matter volume (GMV) as defined using the voxel based morphometry (VBM) in patients with first-episode, antipsychotic-naive schizophrenia.

Subjects and Methods

The study was approved by the local ethical committee and written informed consent was obtained from all subjects. Twenty patients with first-episode schizophrenia (aged 24.2 ± 8.2 years, range 16-41 years, 8 males, 12 females; all right handed, diagnosis based on DSM-IV) and twenty one normal controls (aged 36.4 ± 9.5 years, range 19-55 years, 10 males, 11 females) were recruited. MR examinations were performed before commencing the treatment. High resolution T₁-weighted images were acquired using a 3T MR imaging system (EXCITE, General Electric, Milwaukee, USA) with an 8 channel phase array head coil (TR/ TE 8.5/3.4msec, Flip angle 12°, slice thickness 1mm, voxel size: 0.47×0.47×1mm³, 156 axial slices in total to cover the whole brain). The images were automatically segmented using Statistical Parametric Mapping (SPM2, <http://www.fil.ion.ucl.ac.uk>). All gray and white matter of the brain were analyzed on a voxel-by-voxel basis. The ratio of global G/W was calculated from the resulting segmentation, and the correlation between G/W ratio and age was analyzed using bivariate (Pearson) correlations. A p value of less than 0.05 was deemed to be significant. Additionally, an optimized VBM (2) was also employed to find the correlation between regional GMV and age using voxel-by-voxel regression analysis. An uncorrected p value of less than 0.001 was deemed to be significant.

Results

Significant linear correlation was found between age and global G/W ratio in normal controls ($r = -0.650$, $p < 0.01$) but not in patients with schizophrenia ($r = 0.05$, $p = 0.968$) (Figure 1). Compared with the normal controls, patients with schizophrenia in the present cohort showed reduction in the volume of both global gray matter (-3%) and white matter (-0.3%). The significant reduction in GMV with age in normal controls were observed mainly in the bilateral frontal (Talairach: -41 54 -7; 26 53 10; et. al $P_{\text{uncorrected}} < 0.001$) and temporal lobes (Talairach: -51 25 -12; 46 14 11; et. al $P_{\text{uncorrected}} < 0.001$) (Figure 2). However, no significant association of the reduction in GMV with age was found in patients with schizophrenia.

Discussion

We observed a disassociation of the global G/W ratio with age in patients with schizophrenia, supporting the notion that there may be a destroyed “optimal” balance of gray and white matter in patients. In addition, our finding of the correlation between the GMV reductions and age in normal controls is consistent with previous reports (6) and this represents the normal aging effect on the brain, particularly on the frontal and temporal lobes which are regions crucial to cognitive function. We speculate that the disassociation of the GMV and age in these brain regions, in particular in the frontal lobe, may, in part, explain the impaired cognitive performance in patients with schizophrenia. Further study on a large cohort with wider age span is required to clarify whether G/W ratio and GMV can be used as an indicator of the disease progression in patients with schizophrenia.

Reference.

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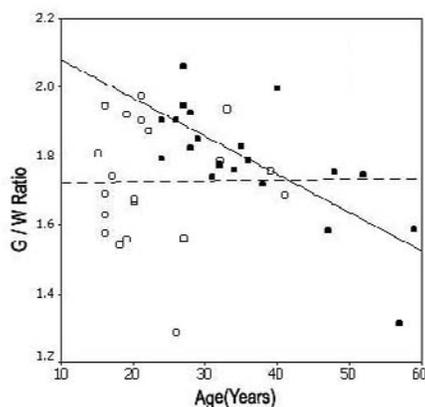


Figure 1. Scatter plot showing the correlation between global gray/white matter ratio (G/W) and age. Solid dots with fitted regression line: normal controls; Circles with dotted regression line: patients with schizophrenia. Note that there was no significant association of G/W ratios with age in first-episode patients ($p > 0.05$).

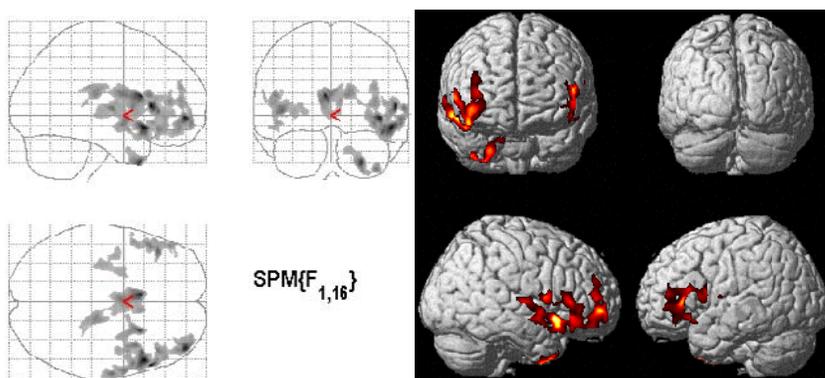


Figure 2. Glass brain images (left panel) and rendering images (right panel) from VBM analysis on normal controls, showing negative correlation between gray matter volume and age mainly in the left frontal (Talairach: -41 54 -7) and temporal lobe (Talairach: -51 25 -12) ($p < 0.001$, uncorrected).