

Aging Effect on Human Brain Transverse Relaxation since Preadolescence

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Introduction

The transverse relaxation (T_2/R_2) mapping has been applied to a wide age range of clinical examinations from autism in children to Alzheimer's disease in old age in addition to white matter abnormalities, brain tumors, schizophrenia, and multiple sclerosis [1-5]. In order to utilize T_2/R_2 mapping to improve the diagnosis of these brain diseases, it is essential to establish the quantitative relationship between age and T_2/R_2 distribution in the normal human brain. Previous normative studies on brain transverse relaxation have shown a general trend of age dependency in either narrow age ranges or small samples [6-10]. The goal of this study was to elucidate a quantitative developmental/aging characteristics and its variability on regional transverse relaxation rates (R_2) in normal human brain without a priori models.

Methods

Seventy-seven 9 to 85 year-old healthy normal volunteers (41 males and 36 females) were studied on two 3 T scanners with a 9-echo T_2 -mapping sequence with TE from 11.8 to 106.2 ms. All the subjects and the parents of the subjects under 18 years old gave informed written consent prior to participation. There was no significant age difference between the two genders nor did the subjects have any neurological or psychiatric history. The R_2 maps with an in-plane resolution of 1 mm were generated using linear regression of the logarithm with home-developed software qMRI. The maps were normalized to the standard MNI space using SPM5 (University College London). There was no significant difference on the R_2 maps obtained from the same subjects with the two scanners. Twenty-five ROIs were manually selected from the R_2 maps at the center of 18 major gray matter and 7 white matter structures where the R_2 distribution within the structure was relatively homogeneous (Fig. 1). The size of ROIs ranged from 21 voxels (e.g., red nucleus) to 107 voxels (e.g., the anterior nucleus of thalamus) in order to provide representative values for the given brain structures. The correlation of R_2 with age was analyzed with generalized additive models using SAS.

Results

Significant age-dependence of R_2 was observed in all the brain structures. However, as illustrated in several representative brain structures in Fig. 2, the relationships between R_2 and age exhibited strikingly different patterns among the structures. In most brain structures, the relationships between R_2 and age were nonlinear ($p < 0.01$), except genu of corpus callosum and bilateral occipital white matter ($p > 0.17$). The R_2 in most gray matter structures, e.g., the hippocampus, amygdala, globus pallidus, thalamus, red nucleus and substantia nigra, showed a quadratic pattern where there was an increase of R_2 in adolescence and young adulthood (< 20 years), then a plateau of R_2 in middle age (20 to as early as 40 or as late as 60 years, which varied among structures), and finally a decline of R_2 in older age; while in the putamen and caudate nucleus, the R_2 -age relationship followed a logarithmic pattern, which increased at a slower rate after adolescence. In contrast, in most white matter structures studied, e.g., genu of corpus callosum, bilatera orbitofrontal and occipital white matter, there was a significant desending trend between R_2 and age. There was no significant lateralization effect on the R_2 -distribution (paired t-test, $p > 0.14$).

Discussion

The present study revealed that the age dependence of R_2 varied with respect to brain anatomy. The relationships between regional R_2 and age showed *nonlinearity* in most brain regions studied. The accelerated trend of R_2 with developmental age detected in most of the deep gray matter structures is likely attributed to tissue iron deposition as observed in a postmortem study: the rise in non-heme iron concentration of the brain is rapid during the first two decades of life and then becomes more gradual [11]. This raises the possibility that tissue iron plays an important role in the changes of brain transverse relaxation during normal development until middle age. The mechanism for the decrease of R_2 in some white matters after childhood and some gray matters in older ages needs to be further investigated. The detailed age dependence of R_2 curves established here provides an important foundation for clinical studies using R_2 mapping.

References

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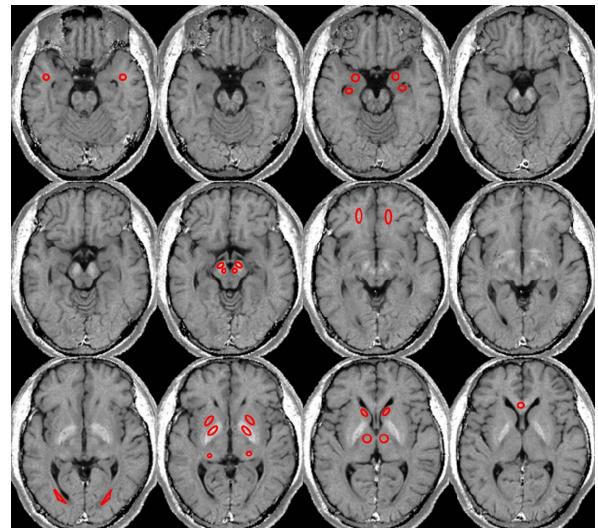


Figure 1. ROIs shown on a normalized R_2 map from a healthy 33-year-old man. ROIs include: temporal white matter, amygdala, head of hippocampus, substantia nigra, red nucleus, orbitofrontal white matter, occipital white matter, putamen, globus pallidus, anterior and posterior thalamus, head of caudate nucleus, and genu of corpus callosum.

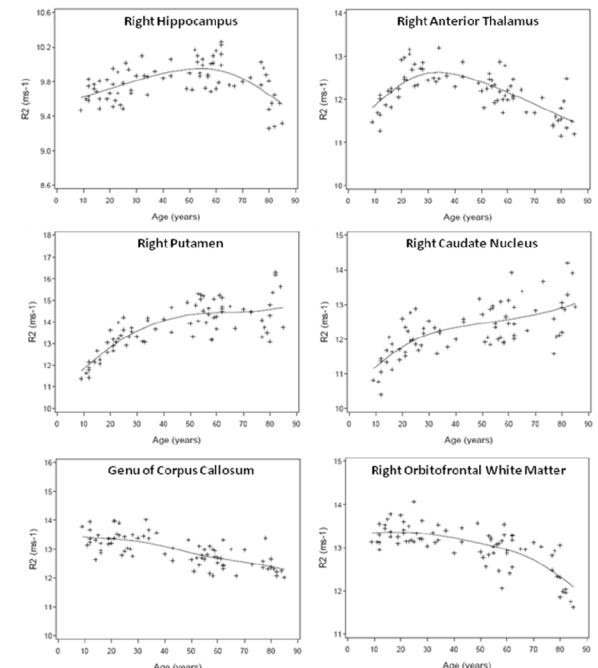


Figure 2. Representative R_2 of right hippocampus, anterior thalamus, putamen, caudate nucleus, orbitofrontal white matter, and genu of corpus callosum.