Assessing the Effect of Age on Voxel-Based Relaxometry of Epileptic Patients

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INTRODUCTION

T2 weighted MR imaging can be helpful in locating epileptogenic lesions since a correlation has been found between the presence of epileptogenic tissue and elevated T2 relaxation time.1 T2 relaxation time (quantitative assessment of T2 relaxation time) is a sensitive tool for identifying T2 abnormalities.2 T2 Voxel Based Relaxometry (VBR) is a technique which performs a voxel-level statistical comparison of quantitative T2 maps to identify regions with significantly elevated T2 relaxation time.3 VBR may thus depict the locations and extents of T2 abnormalities. This whole brain, objective technique has been shown to be useful both as a research tool for examining groups of patients and for clinical evaluation of single patients, and also in cases of cryptogenic focal epilepsy where the seizure focus is uncertain.4 With T2 relaxation and VBR, one important consideration is that causes other than epilepsy may also produce increased T2, leading to false-positive T2 changes attributed to epilepsy. The process of aging, for instance, in healthy individuals may lead to tissue changes that manifest as T2 changes. There is some evidence that T2 relaxation time changes with age.5,6 This may have important implications considering the broad age range of studied patients. To this end, our objective was to assess the effect of age on T2 for VBR analysis using an expanded group of healthy controls with voxel-based statistical analyses.

METHODS

We scanned 44 healthy volunteers (controls) and 25 right temporal lobe epilepsy (RTE) patients who provided written informed consent. A modified Carr-Purcell-Meiboom-Gill (CPMG) sequence was performed at 3 T (Signa VH/i; GE Healthcare, WI). The CPMG sequence parameters were: 8 echoes, TE 30 ms to 240 ms, TR = 2175 ms, 256 x 128 matrix, 24 cm FOV, 15 to 24 slices, 5 mm thick, 1 mm gap. T2 maps were generated using a Levenberg-Marquardt non-linear fitting routine with a baseline to account for cerebrospinal fluid partial-volume. The T2 maps were spatially normalized (T2-weighted template) and smoothed (Gaussian filter, 6 mm full width half maximum) with SPM2 (FIL Methods Group, UK, 2004) using previously described methods.2,7 To ascertain whether age could be correlated with T2 relaxation time, two simple regressions of age and T2 were run with SPM2 (FIL Methods Group, UK, 2004) using previously described methods.8 To determine whether age VBR analysis could be correlated with T2 relaxation time, we performed a single-subject VBR assessment for the controls and for the RTLE patients. Statistical analysis of the smoothed T2 maps was performed using a two-sample student’s t-test between individual controls and the remainder of the controls, and between individual patients and the control group using SPM2 (α = 0.05). For each subject, VBR was performed once with age included as a nuisance variable, and once without. The number and location of significant T2 elevations on VBR maps were recorded based on the presence of VBR significance in the same regions assessed for the ROI analysis, except both grey matter and white matter were considered for those lobes where only white matter ROIs were placed.3

RESULTS

There were 44 controls studied, with a mean age of 37 yr ± 15 yr (standard deviation, SD), a range of 18–70 yr, composed of 24 females (55%). There were 25 right temporal lobe epilepsy (RTLE) patients studied with a mean age of 42 yr ± 13 yr (SD), a range 20–67 yr, composed of 17 females (68%). We broke down our control group into age groups of < 20 yr, > 60 yr, and 5 yr age groups in between. Each age group had a minimum of 2 patients. Age regression at α = 0.001 showed small localized regions of significance, most notably in the putamen and hippocampus (Fig 1). When the regression was repeated at α = 0.05 the areas of significance were much more extensive, covering much larger areas surrounding the putamen and hippocampus and stretching into the amygdala and large significant areas were also present in the frontal lobe white matter. A large degree of significance was detected around the edges of the brain and near areas of CSF. Analysis of the ROIs showed variable slope and R2 values across the brain, but revealed a general trend for white matter T2 to increase with age and grey matter T2 to decrease with age (Fig 1). The trend was significant (p < 0.05) in the frontal lobe white matter, hippocampus, caudate and putamen. Controls had, on average, a reduced occurrence of significant regions and greater variability between individuals than did the RTLE group. A graph of the discrepancies between the two VBR scores shows increased discrepancy between the young and old, with a greater degree of correlation closer to average age (Fig 2).

DISCUSSION

The areas of significance found in the voxel-based linear regression correspond to those regions found to be significant by the ROI-based linear regression. There is good corroboration between the results of the linear regression and the VBR severity scores. Most previous reports have failed to identify any correlation between age and T2 relaxation time. However a previous study found a significant negative relationship between age and T2 time in the caudate, putamen and hippocampus in healthy controls at a significance of α = 0.01 with stepwise and simple regression, which is an agreement with our findings.5 The age related increase in T2 time in the frontal lobes could possibly be a result of normal age related microvascular white matter changes.6 The insular ribbon is discordant with the other findings, though partial volume effects with adjacent CSF may be a confounding factor.

References