Abnormal T2' Relaxation Rates as a Measure of Iron Concentration in HIV-positive subjects

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INTRODUCTION: Iron depositions in the aging brain increase the static magnetic field inhomogeneity relaxation rate R_2' (1). Excess brain iron may contribute to neuronal injury since neuropathological studies have shown high levels of brain iron in selected brain region. R_2' has been used as a surrogate measurement of iron content in the brain, and was found to be higher in subjects aging with neurodegenerative diseases, including patients with HIV (2). R,' also may provide a more specific measure of brain iron deposition than R2 or R2*, since these parameters can be affected by other pathological mechanisms (3). Here, we present whole brain, multi-echo, relaxation data in a group of HIV positive or negative individuals.

METHODS: Eleven HIV-positive (49.9±3.2 year old) and eleven HIV-negative (42.0±5.0 year old) subjects between 20 and 70 years were scanned with a Siemens 3T whole body scanner to obtain T_2 and T_2*-weighted images at ten echo times (TE) using a spiral sequence (22cm FOV, 90° flip angle, 128x128 matrix, 24 5mm thick slices, four interleaves, 4 sec TR). For the T_2-weighted scan the echo times ranged from 8ms to 150ms, and the T_2*-weighted scan echo times ranged from 3ms to 100ms. The volumes at each TE were registered to the standard MNI brain template using an affine 12-parameter algorithm in the FSL software package. Exponential fits to the echo times yielded spatial maps of the static field relaxation rate: $R_2' = R_2^* - R_2 = 1/T_2^* - 1/T_2$. The FSL package was then used to automatically segment the following regions of interest (ROIs): right and left pallidum, thalamus, putamen, caudate, and hippocampus. The values of R_2' within each ROI's were averaged.

RESULTS: The HIV subjects had CD4 counts of 597± /mm3 and nadir CD4 counts of 197± /mm3. They were on antiretroviral medications with relatively controlled viral load or 2. Log. In the left thalamus, there was a trend for higher R_2' in the HIV group compared to the control subjects (p=0.07, covaried for age). Conversely, R_2' tended to be lower in the HIV group in the right pallidus (p=0.07, covaried for age). R_2' increased with age (both groups combined) in the left thalamus (r=+0.51, p=0.015), right thalamus (r=+0.46, p=0.03), and right putamen (r=+0.39, p=0.07). Furthermore, there was a significant interaction, or trends for interactions, between age and HIV status on R_2' in several of the ROIs. In the right thalamus, R_2' increased with age in the control as well as HIV-positive subjects, but the increase was much more pronounced in the HIV-group (Fig. 2b). In contrast, in both left and right putamen, R_2' decreased with age in the HIV-positive subjects, but increased in the controls (Fig. 2c and d).
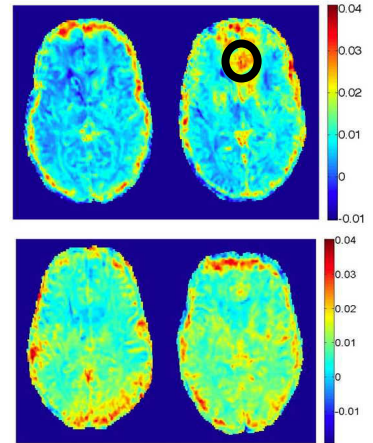
Figure 1: Top: R_2' maps of a 35yr old (left) and 53 yr old (right) seronegative subject. Note increased R_2' in the older subject (ROI). **Bottom:** R_2' map of a 67yr old seronegative (left) and 70 yr old seropositive (right).
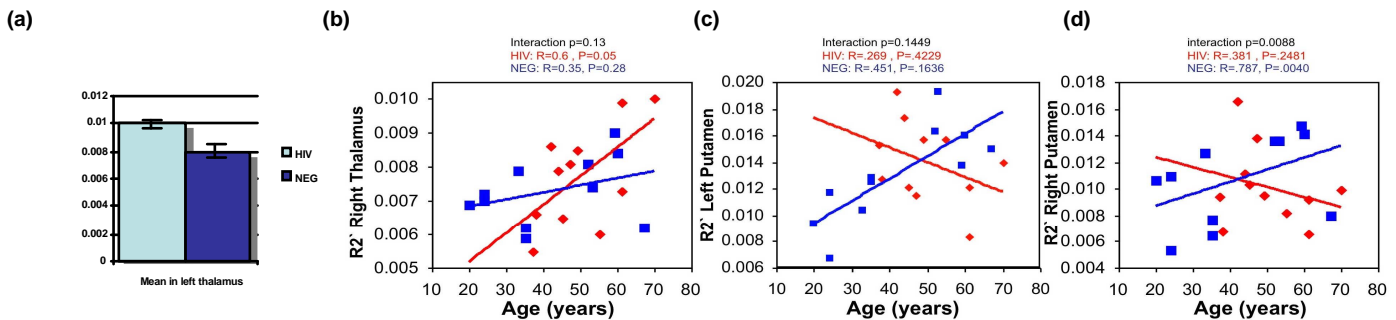
Figure 2.

DISCUSSION: R_2' relaxation rates increase as a result of the magnetic disturbance of iron concentration in surrounding tissues. In agreement with prior studies, R_2' values were found to increase with age in certain subcortical brain structures, indicating increased deposition of iron in the normal aging brain. Similarly, HIV infection was associated with trends for higher iron contents in the thalamus, but slower than age-related increased in R_2' in the thalamus. HIV subjects also showed age-related decline in both putamens, rather than the normal age-related increase in these regions. This interaction effect between HIV status and age occurred because some of the younger (middle-aged) HIV subjects had markedly elevated iron content, with levels similar to much older healthy subjects at ages 70-80 years. The findings suggest that iron deposition may predominately affect the putamen and thalamus of HIV subjects, and may contribute to brain degeneration in younger HIV patients. Further correlations with cognitive performance will determine whether the higher iron content (assessed by R2') might contribute to poorer cognitive performance.

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