T1rho ($T_{1\rho}$) MR imaging in Alzheimer' Disease and Parkinson's Disease

A. Singh[1], M. Haris[1], E. McArdle[1], M. Sochor[1], M. Fenty[1], C. Davatzikos[2], J. Q. Trojanowski[3], E. R. Melhem[4], C. M. Clark[5], R. Reddy[1], and A. Borthakur[1]

[1]MMRRCC, Radiology, University of Pennsylvania, Philadephia, PA, United States, [2]SBIA, Radiology, University of Pennsylvania, Philadephia, PA, United States, [3]Department of Pathology & Lab Medicine, University of Pennsylvania, Philadephia, PA, United States, [4]Radiology, University of Pennsylvania, Philadephia, PA, United States, [5]Department of Neurology, University of Pennsylvania, Philadephia, PA, United States

Introduction:

Alzheimer's disease (AD) accounts for 50–60% of cases of dementia in the elderly. The neuropathological features of AD include widespread neuronal loss, neurofibrillary tangles affecting many surviving neurons, and deposition of beta-amyloid plaques[1]. On the other hand Parkinson's disease (PD) is a neurodegenerative disorder that affects an estimated 1 million people in the US and tens of millions worldwide and is associated with the loss of dopaminergic neurons in the substantia nigra[2]. Diagnosis of both AD and PD can be difficult in elderly patients because some of the key symptoms also may be manifestations of normal aging in both cases (AD and PD). Early and correct diagnosis and treatment of both AD and Parkinson's disease (PD) are crucial for the patient's well being. Structural neuroimaging has the potential to play an important role in the early diagnosis of both AD and PD. It has been shown that both AD and PD individuals showed high Medial temporal lobe (MTL) atrophy compared to controls[3]. However, the age related atrophy in the previous study may contribute and misinterpretate the final results. An alternate contrast mechanism is T1rho ($T_{1\rho}$), the spin lattice relaxation time constant in the rotating frame, which determines the decay of transfer magnetization in the presence of "spin-lock" radio-frequency field. In biological tissue exchange between protons in different environments is expected to contribute $T_{1\rho}$ relaxation. The molecular process that occurs in the milliseconds range influences $T_{1\rho}$ relaxation time constant. The current study was performed with an aim to measure the base line $T_{1\rho}$ in MTL in the brain of Control, AD and PD cohorts and to determine whether the $T_{1\rho}$ value show any significant difference between these cohorts.

Materials and Methods:

Subjects: The Institutional Review Board approved the study protocols. In the current study, we included 54 AD patients (mean age±SD = 73.6±7.8 years), 52 PD patients (mean age±SD = 72.7±9.2 years), and 40 age-matched controls (mean age±SD = 70.7±8.6 years). All patients underwent a standardized clinical assessment including medical history, physical and neurological examination, psychometric evaluation, and brain MRI.

MRI: All these patients underwent a standard MRI protocol on a 1.5 Tesla Siemens Sonata clinical scanner using the vendor-supplied head coil. The written informed consent was obtained from each patient before they underwent for MRI. For $T_{1\rho}$ MRI, a fluid-attenuated $T_{1\rho}$ pre-encoded Turbo Spin-Echo pulse sequence was used (8). The imaging parameters were: TE/TR = 12/2000 ms, TSL (duration of spin lock pulse) = 10, 20, 30, 40 ms, with a spin lock frequency of 500Hz, slice thickness = 2mm, FOV = 22 cm, Matrix size=256x128, bandwidth= 130Hz/pixel, echo train length = 4. The inversion time (TI) was fixed at 860 ms to remove the contribution of the CSF to the $T_{1\rho}$ maps. An oblique coronal $T_{1\rho}$ weighted image of a slice perpendicular to the anterior/posterior commissure (AC/PC) plane was obtained. The slice was chosen to include the head of the hippocampus. Immediately after $T_{1\rho}$ MRI, the entire volume of each subject's brain was imaged in the coronal plane using a T_1-weighted 3D volumetric MPRAGE pulse sequence with 124 continuous slices. The parameters were TR/TE= 3000 ms/ 3.5ms, slice thickness= 1.2 mm, FOV of 24 cm and 192 phase encode steps, and flip angle =8° for a total imaging time of 10 min.

Data Processing: $T_{1\rho}$ maps were generated by fitting each pixel's intensity as a function of the duration of the spin-lock pulse (TSL) by a linear least-squares algorithm[4]. Pixels whose intensities correlated poorly (R2<0.95) with the fitting equation were set to zero. Pixels outside of the brain were also set to zero. $T_{1\rho}$ values were automatically calculated from the gray matter (GM) and white matter (WM) of right and left MTL by an algorithm described previously. For GM and WM segmentation a previously developed method was used to partition the volumetric MPRAGE scans into 92 ROIs incorporating all major cortical and sub-cortical regions[5]. This method deforms MRI scans of different brains into anatomical co-registration with each other, and into co-registration with a standardized template. The template's labels are then transformed to individual scans by applying the elastic transformation that was found to co-register the respective images.

Statistical analyses: For statistical analysis $T_{1\rho}$ value from the left and right side were averaged both for GM and WM. One Way Analysis of Variance (ANOVA) using Bonferroni post-hoc multiple comparisons was performed. Pearson correlation was performed between $T_{1\rho}$ values versus age.

Results:

The average GM and WM $T_{1\rho}$ values in MTL in the brain of control, AD and PD are reported in Table 1. Figure 1 shows $T_{1\rho}$ maps in MTL of control, MCI and AD. Higher $T_{1\rho}$ pixels (in red) were found in the AD subjects compared to control and PD. One way ANOVA showed that both the GM and WM $T_{1\rho}$ value were significantly different between three groups (control, AD and PD). The Bonferroni's multiple comparisons showed that the GM $T_{1\rho}$ was only significant decreased in PD compared to AD, while in case of WM both control and PD showed significant decreased $T_{1\rho}$ value compared to AD. No significant difference was observed either for GM or WM $T_{1\rho}$ between control and PD. The AD group showed 10% increase in GM $T_{1\rho}$ and 9% increase in WM $T_{1\rho}$ value over control while on comparing to PD $T_{1\rho}$ was increased by 12% in GM and 14% in WM. The control showed a 5% increase in GM $T_{1\rho}$ and 6% increase in WM $T_{1\rho}$ compared to PD. We did not find any significant correlation between $T_{1\rho}$ and age in all three cohorts (control, AD and PD).

Discussion:

In the current study, we found increased $T_{1\rho}$ in the MTL in the brain of AD compared to age-matched control and PD cohorts. The PD individuals showed decreased (5-6%) $T_{1\rho}$ value compared to controls. The presence of pathology in AD may contribute to molecular interactions such as exchanging protons from bulk water with protons associated with slowly tumbling macromolecules in the extracellular space resulting in an increased $T_{1\rho}$. The decreased $T_{1\rho}$ in PD is probably due to proton spin dephasing from iron-induced local field inhomogeneities resulting from the increased iron content in the substantia nigra in PD patients. The serial measurement of $T_{1\rho}$ in both AD and PD may provide the nature of disease progression and would contribute to their early diagnosis in the future.

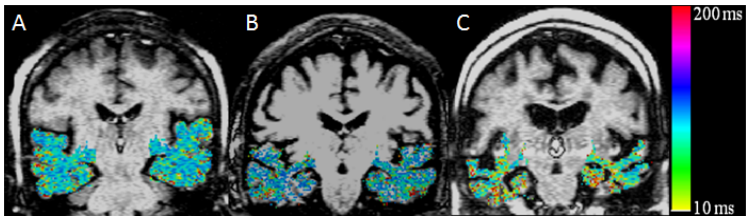

Fig.1 $T_{1\rho}$ maps of the medial temporal lobe (MTL) region overlaid on fluid- $T_{1\rho}$ MRI in the brain of control (A), PD (B) and AD patient (C). Pixels with higher $T_{1\rho}$ (red) are more prominent in MTL of AD patient.

	Gray matter (mean±SE)	White matter (mean±SE)
Control	86.9±1.3	79.9±1.5
AD	90.1±0.9	85.6±1.3
PD	83.9±1.1	76.9±1.4
ANOVA (p value)	0.000	0.000

Table 1. $T_{1\rho}$ value in medial temporal lobe (gray matter and white matter) of control, AD and PD

References:

1. Braak et al. Acta Neuropathol 1991:82:239-59, 2. Gelb et al. Arch Neurol 1999;56:33-9, 3. Tam et al. Neurology 2005;64:861-65, 4. Borthakur A et al. Neuroimage 2008:41:1199-1205, 5. Davatzikos C et al. Neurobiol Aging 2008:29:514-23