Brain T1rho MR imaging in Parkinson Disease: Female vs Male

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Introduction: Parkinson's disease (PD) is a progressive neurological disorder, which progressively deteriorates muscles control, balance, cognitive functions and overall quality of life. There are several evidences that gender based differences in disease progression and disease prevalence are exist in PD patients (1, 2). Epidemiological studies have shown that both incidence and prevalence of PD are higher in male than female, although extent of disease severity symptoms such as tremor, non-motor functions and comorbidity with other disease conditions are more prominent in female than male (2, 3). Magnetic resonance imaging (MRI) techniques have been widely used to assess the structural and functional changes in brain of PD patients. Various neuroimaging modalities such as functional MRI, MR spectroscopy, trace based techniques and spin-lock based T1rho (ρ) imaging have been used to characterize the brain tissue changes in patients with PD (4, 5). T1ρ imaging is a spin lattice relaxation time constant in the rotating frame and has been earlier used to probe the molecular changes in various human pathophysiologies (5, 6). Since PD male and female have different symptoms severity, disease progression, and treatment outcomes, characterization of the brain tissue changes separately in male and female patients may provide a marker to follow-up their treatment responses as well as to predict the disease severity. In the current study, we have evaluated the gender based T1ρ relaxation changes in medial temporal lobe (MTL) and hippocampus in brain of patients with PD.

Materials and methods: This study was performed under an approved Institutional protocol. With informed consent, 60 patients with PD (mean age±SD, 70.4±9.8 years; female, 21; 39, male) and 41 age and gender matched controls (mean age±SD, 70.4±6.2 years; female, 29; 12, male) underwent for a clinical assessment including Mini-mental state examination (MMSE) and a brain MRI on a 1.5-T clinical MR scanner (Siemens Medical Systems, Malvern, PA, USA). T1ρ MRI was performed using a fluid-attenuated T1ρ pre-encoded Turbo spin-echo pulse sequence with TR/TE = 2,000/12 ms, TSL (duration of spin lock pulse) = 10, 20, 30, 40 ms, with a spin lock B1 amplitude of 500 Hz, slice thickness = 2 mm, FOV = 22 cm, matrix size = 256 × 128, bandwidth = 130 Hz/pixel, echo train length = 4 for a total imaging time of 6 min for four images. An inversion time (TI) of 860 ms was used to remove the CSF contribution to T1ρ values. An oblique coronal T1ρ -weighted image of a slice perpendicular to the anterior/posterior commissure plane was obtained. The slice was chosen to include the head of the hippocampus and medial temporal lobe. For brain segmentation a T1-weighted 3D volumetric MPRAGE imaging was performed on each subject using following parameters: TR/TE = 3,000 ms/3.5 ms, slice thickness = 1.2 mm, number of slice=160, FOV of 240×240 cm^2 and 192 phase encode steps, and flip angle = 8° for a total imaging time of 10 min. T1ρ relaxation time was calculated by fitting the T1ρ weighted signal to equation: $M(TSL)=M0_e^{-TSL/T1\rho}$, where M0 is the thermal equilibrium magnetization. The volumetric MPRAGE images were used to automatically calculate T1ρ values from hippocampus and MTL regions as described previously (Fig. 1), (7).

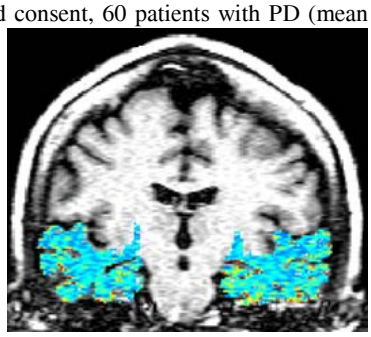

Fig. 1 T1ρ contrast from MTL region overlaid on anatomic fluid attenuated T1ρ -weighted image from a control subject.

A one-way analysis of variance was performed followed by post-hoc analysis using least significant difference to compare the T1ρ values among the male and female between two groups. Pearson correlations between T1ρ versus age and between T1ρ versus MMSE score were performed separately for male and female. A p value of less than 0.05 was considered to be statistically significant.

Results and Discussion:

No significant difference in age was observed across the groups. Significantly reduced T1ρ in left and right MTL's gray matter (p=0.006 and p=0.004), left and right MTL's white matter (p=0.01 and p=0.004), and left and right hippocampus (p=0.003 and p=0.0002) were observed in PD female group compared with those in control female group. When compared with PD male group, the PD female group showed significantly reduced T1ρ values in the left and right MTL's gray matter (p=0.04 and p=0.04), right MTL's white matter, and right hippocampus (p=0.01 and p=0.02).Further, PD female group showed significantly reduced T1ρ values in the right hippocampus (p=0.03) compared with that in control male group (Table 1). No correlations were observed between T1ρvalues, age, and MMSE scores.

Table 1: Brain T1ρ values from control and PD patients in MTL and hippocampus area.

Brain regions	Control T1ρ (ms) values		PD T1ρ (ms) values		P-values
	male (a)	female (b)	male (c)	female (d)	
LG	86.0 ± 8.3	86.8 ± 8.3	85.0 ± 7.9	80.2 ± 8.3	b-d, p=0.006; c-d, p=0.04
RG	85.0 ± 8.2	88.0 ± 8.5	85.6 ± 8.2	80.7 ± 9.4	b-d, p=0.004; c-d, p=0.04
LW	78.5 ± 10.2	79.8 ± 9.7	77.8 ± 10.6	72.4 ± 9.5	b-d, p=0.01
RW	78.9 ± 9.1	81.0 ± 9.3	79.3 ± 9.8	72.8 ± 9.7	b-d, p=0.004; c-d, p=0.01
LH	88.0 ± 13.3	92.0 ± 12.7	86.7 ± 16.8	79.1 ± 13.9	b-d, p=0.003
RH	90.7 ± 14.2	94.5 ± 13.6	88.7 ± 14.7	79.1 ± 13.3	b-d, p=0.0002; a-d, p=0.03; c-d, p=0.02

LG, left gray; RG, right gray; LW, left white; RW, right white; LH, left hippocampus, RH, right hippocampus.

Gender based differences in the T1ρ values were observed in PD patients. Larger T1ρ changes in female than male PD patients suggest that the extent of brain tissue damage is more severe in female. These female-specific tissue changes as reflected by decreased T1ρ values may be due to the physiological and genomic differences between male and female, and might have significant implication in evaluating and treating PD among gender. A follow-up study form early stage of PD is require to properly assess the gender based disease progression and severity.

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