

Transverse Relaxation Mapping of Nigrostriatal Damage in Early Stage Parkinson's Disease

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Introduction:

Parkinson's disease (PD) is a common neurodegenerative disorder affecting motor functions. It is caused by degeneration of dopaminergic neurons located in the substantia nigra (SN). Dopamine is delivered through nigrostriatal pathway to the basal ganglia to control the motor functions. PD is a bilateral disease. However, the disease is always asymmetric in onset and this asymmetry can last for a few years before the motor symptoms appear on the other side of body. The underlying mechanism for this asymmetry is not clear. In this study, we used quantitative evaluation of transverse relaxation parameters to detect this asymmetry. Our hypotheses are that in the early stage of PD the pathological development is asymmetric in the hemispheres corresponding to the clinically affected side and the clinically unaffected side, and this asymmetry can be detected by transverse relaxation parametric mapping. The rationales are: 1), primary PD pathology happens in the SN and putamen, which are iron-rich dopaminergic structures [1,2]; 2), transverse relaxation parametric mapping is a sensitive method for *in vivo* tissue iron measurement [3]; and 3), transverse relaxation changes have been detected in SN and putamen in PD [4-7].

Methods:

Human Subjects: Twenty-seven early stage PD patients with clinical motor symptoms located on one side of body (Hoehn & Yahr Stage I) were recruited from a movement disorders clinic. All subjects gave written informed consent, which was approved by the University Institutional Review Board.

Data Acquisition: All the subjects were evaluated for the Unified Parkinson's Disease Rating Scale (UPDRS) by a clinical movement disorders specialist who was not informed about the results of the MRI studies. The MRI studies were carried out on a Siemens Magnetom Trio 3.0 Tesla scanner (Siemens Medical Solutions, Erlangen, Germany). An eight-channel phased array head coil was used for reception. Three sets of images were collected from each subject: MPRAGE T₁ image, R₂ and R₂* mapping. Total imaging time was around 30 minutes.

Data Processing and Analysis: Transverse relaxation ratios R₂ and R₂* maps were generated using linear regression of the logarithm of MR signal S_(t) = S₀ · e^{-R₂TE} with qMRI (<http://pennstatehershey.org/web/nmrlab/resources/software/qmri>). R₂' = R₂* - R₂. Region of interest studies were conducted on SN and putamen of each hemisphere (Figs. 1 and 2). The ROIs were manually segmented by three evaluators that were blinded to the subjects' clinical conditions. One subject's SN was not segmented due to movement artifacts in the region. To study the asymmetry in early PD subjects, paired *t*-tests were conducted on the R₂, R₂*, R₂', and structure volume between the clinically affected and unaffected hemispheres.

Results:

The average transverse relaxation ratios of SN and putamen in the contralateral and ipsilateral hemisphere, with reference to the clinically affected (symptomatic) body side were listed in Tables 1 and 2. The R₂* in the symptomatic SN was significantly higher than the nonsymptomatic side (paired *t*-test, n = 26, p = 0.03). The R₂' in the symptomatic SN was significantly higher than the nonsymptomatic side (p = 0.04). There was no significant difference between the symptomatic and nonsymptomatic SNs in R₂ (p = 0.14) or in the volume of SN (p = 0.20). There was no significant difference between the symptomatic and nonsymptomatic side putamen in R₂, R₂*, R₂' and the volume of putamen (paired *t*-test, n = 27, p = 0.30, 0.12, 0.18, and 0.50, respectively).

Conclusion:

At the early stage of PD, the R₂* and R₂' in the SN contralateral to the symptomatic body side were significantly higher than the ones in the ipsilateral side. This supports our hypothesis of the asymmetry of pathological development in the two hemispheres at the early stage of PD, and this asymmetry can be detected by transverse relaxation mapping. In addition, the asymmetry of R₂* and R₂' in the two hemispheres suggests more iron deposition in the symptomatic SN, which may be a contributing factor to the SN degeneration in PD.

References:

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Table 1. Segmented Transverse relaxation rates of SN (n = 26)

Substantia Nigra	Volume (mm ³)	R ₂ (sec ⁻¹)	R ₂ * (sec ⁻¹)	R ₂ ' (sec ⁻¹)
Symptomatic	212.6±54.6	14.8±1.3	35.5±5.1	20.9±4.4
Non-symptomatic	219.4±54.2	14.6±1.2	34.0±5.3	19.5±4.5

Table 2. Transverse relaxation rates of putamen (n = 27)

Putamen	Volume (cm ³)	R ₂ (sec ⁻¹)	R ₂ * (sec ⁻¹)	R ₂ ' (sec ⁻¹)
Symptomatic	4.7±0.4	14.8±0.6	25.4±2.2	10.6±1.8
Non-Symptomatic	4.6±0.4	14.8±0.6	25.8±2.3	10.9±1.9

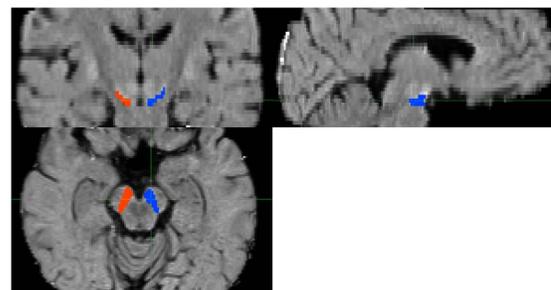


Fig. 1. Segmented SN overlaid on R₂ map. Orange: right SN; blue: left SN.

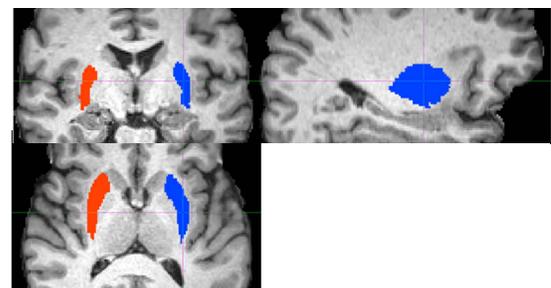


Fig. 2. Segmented putamen overlaid on T₁-weighted MPRAGE image. Orange: right putamen; blue: left putamen.