Direct Visualization of Parkinson's Disease by In Vivo Human Brain Imaging using 7.0T MRI

S-H. Oh[1], J-M. Kim[2], S-Y. Park[1], D-H. Kwon[1], H-J. Jeong[1], M-K. Woo[1], Y-B. Kim[1], J. Huston III[3], K. H. Lee[4], B. S. Jeon[2], and Z-H. Cho[1]

[1]Neuroscience Research Institute, Gachon University of Medicine and Science, Incheon, Korea, Republic of, [2]Departments of Neurology, College of Medicine, Seoul National University, Seoul, Korea, Republic of, [3]Department of Radiology, Mayo Clinic, Rochester, United States, [4]4Department of Neurosurgery and Department of Physiology and Biomedical Engineering, Mayo Clinic, Rochester, United States

INTRODUCTION: Parkinson's disease (PD) is a common neurodegenerative disorder. Through out the world, the incidence of PD has increased dramatically with the aging of society. In the vast majority of cases, the disease is idiopathic and the diagnosis is dependent on constellation of symptoms. Thus, the definitive diagnosis is not available until post-mortem histologic analysis, where degeneration of the subtatia nigra pars compacta (SNc) dopaminergic system is seen as depigmentation of SN. The neurodegeneration SNc result in the release of neuromelanin into the adjacent tissue, where it is phagocytosed and carried away by macrophages. It is believed that over 60% of dopaminergic neurons are lost before a patient begins to show clinical symptoms of PD, such as bradykinesia, cogwheel rigidity, and tremor. Thus, *in vivo* direct observation of the SNc in the human brain has been one of the most sought-after goals in PD research, as it has the potential to lead to noninvasive pre-mortem diagnosis of PD. Images obtained using 7.0T MRI began to show deep brain areas [1-2]. These findings suggest that 7.0T MRI could be used to observe the degeneration of the SN in PD patients. Here, we demonstrate that there are visible and distinctive differences in morphology of SNc in PD patients when compared to normal controls and suggest that 7.0 T MRI may be a useful tool in diagnosis of PD.

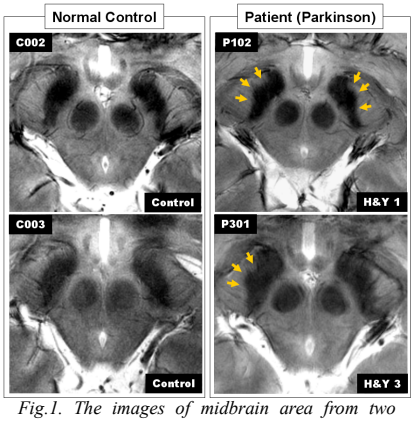

Fig.1. The images of midbrain area from two typical normal controls and Parkinson's patients

MATERIALS AND METHODS: 7.0T T_2*-weighted MR images of the SN were obtained from 10 patients with PD and 9 age-matched control subjects. The MRI used was a 7.0T MRI scanner (Siemens). All images were acquired using a 2D T_2*-weighted gradient echo sequence aligned with AC-PC line. (TR/TE = 750/17.8 ms; flip angle = 45°; in-plane resolution = 0.25 mm; and the slice thickness was 2 mm). For the quantitative analysis, we have segmented SN, and then the center of mass was obtained to locate a center point. From this center point, we have defined the midline of SN along the direction of anterior-posterior (A-P) which divides the lateral and the ventral aspects of SN. We select the lateral boundary of each subject, and then these boundaries are normalized based on the midline of SN. To make the reference lateral boundary line between SN and CC, we have calculated mean boundary line of control group and used as a reference line. We then measured distance profiles from the midline to the lateral boundary of SN and calculated sum of absolute differences for PD and normal control i.e., sum of absolute differences between individual data along the midline and reference. We referred this sum of absolute difference values as 'Undulation value'.

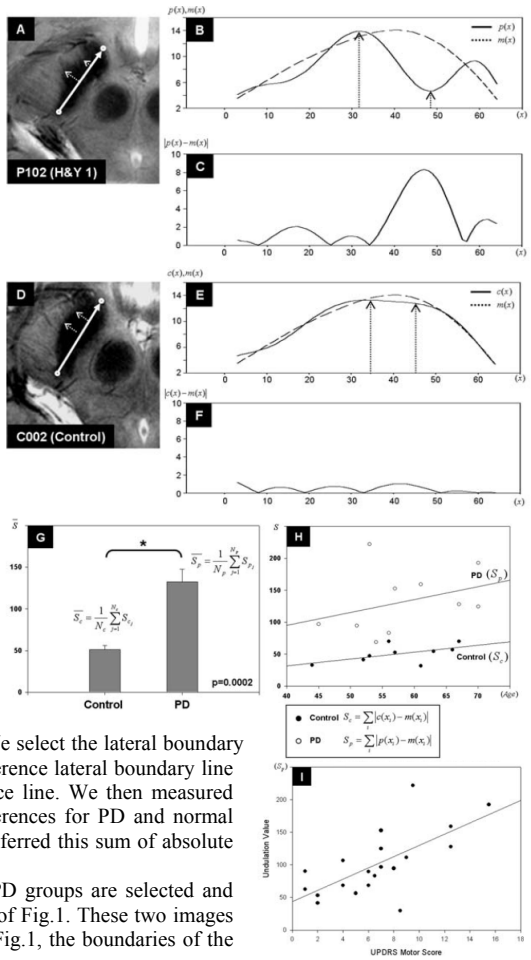

Fig.2. Results of analysis in typical PD patient and normal control.

RESULTS AND DISCUSSION: Representative samples of 7.0T images of the normal control and PD groups are selected and compared. First, two typical axial images of age-matched normal controls are shown in the left column of Fig.1. These two images clearly show the typical smooth boundaries between the SN and CC. However, in the right column of Fig.1, the boundaries of the two PD cases are severely serrated in both PDs and clearly distinguish the two groups. More specifically, the boundaries of PD patients are no longer smooth 'arch' shaped, but rather appear serrated, suggesting probably due to the degradation of cells in the SN. These clear distinctions appear an important maker for the diagnosis of PD *in-vivo* hither to unable to do with any other devices. Fig.2(A-C) and (D-F) are the results of analysis in typical PD patient and normal control, respectively. Representative images of a PD and a normal control obtained from 7.0T T_2*-weighted SN images are shown in (A) and (D). In these images, white solid lines represent midline which divides the lateral and the ventral aspects of SN and white dotted lines represent distance from the midline to the lateral border of SN. Distance profiles of individual PD for the lateral borderline and reference line are shown in (B) and same process is applied for normal control and the results is shown in (E). When we take the absolute differences between the reference and individual data, one obtains a typical data as shown in (C) and (F) for PD and normal control, respectively. As shown, the difference of PD patient is much larger than normal control (this example is the case of P102 patient and C002 normal control). Fig.2(G) shows a group difference which is calculated by SAD (Sc and Sp, referred this as 'undulation value' for control and PD, respectively) of the individuals divided by the number of control subjects and patients who participated in the experiment. In case of the normal control we averaged both (left and right) side while in the case of the PD patient, we measured only the most affected side value. As it is seen, the values were significantly different between the two groups (p=0.0002) and show much higher value in the PD patient than the normal control. Within each PD and control groups, correlation analysis show that, there is substantial age dependent correlation as well, especially for the patients (see Fig.2(H)). As seen, the 'undulation value' of PD group (Sp) is larger than normal control (Sc). Compare the two correlation lines, the slope of the PD (0.314) is lager than normal control (0.117) (see Fig.2(H)). In addition to age dependent correlation we have also measured UPDRS motor score dependent correlation and the result is shown in Fig.2(I). In this case we measured both side of the 'undulation value' of SN (Sp) and UPDRS motor scores in PD patients. As the UPDRS motor score increase, the 'undulation value' also increased and the slope of correlation line was 0.457. This correlation analysis shows that, there is substantial UPDRS motor score dependent correlation. These statistical results would obviously be useful in setting the criteria for diagnosis of PD patients in quantitative manner.

CONCLUSION: The most interesting and important finding of these 7.0T MR imaging study appears to be the clear visualization and eventual quantitation of PDs and normal controls based on the difference in the gross anatomical shape and the quantitative 'undulation values' between the controls and PDs. From the quantitative observation and quantitative analysis such as the 'undulation value', *in vivo* 7.0T T2*-weighted MR imaging could provide direct visualization of morphological deformation as well as quantitative estimation of the PDs from that of the normal controls in-vivo. In conclusion, this study has demonstrated that using 7.0T MRI, one can visualize the pathologic features of PD within the SN.

REFERENCES: [1] Cho Z.H., et al., *IJIST*, 2008; **18(1)**:2-8, [2] Cho Z.H., et al., *Neuroimage*, 2010; **49(3)**:2134-2140

ACKNOWLEDGEMENT: This work was supported by the Korea Science and Engineering Foundation (KOSEF) grant funded by the Korea government (MOST) (Grant no. 20100002134).