Quantitative assessment of the substantia nigra, red and subthalamic nuclei in Parkinson's disease using susceptibility weighted imaging

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INTRODUCTION

The substantia nigra (SN), subthalamic nucleus (STN), and red nucleus (RN) are important structures in the study of Parkinson's disease (PD) and all three structures contain high concentrations of iron. A hallmark of PD is the increased deposition of iron in the SN and RN as well as the loss of dopaminergic neurons in the SN pars compacta. While susceptibility weighted imaging (SWI) [1] is unable to accurately measure the loss of dopaminergic neurons, it is sensitive to iron and susceptibility mapping has been used to segment the SN [2,3]. Deep brain stimulation of the STN is crucial in the treatment of PD and recent work has shown an image from an intermediary processing step, the filtered phase map, to provide more accurate results when segmenting the STN (see Fig. 1 for an example in visualizing the SN) [4]. In this abstract, volumetric measurements of the SN, STN, and RN are compared between PD and control groups. Additionally, the phase, which is a surrogate marker for iron content, in the SN, STN, and RN is also compared between PD and control groups.

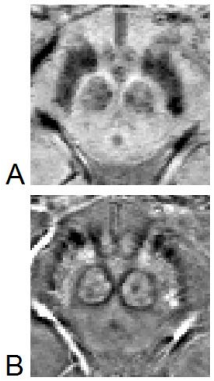

Fig. 1. A comparison of the SWI (A) and phase maps (B).

METHODS

Data Acquisition: A PD group consisting of 17 subjects (aged 63.8±9.5 years; UPDRS score = 36,1±13,2) and a control group consisting of 13 subjects (aged 71.6±5.5 years) was used in this study. The subjects in the PD group were clinically diagnosed PD patients and all subjects signed a consent form in accordance with our institutional review board requirements. All imaging data were acquired using a 3 T scanner (Skyra, Siemens Medical Solutions) using the 20 channel receive only standard head/neck coil. Susceptibility weighted imaging was performed using a three-dimensional gradient echo sequence with the following parameters: TE/TR=20/50 ms, 56 contiguous slices, 384×288 imaging matrix, 229×172 mm (0.59×0.59×1.5 mm), 1 average, flip angle (FA) = 17°, and 50 Hz/pixel receiver bandwidth.

RN and SN Segmentation: The RN and SN were segmented using the same procedure. A region of interest (ROI) was chosen in the midbrain tegmentum. The mean (μ) and standard deviation (σ) of the filtered phase map were calculated for the ROI. Next, a ROI was chosen, covering the entire brainstem, and voxels in this ROI that exhibited a phase value larger than μ+1.5σ were assumed to be in either the SN or RN.

STN Segmentation: A region of interest (ROI) large enough to contain the STN was chosen in the phase map. Then the STN was segmented using the following steps:

(1) The floor of the third ventricle and infundibular recess was identified.

(2) Target ROIs for STN were drawn from the following criteria: two circular ROIs with radius 3 mm, centered 3 mm left / right and 2 mm posterior to the base of the third ventricle.

(3) Voxels within the ROI whose intensity is equal to or higher than μ+1.5σ were considered to be part of STN.

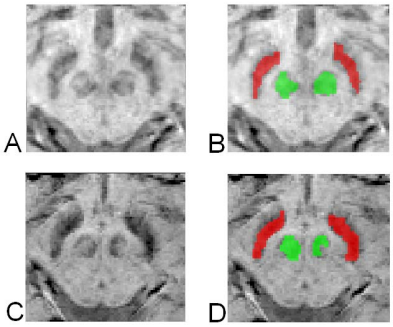

Fig. 2. A comparison of the SN and RN for a control subject (A & B) and subject with PD (C & D). The SN (red) and RN (green) masks are overlaid on the SWI images in B & D.

RESULTS AND DISCUSSION

Univariate analysis showed a statistically significant difference between the phase in the SN for the PD and control groups (p=0.003), indicating that excess iron is deposited in the SN after onset of PD. However the estimated SN volume did not offer a statistically significant difference between the PD and control groups, (p=0.19). The estimated SN volume for the control and PD groups was 677.0±87.5 mm^3 and 686.4±122.0 mm^3, respectively. Fig 2 offers a visual comparison of phase and volumetric estimates between the segmented SN, RN, and STN for a subject from each of the two groups.

This study analyzes group differences between subjects with PD and controls and found significant differences in the phase of the SN and volume of the RN across the two groups. While no significant difference was found in the phase values in the RN (PD phase = -0.066±0.020 radians; control phase = -0.075±0.018 radians; p=0.11), a statistically significant difference in the RN volume between the two groups was found (PD volume = 391.5±101.7 mm^3; control volume = 442.8±59.3 mm^3; p=0.034). No statistical difference of the phase values in the STN for the two groups was found (PD phase = -0.12±0.020 radians; control phase = -0.12±0.020 radians; p=0.48) and no statistical difference between the two groups was found for the STN volume (PD volume = 107.6±73.7 mm^3; control volume = 118.7±26.4 mm^3; p=0.07).

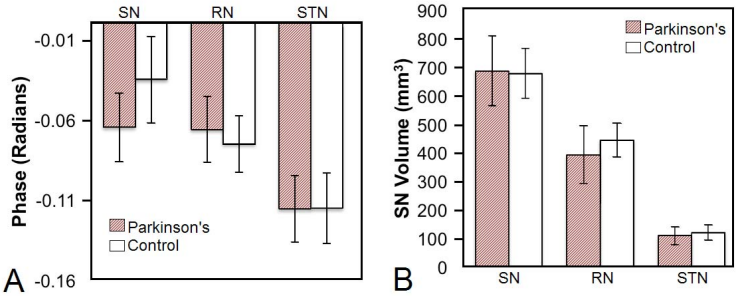

Fig. 3. A comparison of the phase and volumes of the PD and control groups the SN, RN, and STN.

The volumetric estimates seem to be in accord with the Braak hypothesis [5], which states that inferior portions of the brain stem will degenerate prior to superior portions after onset of PD. An eleven percent reduction in the RN is seen in the PD group when compared to the control group and a nine percent reduction is seen in the STN when the PD group is compared to the control group. One interpretation of this is that degeneration in the RN is in a more advanced stage than the STN. In addition, the increase in iron in the SN is also in accordance with previous findings that there is increased iron deposition in subjects with PD [5]. A possible reason for the non-significant volume differences in the SN between the PD and control groups may be the insensitivity of SWI to neuromelanin, which is a byproduct of dopaminergic neurons, degenerates in PD [6], and is sensitive to magnetization transfer contrast (MTC) [7].

CONCLUSION

The results of this study found statistically significant volumetric difference between PD and control groups in the RN and the phase difference between the two groups in the SN. Analysis of more subjects is currently underway to strengthen these preliminary findings allowing compelling conclusions in future.

REFERENCES: [1] Haacke, *et al*. Magn Reson Med 52:612 (2004); [2] Lotfipour, *et al*. Journal Magn Reson Imag 35:44 (2012); [3] Gupta, *et al*. Neuroradiol 52:1087 (2010); [4] Vertinsky, *et al*. Am J Neuroradiol 30:1717 (2009); [5] Braak, *et al*. Neurobio Aging 24:197 (2003); [5] Dexter, *et al*. Brain 114:1953 (1991); [6] Fearnley, *et al*. Brain 114: 2283 (1991); [7] Schwarz, *et al*. Movement Disorders 26:1633 (2011)