Comparison of Neuromelanin MRI with FP-CIT SPECT in Parkinson Disease

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Target Audience Neuroradiologists and Neurologists interested in Parkinson disease.

Purpose Neuromelanin (NM) is a complex polymeric molecule present in the human central nervous system[1] with the highest levels in the pigmented neurons of the substantia nigra (SN).[2] NM accumulates normally with age in human SN but is relatively depleted in patients with Parkinson disease (PD). PD is a neurodegenerative disease mainly characterized by a progressive loss of pigmented SN neurons which results in a striatal dopaminergic innervation loss. Single photon emission computed tomography (SPECT) with FP-CIT is an establish method to measure density of striatal dopamine reuptake transporters (DAT) and therefore striatal dopaminergic innervation.[3] Preliminary studies suggest that neuromelanin-sensitive MRI (NM-MRI) may provide an indirect measurement of the NM content in the SN.[4] The possible relation between SN vulnerability, the presence of NM, and the consequent dopaminergic loss at a striatal level has not been yet elucidated. The aim of this study was to compare NM-MRI measurements between Parkinson disease patients (PD group) and healthy controls (HC group), and to compare NM-MRI measurements with and FP-CIT SPECT binding values in order to provide new insights on the role of NM in the dopaminergic nigrostriatal system.

Methods We prospectively examined 18 PD patients (13 males; 46-72 years old; disease duration: 2-13 years) and 11 age-matched healthy controls (5 males; 46-86 years old) using the NM-MRI sequence obtained on a 3T scanner (Achieva, Philips Medical Systems, the Netherlands). The scan consisted of a T1-weighted fast spin echo sequence with magnetization transfer preparation pulses (TE/TR=12/670 ms, ETL=4, FoV=216x164 mm, acquisition/reconstruction resolution=0.5x0.6x3.0 mm/0.5x0.5x3.0 mm, five averages, acquisition time approx. 8 min). The background region and the SN were segmented from the NM-MRI images following the method proposed by Chen et al.,[5] (Fig. 1) using 3D Slicer (http://www.slicer.org). The mean contrast-to-noise-ratio (CNR) between SN and the background region, and the volume of the SN (number of voxels) were computed.

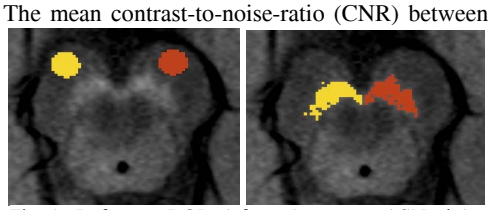

Fig. 1. Reference ROIs (left) and segmented SN (right).

Twelve of the PD subjects and a second group of 15 HC (4 males; 44-74 years old) underwent a FP-CIT (DaTSCAN, GE-Healthcare, UK) SPECT on a triple detector gamma-camera (Prism 3000, Philips Medical Systems, the Netherlands). FP-CIT binding values of the caudate nucleus (CN) and putamen (PT) were calculated on the basis of VOIs defined with the Basal Ganglia Matching Tool.[6] Imaging studies were performed when patients were on medication (L-Dopa 300-700 mg/day, L-Dopa equivalent daily dose: 240-752 mg/day). For statistical comparisons and correlations we applied the Wilcoxon rank-sum test and the Spearman rank-order correlation coefficient (Rho). Data are stated as mean ± standard deviation.

Results The PD group showed significantly lower CNR (left 4.46±0.35, right 4.36±0.47) and SN volume values (left 337±75, right 383±114) than HC (CNR left 4.87±0.37, right 4.84±0.43; SN volume left 455±68, right 475±95; $p<0.01$ for all analysis) (Fig. 2). DAT binding values were significantly reduced in PD (CN left: 3.41±0.77, right: 3.59±0.95; PT left: 1.82±0.59, right 2.32±0.79) relative to HC (CN left: 4.93±0.93, right: 4.95±0.97; PT left: 4.6±0.83, right 4.65±0.83; $p<0.01$ for all analysis), thus confirming the clinical diagnosis. DAT binding values positively correlated with both CNR (left: CN: Rho=0.64, PT: Rho=0.54; right: CN: Rho=0.70 PT: Rho=0.67) and SN volume (left: CN: Rho=0.63, PT: Rho=0.57; right: CN: Rho=0.83 PT: Rho=0.87) (Fig. 3).

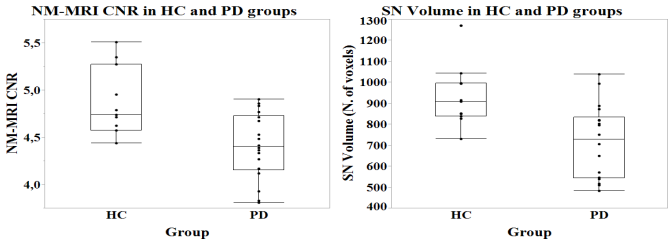

Fig. 2. Comparison of mean CNR (left) and SN volume (right) between HC and PD groups.

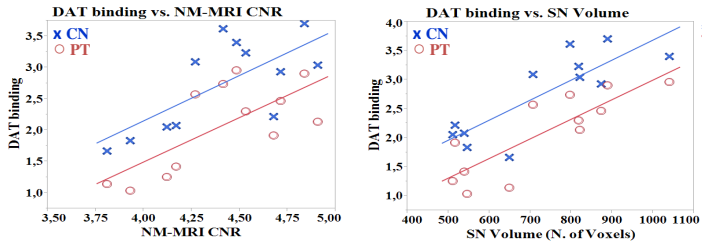

Fig. 3. Correlation between mean CNR (left) and SN volume (right) with mean DAT binding values of the caudate nucleus (CN, blue) and putamen (PT, red).

Discussion The main finding of this study is the positive correlation between NM content in the SN as seen by NM-MRI and the dopaminergic striatal innervation, suggesting that PD progression may be assess using the NM-MRI approach. We also confirmed that NM-MRI can differentiate between HC and PD groups. The correlation between NM-MRI and FP-CIT SPECT is a novel result supporting the idea that NM reduction and loss of dopamine secreting neurons in PD are associated processes, and suggesting that NM in the SN neurons may play a neuroprotective role.

Conclusion NM-MRI may be useful to quantify SN pathology in subjects with PD, which closely correlates with dopaminergic striatal innervation loss.

References

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