

## Relationship between neuromelanin-weighted MRI contrast and PET radiotracer binding to dopamine transporter in substantia nigra

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**Target Audience:** Neurologists and scientists who are concerned with Parkinson's disease and presynaptic dopaminergic functions

**Introduction:** Neuromelanin (NM) is a pigment that accumulates in the cell body of dopaminergic neurons in the substantia nigra (SN). The role of NM in dopaminergic function is still unclear, but the complex molecular structure of NM contains iron that shortens the longitudinal relaxation time and produces positive signal on T1 weighted images [1]. It is also known from studies with positron emission tomography (PET) showed that dopaminergic neurons in the SN also possess dopamine transporters (DATs). Since both NM and DAT exist in the cell body of dopaminergic neurons, there must be some relationship between the signals these two imaging modalities provide. We performed both [<sup>18</sup>F]FE-PE2I PET and NM MRI on selected groups of subjects to assess the presynaptic function of dopaminergic neurons in the SN.

**Materials and Methods:** Images were acquired for three groups: young healthy subjects (YHS: N=6), aged healthy subjects (AHS: N=6) and aged Parkinson's disease patients (APD: N=7). A dynamic PET scan (Siemens, HR+) was performed for 90 min after intravenous injection of [<sup>18</sup>F]FE-PE2I. Neuromelanin-weighted (NMW) images were acquired with a 3T MRI scanner (Siemens, Verio) using a 2D fast spin-echo sequence (TR/TE: 550/11 ms, resolution: 0.45 x 0.64, slice thickness: 2.5 mm). T1-weighted images were also acquired to aid spatial registration between the PET and NMW images. Registration and inter-subject anatomical normalization were performed with the statistical parametric mapping software (SPM8). The BP<sub>ND</sub> of dopamine transporter was calculated with a simplified reference tissue model using the cerebellum as a reference region. The anatomically normalized BP<sub>ND</sub> and NMW images were averaged across subjects before regions-of-interest (ROIs) were defined on the averaged images. The ratio of the pixel intensities in the SN and decussation of the superior cerebellar peduncles (R<sub>NM</sub>) was calculated, and R<sub>NM</sub> and BP<sub>ND</sub> were averaged over the bilateral SN ROIs. Statistical tests were performed with custom Matlab scripts. A p-value of less than 0.05 was considered significant.

**Results:** Fig. 1 shows images of the DAT-BP<sub>ND</sub> and R<sub>NM</sub> averaged within each subject group. The R<sub>NM</sub> was 1.18 ± 0.03, 1.20 ± 0.02 and 1.17 ± 0.03 for YHS, AHS and APD, respectively. Similarly, the DAT-BP<sub>ND</sub> was 0.64 ± 0.06, 0.44 ± 0.16 and 1.29 ± 0.04 for YHS, AHS and APD, respectively. Fig. 2 is a scatter plot of DAT-BP<sub>ND</sub> versus R<sub>NM</sub>. Negative correlations between the DAT BP<sub>ND</sub> and R<sub>NM</sub> were found (YHS: -0.11, AHS: -0.26 and APD: -0.53), but the results were not statistically significant.

**Discussion:** Both the DAT BP<sub>ND</sub> and R<sub>NM</sub> in the SN are affected by the age of the subject, which indicates that an aging effect should be considered when using these metrics. Multimodal imaging can produce more accurate measurements for the diagnosis of Parkinson's disease because the AHS and APD groups can be resolved on the scatter plot despite there being an overlap for the two groups when using either metric alone.

**Conclusions:** The R<sub>NM</sub> provides information about the presynaptic function of dopaminergic neurons in the SN that is supplementary to DAT PET. However, the role of NM in the dopaminergic system is still controversial and further studies are necessary.

**References:** [1] Sasaki M, et al., Clin Neuroradiol. 2008;18(3):147–53. [2] Ito H, et al., NeuroImage. 2008 Jan 15;39(2):555–65.

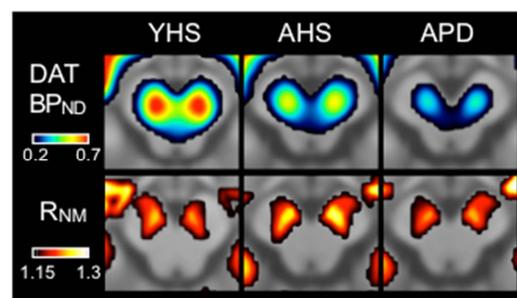


Fig. 1. Averaged images of dopamine transporter binding (DAT BP<sub>ND</sub>) and Neuromelanin-related signal ratio (R<sub>NM</sub>) for the three subject groups

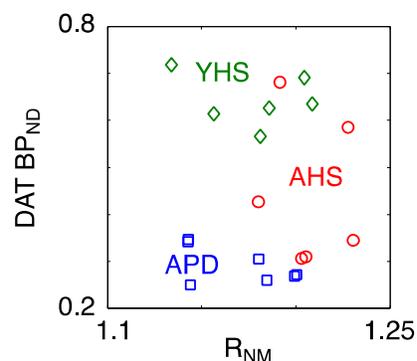


Fig. 2. Scatter plot of DAT BP<sub>ND</sub> vs R<sub>NM</sub>