Association of neurodegenerative markers with T2 hypointensities in the basal ganglia

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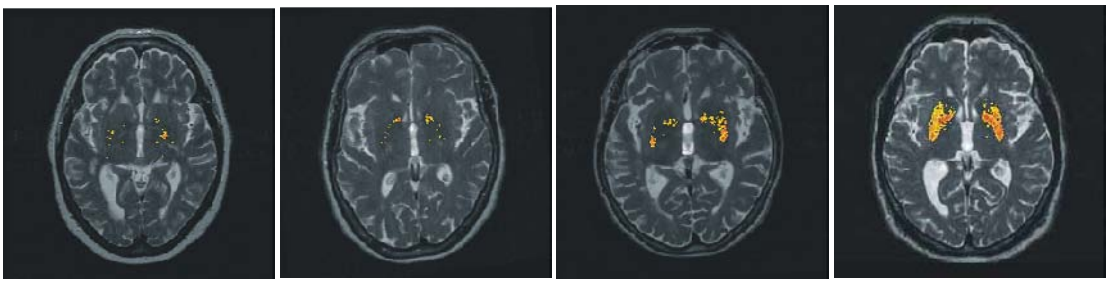
Synopsis:
Hypointensities on T2-w MRI in the basal ganglia is a frequently observed finding, and is thought to be associated with age. Due to absence of adequate scoring system of these hypointensities, its clinical relevance is still unknown. In the present study we quantitatively determined the hypointense lesion load in the basal ganglia in a large cohort of atherosclerotic patients. Our data show a significant correlation between the basal ganglia lesion load with atrophy ($p<0.01$) and intracranial normalized MTR peak height ($p<0.05$). No association was found with age or gender. Therefore hypointensities in the basal ganglia may be an easy assessable marker of overall neurodegeneration, independent from age and gender.

Introduction:
An age-related progressive shortening of T2 relaxation time, resulting in a decrease in signal intensity on T2-weighted Magnetic Resonance Imaging (MRI), has been found in the basal ganglia in several studies. It is thought that this process follows a age related preferential pattern in which the globus pallidus becomes hypointense in early adulthood whereas the putamen is involved after the age of approximately 70 years (18). This age related increase in signal hypointensity is largely attributed to increasing iron concentration. In this respect, excessive deposition of iron has been reported in neurodegenerative diseases like Alzheimer's, Parkinson's, Huntington's disease and Multiple Sclerosis. It has been put forward that hypointensities of the basal ganglia on MRI might be associated with cerebral neurodegenerative processes. The aim of the present study is to investigate whether the presence of hypointense basal ganglia on T2-weighted MRI is associated with radiological signs of neurodegeneration (deep and periventricular white matter hyperintensities (WMH), atrophy and Magnetization Transfer (MT) Ratios.

Method:
558 patients (mean age 77.4 $\pm$ 3.4y, 42%-m/58%-w) were analyzed. Patients were screened for atherosclerotic risk factors. Inclusion criteria for this study were: men or women aged 70-82 years; total cholesterol 4.0-9.0 mmol/L; stroke, transient ischemic attack, myocardial infarction, arterial surgery, or amputation for vascular disease >6 months before study entry; $\geq$1 of the following risk factors for vascular disease: current smoker; hypertension, currently receiving drug treatment; known diabetes mellitus or fastening blood glucose >7 mmol/L. All imaging was performed on a 1.5T MR system (Intera Philips Medical Systems, Best, The Netherlands). In addition to dual fast spin echo [TR = 3000 msec; TE = 27/120 msec; flip angle = 90°; section thickness = 3 mm; number of sections = 48; no section gap; whole brain coverage; FOV = 220; scan percentage = 80%; matrix = 256] and fluid-attenuated inversion recovery (FLAIR) [TE = 100 msec; TR = 8000 msec; flip angle = 90°; section thickness = 3 mm; sections = 48; no section gap; whole brain coverage; FOV = 220; RFOV = 80%; scan percentage = 75%; matrix = 256], MTI of the brain was performed using a 3-dimensional (3D) gradient-echo pulse sequence [28 axial slices, slice thickness = 5 mm; no gap; TR/ TE msec 106/6; flip angle = 12°; field of view = 220 x 220 mm; matrix = 256 x 256, a sinc-shaped saturation pulse 1100 hertz below frequency of water was added]. These scan parameters were chosen to minimize T1 and T2 weighting, resulting in a proton-density contrast in the absence of MT saturation pulses. Two consecutive sets of images were acquired; the first was performed in combination with the MT saturation pulse, and the second without. To calculate the volume of basal ganglia hypointensities, we used in home developed software.[1] In the short: Based on normalized MRI T2-w images, each pixel intensity in the basal ganglia was analyzed according to a threshold with was optimized using a gold standard (manual segmentations) and subsequent ROC curve analysis. Associations between the hypo intensity load in the basal ganglia and neurodegenerative parameters were calculated using linear regression analysis corrected for age and gender.

Results:
The figure below shows 4 examples indicating a basal ganglia lesion load ranging from mild (left) to severe (right)



For the entire patient group we found a mean hypo intensity load of 0.99 ml (range 0.00 - 4.16, 95% CI: 0.93 – 1.06). We found a significant correlation between the basal ganglia lesion load and atrophy ($p<0.01$) and intracranial normalized MTR peak height ($p<0.05$) (both corrected for age and gender). No association was found with periventricular nor with deep white matter lesion load (expressed in ml). Also, no separate associations between hypo intensity load and age or gender was found.

Conclusion:
Hypointensities in the basal ganglia, frequently observed on T2-w MRI, may be an easy assessable marker of overall neurodegeneration, independent from age and sex.

[1] Marker for T2 Hypointensity Load, R.S. Jasinschi, A. Ekin, A.C.G.M. van Es, M.A. van Buchem, R. Engbers, A. van Muiswinkel, J. van der Grond, *ISMRM* 2007
[2] Shape-directed, landmark-based deep gray matter segmentation for quantification of iron deposition, A. Ekin, R.S. Jasinschi, J. van der Grond, M.A. van Buchem, and A. van Muiswinkel, *Proc. of SPIE on Med. Imag.*, 2006.