Iron in basal ganglia causes weak reproducibility of T2-weighted images at 3.0 Tesla

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Introduction

The basal ganglia play a role in a highly complex and widely distributed neural network in which sequences of activation and inhibition are coded in both time and space with exquisite precision [1]. Many common neurological and psychiatric disorders, such as Parkinson disease, attention deficit-hyperactivity disorder, Huntington disease, and Tourette syndrome are primarily due to basal ganglia dysfunction, and many other diseases such as schizophrenia and drug addiction are influenced by the basal ganglia [1]. The basal ganglia consist of the caudate nucleus, putamen, globus pallidus, subthalamic nucleus, and substantia nigra; the caudate and putamen together are collectively known as the striatum. As the basal ganglia are interconnected with all lobes of the cerebrum, and are in a key position to modulate all aspects of mental life, the basal ganglia is the focus of many quantitative MRI investigations [2].

It is important to study and report the reproducibility of quantitative MRI methods, as individual changes associated with a certain pathology, progression of disease, advancing age, or intervention can only be detected when the deviation from normal values is larger than the reproducibility of that particular measurement. Therefore, knowing the reproducibility limits in terms of physical quantities provides information to which extent measured tissue values can be classified as normal or abnormal. Reproducibility is defined as the extent to which repeated measurements on the same subject are in agreement. We set out to assess the reproducibility of T2 relaxometry of the whole cerebrum (including the basal ganglia) on a clinical 3.0 T MR system.

Material and Methods

10 healthy volunteers were imaged twice (on two separate days) with a 3.0-Tesla whole-body unit (Philips Achieva, The Netherlands), using an 8 channel SENSE head coil. For anatomic reference, a T1-weigthed 3D TFE was acquired with the following parameters: repetition time (TR) 9.91 ms, echo time (TE) 4.6 ms, inversion time (TI) 3 s, flip angle 8°, matrix 256x256x160, field of view (FOV) 256x256x160 mm^3, 1 mm adjacent coronal slices. For T2 quantification a 3D TSE-Dual was performed, using: TR 2500 ms, TE_1 10 ms, TE_2 110 ms, matrix 256x256x100, FOV 256x256x200 mm^3, 2.0 mm adjacent coronal slices, SENSE factor 1.5 (left-right). T2 was calculated (in ms) on a voxel-by-voxel basis using the signal intensities of the images obtained at the two echo times. The T2-map was spatially normalized into common coordinates along with the spatial normalization procedure of the TE_2 image. Descriptive statistics were derived on a voxel-by-voxel basis, using the coefficient of variation (CV), and the intraclass correlation coefficient (ICC). Following the methods of Bland and Altman, the CV was estimated by calculating the overall mean within-subjects standard deviation (SD_{ws}) of a given measurement and dividing it by the mean measurement value for all subjects [3]. Additionally, an ICC was calculated, using a one-way random model [4], according to $ICC = SD_{bs}^2 / (SD_{bs}^2 + SD_{ws}^2)$, where SD_{bs} represents between-subjects standard deviation. To correct for imperfections in the spatial matching between the two scan sessions, the T2-maps were smoothed using a Gaussian kernel with a FWHM value of 6 mm.

Results (Figure 1)

In Figure 1A a typical normalized T2-weigthed image (TE = 110 ms) is shown (red arrows indicate decreased signal intensities). In Figure 1B-C, the areas that display high CV (1B) and low ICC (1C) values for the T2 measures are projected on a transverse T1-weighted slice. Several regions display less favorable reproducibility characteristics (expressed by high CV values or low ICC values). Some of these regions (indicated with blue arrows in Figure 1B) display a large variability in CSF content (e.g. near the dorsal horns of the ventricles). The areas (indicated with green arrows in figure 1C) that display less favorable reproducibility characteristics on the ICC are part of the basal ganglia, anterior to the thalamus, which includes the head of the caudate nucleus, the putamen, and the internal capsule.

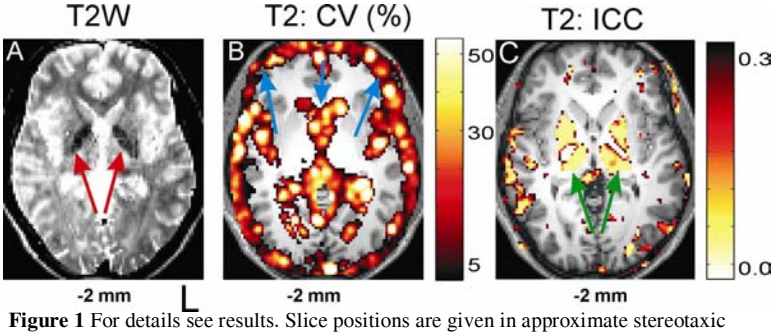

Figure 1 For details see results. Slice positions are given in approximate stereotaxic Talairach z-coordinates

Discussion

The prominent decrease of T2-weighted signal intensity in basal ganglia, can be attributed to high levels of iron leading to T2-shortening of bulk water protons by means of a mechanism involving diffusion of water through local magnetic field gradients generated by iron [5]. The primary form of tissue iron storage is ferritin, which stores excess iron atoms that are not immediately engaged in metabolic activities [6]. The voxels that have large CV values for the T2-map (figure 1B) all have (partial) contribution from the CSF. As the dual spin echo technique used to obtain T2-maps was specifically aimed at determining reliable T2 values for cerebral tissue, the calculated T2 of CSF containing voxels is inaccurate, which results in high CV values for those voxels. The brain regions close to the CSF spaces (i.e. ventricles and pericortex) display large CV values due to the highly variable local size of CSF space throughout the volunteer population. This was confirmed by high between-subject variance in these regions (data not shown). However, the CV has major limitations as a measure of precision, the most important of which is the dependence on the magnitude of the measured value. Therefore, a single value for CV not necessarily describes the true precision and ICC might give a better indication of the reproducibility.

In Figure 1C it can clearly be seen that the iron-rich basal ganglia display low ICC values. The shortening of T2 values due to iron is a well known phenomenon, that has even lead to the characterization of iron concentrations using MRI [6,7], however, we show here that at 3.0 Tesla this susceptibility effect is not very reproducible. The poor reproducibility of the basal ganglia was confirmed by high within-subjects variance in these regions, furthermore the same regions displayed weak reproducibility in a diffusion tensor imaging experiment (data not shown). We can only speculate whether this poor reproducibility is of biological origin, or might be due to slightly different positioning and orientating during the two examinations. As the basal ganglia are of non-spherical shape, its orientation in the magnetic field can be important. Nevertheless, the weak reproducibility in the basal ganglia is important to consider when one is planning to perform an MRI examination aimed at studying the basal ganglia, using T2-weigthed sequences (e.g. for T2 relaxometry, diffusion tensor imaging or fMRI).

References

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