Mapping Human Subcortical Areas in Vivo Based on T2*-weighted, R2* and Phase Images at 7 T

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Introduction: Subcortical brain regions such as the basal ganglia and thalamus have important roles in brain function that may be compromised by a number of diseases. Their accurate localization is often challenging with clinical MRI contrast such as T1 and T2 that are optimized to distinguish the main tissue compartments of CSF, grey matter (GM) and white matter (WM). Previous work has shown that magnetic susceptibility contrast (T2* weighted magnitude, R2*, and phase images) may provide additional contrast in subcortical regions[1]. Here, we set out to generate a brain atlas with the aim to distinguish the sub-regions in the subcortical areas that are not clearly visible in a conventional T1-based atlas[2].

Materials and Methods: Ten healthy volunteers (F/M = 5/5, age = 45.9±12.1, 22 – 66 yrs) participated in this study. A 2D multi gradient-echo acquisition (GRE) was performed with the following parameters: TE = 15.5/ 30.0/ 44.5 ms, TR = 2 s, resolution = 0.31×0.31 mm^2, slice thickness/gap = 0.8/0.2 mm, flip angle= 75°, bandwidth= 62.5 kHz, SENSE acceleration rate = 2. Quantitative R_2^* maps were derived from mono-exponential fitting. The unwrapped phase maps were calculated from the first echo (TE = 15.5 ms) phase data using FSL and the background phase was derived by convolving a Gaussian kernel (FWHM = 5 mm) with the unwrapped phase map. Continuous phase maps were then generated by subtracting the background phase from the unwrapped data. A standard T1-weighted (T1-W) 3D MP-RAGE image was also acquired for each volunteer at 1×1×1 mm^3 resolution. To generate the brain atlas, image registration between subjects was performed based on the T1-W data as follows. First, the T1-W data from individual volunteers was registered to the MNI standard brain using a combination of linear and nonlinear registration. Similarly, linear registration was used to align the GRE magnitude images (TE = 30 ms) to the T1-W images. Finally transformation operations from both registrations were used to align and average each contrast across subjects.

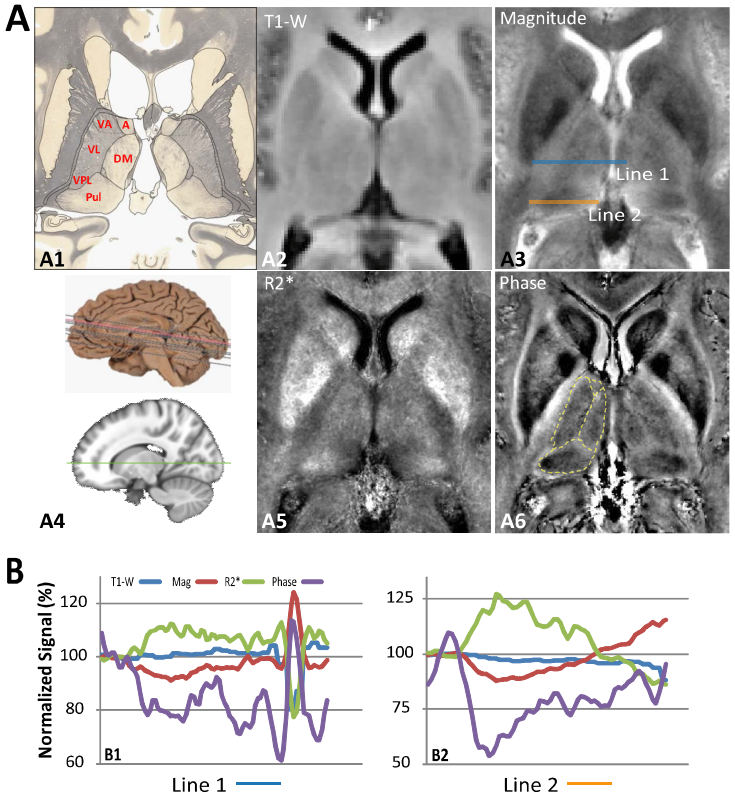

Fig. 1: ***A)*** *One axial slice showing contrast at subcortical regions from group averaged T1-W, GRE-magnitude, R2* and phase images, in comparison with tissue myelin stain image at the similar location (the slice direction are slightly different between MRI and stain image, as shown in **A4**). A: anterior; DM: dorsomedial; Pul: pulvinar; VA: ventral anterior; VL: ventral lateral; VPL: ventral posterolateral;* ***B)*** *Line profiles in the areas marked on **A3**.*

Results: In **Fig. 1A** a single axial slice of the group-averaged MR images containing Caudate Nucleus (CN), Putamen (PU), Globus Pallidus (GP) and thalamus (TH) is compared with a myelin staining image from a similar location, showing the main anatomical structures[3]. The PU and GP are identifiable in all MRI images, although their contrasts appear much stronger in susceptibility contrast images (magnitude, R2* and phase). The CN is poorly visible in the magnitude image but shows the strongest contrast in the phase image. The TH is not clearly distinguishable from the surrounding WM in the T1-W image but it shows a clear boundary in magnitude, R2* and especially the phase images. Some sub-regions of the thalamus including the ventral lateral thalamus (VL), dorsomedial thalamus (DM) and pulvinar (Pul) are distinguishable in magnitude and R2* images, with the strongest contrast seen in the phase image. To facilitate comparison of contrasts in the various images, the intensity of the images were normalized to the range of [0, 1]. Line profiles of normalized image intensity through the DM, VL and part of nearby internal capsule (Line 1 in **Fig. A3**), as well as through Pul and nearby internal capsule (Line 2 in **Fig. A3**) were shown in **Fig. 1B**. T1-W shows a relatively flat line across the regions, indicating little contrast between thalamus and neighboring WM. Interestingly, the phase image shows strong contrast reaching about 20% decrease in VL and DM (**Fig. B1**) and close to 50% decrease in Pul (**Fig. B2**) (values relative to internal capsule of WM). The magnitude contrasts decreased 6-9% in VL and DM and 13% in Pul. The R2* contrasts shows 8-10% increase in VL and DM, and 25% increase in Pul.

Discussion: In subcortical brain regions, brain atlases generated from susceptibility weighted images, and phase images in particular, show a much stronger contrast than an atlas based on T1-W images. This contrast is attributed to susceptibility induced magnetic field shifts generated by the increased iron content in the GM of this area[4]. Regions in WM such as the internal capsule and optical radiation have abundant myelin, which results in an overall diamagnetic field shift, accentuating the paramagnetic shift in the iron rich basal ganglia and thalamus. Some of the sub-regions in the thalamus are distinguishable in the GRE magnitude, R2* and phase images. Since all sensory pathways relay through distinct region-specific thalamic nuclei, the parcellation of sub-thalamic regions based on susceptibility contrast images may provide anatomic guidelines to neuroimaging studies investigating thalamic function and thalamo-cortical pathways.

References: 1. Duyn J, *PNAS*, 2007; 2. Ahsan RL, *NI,* 2007; 3. Nolte J, *The Human Brain*, 2002; 4. Yao B, *NI*, 2009; 5. Yao B, *Radiology*, 2011