Improved direct localization of the human pedunculopontine nucleus (PPN) by 3D FLASH MRI at sub-millimeter resolution

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Introduction: The pedunculopontine nucleus (PPN) is a potential target for deep brain stimulation to address symptoms of gait freezing and postural instability in Parkinson's disease. Proton density-weighted (PD-w) MRI has been recommended to locate its position [1] in the reticulate formation of the mid brain notorious for its poor contrast on T1-w MRI. We expected to improve contrast and delineation of the PPN area a) by increasing the spatial resolution in 3D MRI, and b) by eliminating the residual influence of T1 from the PD-w images. This strategy has been successfully applied to depict the deep cerebellar nuclei [2]. To achieve these goals, a two-point multi-echo FLASH (Fast Low-Angle Shot) protocol [3] was performed to determine the signal amplitude S0 and the longitudinal relaxation time T1.

Methods: Upon assessment of the PPN on amplitude maps of a previous whole brain study performed at 0.95 mm resolution [4], seven healthy volunteers were examined with an identical protocol but at 0.8 mm resolution. A multi-echo FLASH sequence provided 3D data sets of predominant T1-w and PD-w (TR = 30 ms, flip angle = 20° and 7°, respectively). Eight bipolar gradient-echoes (TE = 2.3/5.2/8.2/11.2/14.2/17.2/20.2/23.2 ms) were acquired at a rather high bandwidth (370 Hz/pixel) and averaged, thus reducing susceptibility-related distortions and increasing the signal-to-noise-ratio (SNR) [5]. This high-resolution protocol was adapted to yield clinically feasible measurements (16 minutes) on a 3T whole-body MR system (Tim TRIO, Siemens, Erlangen, Germany, 32-channel head coil) and tested on 2 patients with Parkinson's disease. A 5 cm axial-oblique slab from the frontal pole to the occipital pole (205x180 mm FOV) covered the diencephalon, mesencephalon, and the upper part of the cerebellum. Each measurement took about 4 minutes using partial acquisition (6/8 partial Fourier in phase and slice directions, generalized auto-calibrating partial parallel acquisition (GRAPPA) in phase direction) and was repeated twice to compensate for the reduced SNR at 0.512 microliter voxel size. In addition, sagittal 3D MP-RAGE data were acquired at 0.9 mm isotropic resolution for anatomical reference (Fig. 1). Following conversion into nifti format, these were interpolated to 0.5 mm resolution to serve as a reference to register the four slab-selective dataset to account for patient movements. Co-localized maps of the signal amplitude S0 and the longitudinal relaxation time T1 were calculated as described in [4]. No correction for radio-frequency (RF) inhomogeneities was performed since slowly varying RF bias did hardly affect local contrast. BrainPath planning software (Neurostar, Sindelfingen, Germany) was used to reconstruct axial images at a plane perpendicular to the midline of the fourth ventricular floor.

Results: S0 maps showed high contrast in the PPN region and allowed a better identification of mid-brain white matter structure surrounding the PPN than the PD-w images, whereas T1-w images and T1 maps showed poor contrast. The PPN could be directly localized according to [1] within the gray matter lying lateral to the superior cerebellar peduncle (SCP: green) and its decussation, next to the central tegmental tract (CTT: blue) and medial to the lemniscal system (LS: yellow) as shown in fig. 2 a'-c'. Short axis views of the amplitude maps allowed a localization of the PPN along its whole extent (Fig. 2 a-c). At 0.95 mm resolution the lemniscal system was clearly delineated only in one of eight subjects. Despite a lower SNR, the lemniscal structures were clearly visible in all healthy subjects examined at 0.8 mm resolution. The S0 contrast was not compromised by pathological changes in the two patients examined so far.

Discussion: Landmarks along the whole length of the PPN were unequivocally depicted on S0 maps calculated from 3D FLASH MRI at 0.8mm isotropic resolution, other than on 2D PD-w gradient echo MRI at 1.5T [1]. Thus, a more reliable direct localization of the human pedunculopontine nucleus could be achieved. Resolution was more important than SNR. A residual degree of T1-weighting in our 3D PD-w data was removed by calculating S0 maps. Multi-echo averaging imposed some additional T2* weighting corresponding to the mean TE [5]. This further enhanced the contrast between reticulate formation and surrounding white matter tracts. In case of poor compliance/motion, any of the rather short blocks may be easily discarded and re-run.

References: [1] Zrinzo et al., Brain 131:1588-98 (2008); [2] Deoni, Catani NeuroImage 37:1260-6 (2007); [3] Deoni et al. MRM 49:515-26 (2003); [4] Helms et al., MRM 59:667-72 (2008); [5] Helms, Dechent JMRI 29:198-204 (2009);

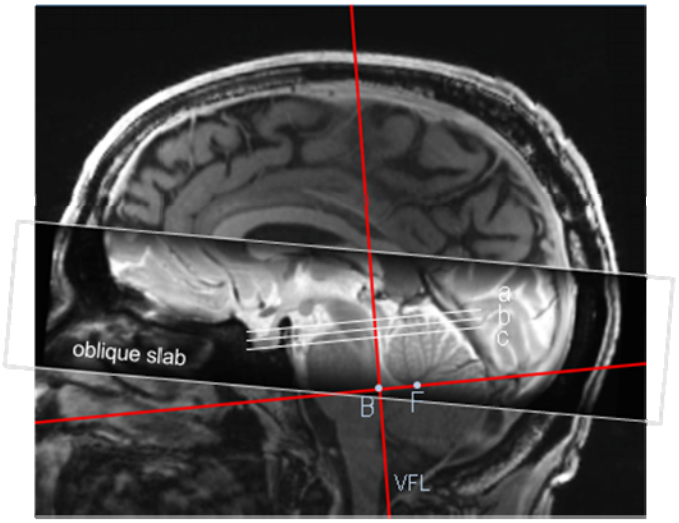

Fig. 1: Oblique slab of a S0 map coregistered to a 3D MP-RAGE dataset for anatomical reference. White lines a-c indicate the axial slice positions in an infratentorial reference system at a plane perpendicular to the midline of the fourth ventricular floor: on the mid-sagittal plane the red VFL line is tangential to the fourth ventricular floor with the red line BF perpendicular to VFL; point B is the origin of the reference system; point F is the fastigium of the fourth ventricle. Slice position a: level of rostral PPN and mid-inferior colliculi. Slice position b: through middle of PPN. Slice position c: level of caudal PPN (5mm caudal from position a).

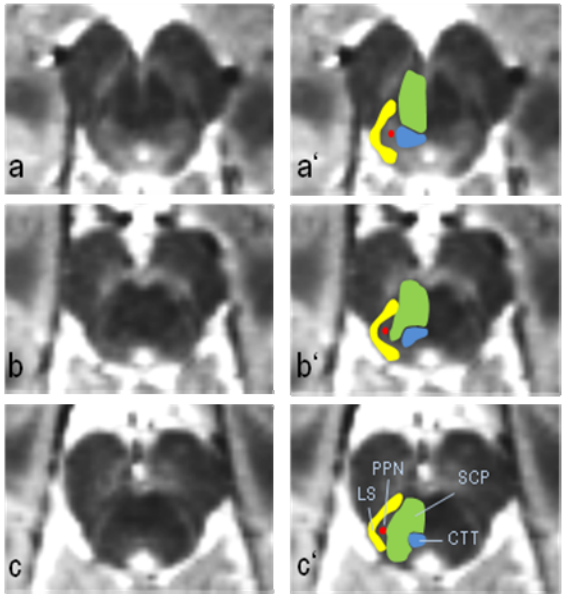

Fig. 2: Axial sections a-c of the calculated S0 maps of a representative volunteer showing the PPN in its cranio-caudal extent as displayed in fig. 1 a-c. The PPN could be directly localized a'-c' within the gray matter lying lateral to the superior cerebellar peduncle (SCP: green) and its decussation, next to the central tegmental tract (CTT: blue) and medial to the lemniscal system (LS: yellow). The PPN is represented by a red circle.