HIGH-RESOLUTION PHASE, SUSCEPTIBILITY-WEIGHTED AND BOLD FMRI MEASUREMENTS OF THE HUMAN LATERAL GENICULATE NUCLEUS AT 7T

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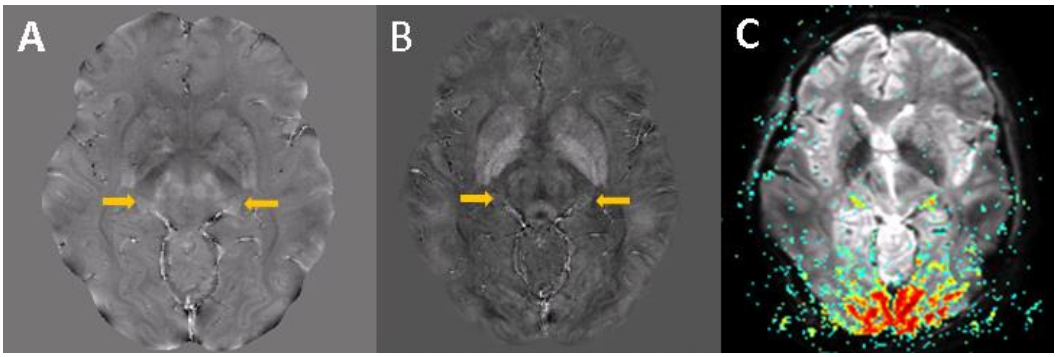
Introduction The lateral geniculate nucleus (LGN) is a small thalamic nucleus that serves as an important relay station in the projection of visual inputs to the striate cortex. Its small size (maximum diameter of 4-6 mm[1]) and proximity to other small subcortical structures which have similar signal intensities on T_1 and T_2 weighted MRI images make its definition in such images technically challenging [2,3]. Previously, proton density (PD) weighted images have been used to aid the detection of the LGN, as it appears bright on these images [2]. Recent improvements in functional MR imaging have enabled the use of blood-oxygen-level dependent (BOLD) contrast to define the LGN based on its responses to visual stimuli. Here, we combined anatomical and functional imaging at 7 T to detect and delineate the LGN. We show that imaging with phase-sensitive contrast can be used in combination with fMRI to easily and accurately detect and delineate the LGN in healthy volunteers. Both phase and functional MR imaging benefit from the increased signal-to-noise ratio at 7T, which can afford substantial improvements in spatial resolution.

Methods Two healthy subjects participated with consent according to regulations and ethics approval of the University of Nottingham Medical Ethics Board. Scanning was performed at 7T (Philips Achieva) using a 16- channel receive coil and a head only volume transmit coil. T2*-weighted structural images (0.5 mm isotropic resolution) were acquired using a 3D spoiled gradient echo sequence (FOV:192×164×25 mm^3, TE = 20 ms, TR = 50 ms, flip angle 14°, SENSE factor 2, EPI factor 3, imaging time 2.2 mins). Functional MRI was performed using single-shot multi-slice gradient echo, echo-planar imaging with the following parameters: 16 slices, FOV: 200×200 mm^2; 1.25 mm isotropic resolution; TE = 25 ms, TR = 2000 ms; flip angle, 90; SENSE factor 2, phase encoding RL. The visual stimulation paradigm consisted of a flickering checkerboard stimulus which alternated every 10 s between the left and right visual field (1-8º eccentricity). The stimulus was projected onto a screen at the end of the scanner bed and viewed by the subject using prism goggles. Subjects were instructed to focus on the fixation cross at the centre of the screen and performed attentionally demanding 'fixation dimming' task. Each functional scan (8 cycles each lasting 20 s; total time 160 s) was repeated eight times. At the end of each session, a T1-weighted MPRAGE data set was acquired with the same slice geometry as the EPI data to facilitate subsequent registration and display of functional data. To allow comparison to previously published results, data were acquired axially with posterior angulations relative to the standard axial plane (AC-PC line) as described by Horton [2].

Data analysis: A binary mask of the brain was produced using BET (FSL; FMRIB, Oxford). PRELUDE was used to unwrap the resulting phase images within the mask. A high-pass filter was used to remove unwanted, non-local phase changes and the data were scaled by $\gamma B_0 TE$ to yield field maps in ppm. Susceptibility maps were created by division of the field map in k-space by the dipole convolution kernel, $C(k) = \frac{1}{3} - \cos^2 \beta$ where β is the angle between k and kz . The 'division by zero' problem occurring on a conical surface in k-space at β = 54.7º was overcome by using a simple threshold-based method [4]. fMRI data were analysed using mrTools software (NYU http://www.cns.nyu.edu/heegerlab/wiki/; VISTA, Stanford) implemented in Matlab (Mathworks, Natick, MA). Individual scans were first motion corrected, then averaged together and analysed using standard Fourier-based methods to produce coherence and phase maps of the BOLD response at each voxel. For direct comparison, fMRI data were co-registered to the high-resolution T2* weighted GRE images as well as phase and susceptibility maps.

Results The LGN appears bright on both phase and susceptibility maps, but the borders of the LGN appear clearer in phase maps. The location and size of the LGN in the anatomical images is consistent with previous histological reports: it is enclosed by the posterior limb of the internal capsule, the optic radiation, and the lateral recess of the ambient cistern. Figure1 shows the LGN appearance on (A) unwrapped, high pass filtered phase image, (B) a susceptibility map, and (C) on a statistical map of fMRI activation (thresholded coherence, c>0.4) superimposed on the mean EPI image. Stimulus-related BOLD responses were clearly visible on 5 consecutive slices (thickness = 1.25 mm).



Discussion Unwrapped and high pass filtered phase data obtained with high-resolution T2*-weighted imaging provide an excellent method of detecting and delineating the lateral geniculate nucleus. Susceptibility maps derived from these phase images showed hyperintensity in the LGN, but boundary definition was clearer on the phase images, which might be expected due to known distortions of phase distributions at the edges of susceptibility perturbers [4]. In similar work Vertinsky et al [5] previously recommended using phase images to detect the medial geniculate body. Previous structural studies have generally imaged the LGN coronally [2], but in this work we used axial imaging to provide robust fMRI data at the base of the brain at 7T. To our knowledge, this is the first study that explicitly correlates the LGN on phase and susceptibility maps with functional MRI data. Future plans include scanning more healthy subjects to establish a baseline in healthy controls. We are also planning to use this protocol to image the LGN in patients with clinically isolated syndrome (an early manifestation of multiple sclerosis, MS), who present with optic neuritis and are known to have a temporarily perturbed vision. Obtaining anatomical and functional data in such patients may help elucidate the mechanisms underlying (and the recovery from) the visual disturbances associated with MS.

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References**:** [1] T. J. Andrews et al. The journal of Neuroscience, 1997,**8**,2859-2868. [2] J. C. Horton et al. Arch Neurol,1990,**47**,1201-1206. [3] N. Fujita et al. AJNR,2001,**22**,1719-1726. [4] Wharton et al Magnetic Resonance in Medicine 2010,**63**, 1292–1304 [5] A.T. Vertinsky et al. AJNR,2009,**30**,1717–1724.