Voxel-based morphometry at 3 Tesla: which T1-weighted sequence is best?

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Introduction: When investigating subtle structural brain differences between subject populations using voxel-based morphometry (VBM), large groups are often desired, leading to the participation of multiple imaging centers. The stability of the VBM process, over time and across sites, is crucial in such studies to enhance the power of statistical results. The accuracy of VBM results is equally important as it ought to represent a biologically meaningful measure of disease activity or regression. We recently presented an evaluation of T1-weighted anatomical protocols at 3T in terms of basic image quality metrics [2]. The purpose of this study is to evaluate the same sequences, FLASH, MP-RAGE and MDEFT, from the perspective of VBM, to determine which sequence is best suited to this particular analysis technique.

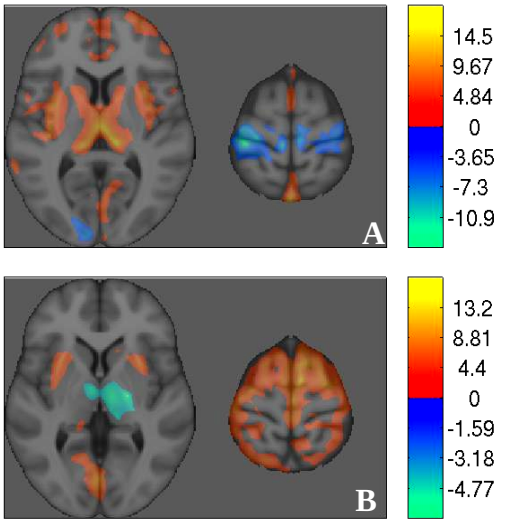

Figure 1: t-map of [GM]: A) MP-RAGE (cool) - MDEFT (hot); B) FLASH (cool) - MDEFT (hot)

Methods: Nine volunteers were scanned twice on a Siemens Trio 3T MRI system with an 8-channel receive-only head coil. The FLASH sequence corresponds to the default Siemens 3D high-resolution brain imaging protocol distributed with the Trio, with α/TE/TR set to 18°/5.67ms/ 19ms and elliptical k-space coverage. The MP-RAGE sequence was adapted from the ADNI protocol [1], with TI/α/TE/Tes/TR set to 960ms/9°/4.19ms/9.9ms/2420ms. Our implementation of MDEFT [2] has TI/τ1/α/TE/Tes/TR set to 680ms/319.6ms/22°/ 4.26ms/10.6ms/1608.4ms and centric-interleave partition encoding. For both MP-RAGE and MDEFT, no segmentation was performed, and a full echo was acquired. All three sagittal acquisitions have matching fields-of-view of 176×224×256 mm^3, 1mm isotropic resolution, 150 Hz/px bandwidth and scan times of 9 min 28 sec (within 5%).

The images were corrected for non-uniformity using N3 [4], and linearly registered using ANIMAL [5] to the ICBM 152 non-linear symmetric brain template. We performed a VBM analysis of grey matter (GM) tissue density between the sequences in a pair-wise manner. The GM tissue maps, created by INSECT [6], were smoothed by an isotropic 8mm FWHM Gaussian kernel prior to statistical analysis. The significant differences between the sequences, for both local maxima and clusters, were inferred using the most limiting of non-isotropic random field theory and Bonferroni correction for $p<0.05$ [7]. We also performed a VBM study of GM density variability by analyzing the difference between the scan-rescan GM tissue maps.

Results: t-maps indicating significant differences in GM concentration estimates between sequences are illustrated in Figure 1. MP-RAGE has higher GM density than MDEFT in the motor and somato-sensory cortex, as well as in the left occipital pole as seen in Figure 1A. MDEFT has higher GM density in the frontal cortex, along the longitudinal fissure, some parts of the temporal and cerebellar cortex, as well as in deep GM structures including the caudate, putamen, globus pallidus and thalamus. Figure 1B shows that FLASH has higher GM density than MDEFT in the thalamus, brain stem, along the lateral fissure and the amygdala. Whereas MDEFT shows higher GM density along the longitudinal fissure, in the left cerebellar cortex, putamen, claustrum and the cortex along the top of the frontal and parietal lobes.

Figure 2 illustrates regions of significant difference in GM concentration variability between sequences. Figure 2A shows that MP-RAGE has more clusters of higher variability than MDEFT, for a total volume of 64,523 mm^3 in comparison to only 9,502 mm^3. Figure 2B shows large areas of higher variability in FLASH than in MDEFT, including mainly deep GM structures, for a total volume of 152,403 mm^3. MDEFT does not have any areas with significantly higher GM concentration variability than FLASH.

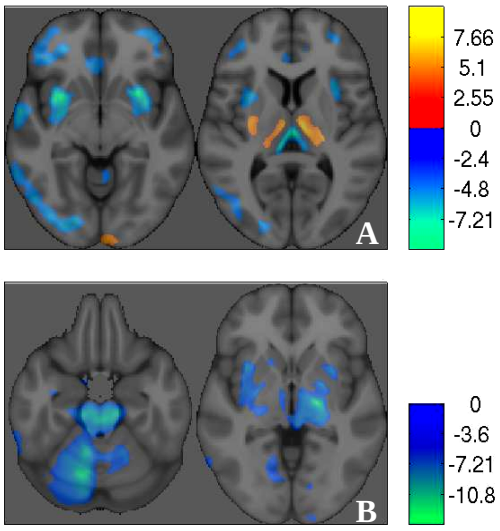

Figure 2: t-map of [GM] variability: top, MP-RAGE (cool) - MDEFT (hot); bottom, of FLASH (cool) - MDEFT (none)

Discussion: First and foremost, this study demonstrates that the choice of acquisition sequence has a significant effect on VBM results, for both regional accuracy and variability. It is thus critical that acquisition protocols be standardized in multi-centre and longitudinal studies. The differences in GM density and corresponding scan-rescan variability may be caused by the following sequence characteristics and their impact on each step of the VBM analysis: signal-to-noise ratio, contrast, uniformity, k-space weighting, and image artifacts such as pulsation, ghosting, etc. The main advantage of VBM is that it analyses the whole brain without bias for a specific area or structure. The pulse sequences should therefore be designed with minimal regional bias also. MDEFT appears best suited for the VBM technique as it shows reasonably accurate measures of GM over the whole brain, and has significantly lower GM density variability than both FLASH and MP-RAGE.

References: [1] www.loni.ucla.edu/ADNI/Research/Cores; [2] Tardif & Pike, Proc. ISMRM 15:210 (2007); [3] Warnking & Pike, Magn Reson Med 52:1190-9 (2004); [4] Sled *et al.*, IEEE Trans Med Imag 17:87-97 (1998); [5] Collins *et al.*, Hum Brain Map 3:190-208 (1995); [6] Cocosco *et al.*, Med Imag Anal 7:513-27 (2003); [7] Worsley *et al.*, Hum Brain Map 4:58-73 (1996).