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Voxel-based morphometry at ultra-high fields. A comparison of 7 T and 3 T MRI data

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ABSTRACT

Recent technological progress enables MRI recordings at ultra-high fields of 7 T and above leading to brain images of higher resolution and increased signal-to-noise ratio. Despite these benefits, imaging at 7 T exhibits distinct challenges due to B1 field inhomogeneities, causing decreased image quality and problems in data analysis. Although several strategies have been proposed, a systematic investigation of bias-corrected 7 T data for voxel-based morphometry (VBM) is still missing and it is an ongoing matter of debate if VBM at 7 T can be carried out properly. Here, an optimized VBM study was conducted, evaluating the impact of field strength (3 T vs. 7 T) and pulse sequence (MPRAGE vs. MP2RAGE) on gray matter volume (GMV) estimates. More specifically, twenty-two participants were measured under the conditions 3 T MPRAGE, 7 T MPRAGE and 7 T MP2RAGE. Due to the fact that 7 T MPRAGE data exhibited strong intensity inhomogeneities, an alternative preprocessing pipeline was proposed and applied for that data. VBM analysis revealed higher GMV estimates for 7 T predominantly in superior cortical areas, caudate nucleus, cingulate cortex and the hippocampus. On the other hand, 3 T yielded higher estimates especially in inferior cortical areas of the brain, cerebellum, thalamus and putamen compared to 7 T. Besides minor exceptions, these results were observed for 7 T MPRAGE as well for the 7 T MP2RAGE measurements. Results gained in the inferior parts of the brain should be taken with caution, as native GM segmentations displayed misclassifications in these regions for both 7 T sequences. This was supported by the test–retest measurements showing highest variability in these inferior regions of the brain for 7 T and also for the advanced MP2RAGE sequence. Hence, our data support the use of 7 T MRI for VBM analysis in cortical areas, but direct comparison between field strengths and sequences requires careful assessment. Similarly, analysis of the inferior cortical regions, cerebellum and subcortical regions still remains challenging at 7 T even if the advanced MP2RAGE sequence is used.

Introduction

Structural magnetic resonance imaging (sMRI) has become a reliable and well-established research method for the detailed assessment of anatomical brain data in vivo. Normal brain development as well as brain abnormalities can be studied by comparing different study populations of interest (May and Gaser, 2006). A regularly applied method for such investigations is voxel-based morphometry (VBM), where local volume or concentration of gray matter is measured by performing a voxel-wise comparison between or within groups (Ashburner and Friston, 2000; Wright et al., 1995). Several studies have applied this technique to assess structural brain changes in terms of aging (Good et al., 2001; Draganski et al., 2011), brain pathology (Nugent et al., 2006; Teipel et al., 2005; Van Tol et al., 2014), or neuroplasticity (Kraus et al., 2014; Maguire et al., 2000). Routinely, a T1-weighted, magnetization-prepared rapid gradient echo (MPRAGE) sequence (Mugler and Brookeman, 1990) at a field strength of 3 Tesla (3 T) is used, as this sequence achieves excellent image contrast between gray matter (GM), white matter (WM) and the cerebrospinal fluid (CSF) (Van der Kouwe et al., 2008). Technological progress during the last few years now enables MRI recordings at ultra-high fields of 7 Tesla (7 T) and above, leading to brain images of higher resolution and to a substantial increase in the signal-to-noise ratio (Hahn et al., 2013; Sladky et al., 2013; Bazin et al., 2013). Despite these benefits, structural imaging at 7 T exhibits distinct drawbacks, such as intensity inhomogeneities, which cause severe problems in automated MRI data analysis (Belaroussi et al., 2006). This so-called bias field, generated by the inhomogeneities of the transmit $B1^+$ and receive $B1^-$ fields at increased high static magnetic fields (B0), leads to intensity variations across the

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entire brain. While reception $B1^-$ inhomogeneities are easily removed, transmission $B1^+$ field inhomogeneities are more severe, as they effectively change the contrast (Marques et al., 2010). These inhomogeneities strongly affect image quality and impede the process of image segmentation and quantitative data analysis at ultra-high fields. Several strategies have been suggested to account for this problem (Marques et al., 2010), whereby a method proposed by Van de Moortele showed promising results (Van de Moortele et al., 2009). Following this approach, a separate proton density weighted 3D gradient echo (GRE) image is acquired in addition to the MPRAGE image aiming for bias field reduction. Another sophisticated way of dealing with these inhomogeneities is by using the magnetization-prepared 2 rapid acquisition gradient echo, or MP2RAGE pulse sequence (Marques et al., 2010), which is a modified version of the conventional MPRAGE sequence adopting the approach of Van de Moortele by integrating the acquisition of the 3D GRE image. The spatially uniform contrast of the MP2RAGE sequence is achieved by a rapid acquisition of the two volumes at different inversion times, where the images are afterwards combined and sources of inhomogeneities are compensated for. While the first inversion time is used to produce a T1-weighted image, the second inversion time is long and therefore produces an approximate proton density-weighted contrast. The combination of these two images delivers a synthetic image with strong contrast between the different tissue types across the entire brain. Hence, strategies for imaging at 7 T exist and studies for cortical thickness measurements have already been conducted (Fujimoto et al., 2014; Lüsebrink et al., 2013). However, VBM utilizes a different approach in assessing brain anatomical changes compared to cortical thickness measurements and it still remains a matter of debate if VBM analyses can be carried out at 7 T ultra-high fields properly in all brain areas. To address this issue, whole-brain VBM analysis was conducted using ultra-high field data (7 T) and comparison to the 3 T standard was carried out to assess reliability for each brain region. Furthermore, two different pulse sequences (MPRAGE, MP2RAGE) were tested at 7 T to observe their influence on gray matter volume estimates. In addition, test–retest analysis at two time-points was conducted to support reliability of gained VBM results. Taken together, we aimed to provide a thorough analysis for which brain regions VBM yields reliable results for ultra-high fields and the respective sequence. Our investigations will be useful for further VBM studies at ultra-high fields to draw attention to brain areas, which are problematic at 7 T.

Materials and methods

Participants

22 healthy subjects (mean age ± SD = 26.5 ± 6.2 years, 13 females) without any neurological or psychiatric disorders were included in this study and scanned at 3 T (MPRAGE) and 7 T (MPRAGE and MP2RAGE). Out of these 22 participants 10 subjects (mean age ± SD = 26.36 ± 7.3, 6 females) underwent the same procedure at a second time point to assess test–retest reliability measurements (mean days between measurements ± SD = 81 days ± 49). All participants were recruited via advertisement at the Medical University of Vienna, Austria and underwent a general physical and neurological examination at the screening visit including medical history, electrocardiogram and routine laboratory tests. Inclusion criteria were age between 18 and 50, general health based on history, physical examination electrocardiogram, laboratory screening and Structured Clinical Interview (SCID I & II) for DSM IV. Exclusion criteria comprised any severe diseases, implants or metal parts, current substance abuse and pregnancy. All participants provided written informed consent after written and oral presentation of an information form and they received reimbursement after participation. The study was approved by the Ethics Committee of the Medical University of Vienna and procedures were performed according to the Declaration of Helsinki.

Data acquisition

Structural MRI was carried out at the MR Centre of Excellence at the Medical University of Vienna, Austria, with a 3 Tesla whole-body scanner (Siemens Tim Trio, Erlangen, Germany) and an ultra-high field whole-body 7 T MRI scanner (Siemens Magnetom) using 32-channel head coils at both scanners. Participants were measured at 3 T (MPRAGE, T1; 256 × 240 matrix, 160 slices, voxel size 1 × 1 × 1.1 mm^3, TE = 4.21 ms, TR = 2300 ms; TI = 900 ms; $\alpha = 9°$; total acquisition time 7 min, 46 s) and 7 T with a MPRAGE sequence (T1; 320 × 310 matrix, 224 slices, voxel size 0.7 × 0.7 × 0.74 mm^3, TE = 3.66 ms, TR = 1980 ms; TI = 900 ms; $\alpha = 9°$; total acquisition time 8 min, 58 s) and a MP2RAGE sequence (T1; 384 × 312 matrix, 192 slices, voxel size 0.68 × 0.68 × 0.74 mm^3, TE = 3.07 ms, TR = 4096 ms; TI_1 = 900 ms; TI_2 = 3190 ms; $\alpha_1 = 4°$; $\alpha_2 = 5°$; total acquisition time 11 min, 20 s) using optimized parameters for each sequence (Fig. 1). MP2RAGE images were calculated from images acquired with inversion times TI_1 and TI_2 following the procedures of Marques et al. (2010). Second-order shimming was performed for both MPRAGE and MP2RAGE sequences on both scanners prior to data acquisition. The scanners used in this study were calibrated by the manufacturer (SIEMENS Healthcare, Erlangen, Germany) upon installation of the gradient systems in order to account for gradient nonlinearity effects, which otherwise might introduce image distortions (Caramanos et al., 2010). Anonymized MRI data will be made available upon request (e-mail to the corresponding author).

Voxel-based morphometry

VBM analysis was carried out in SPM8 (http://www.fil.ion.ucl.ac.uk/spm) using the VBM8 toolbox (http://dbm.neuro.uni-jena.de/vbm/)

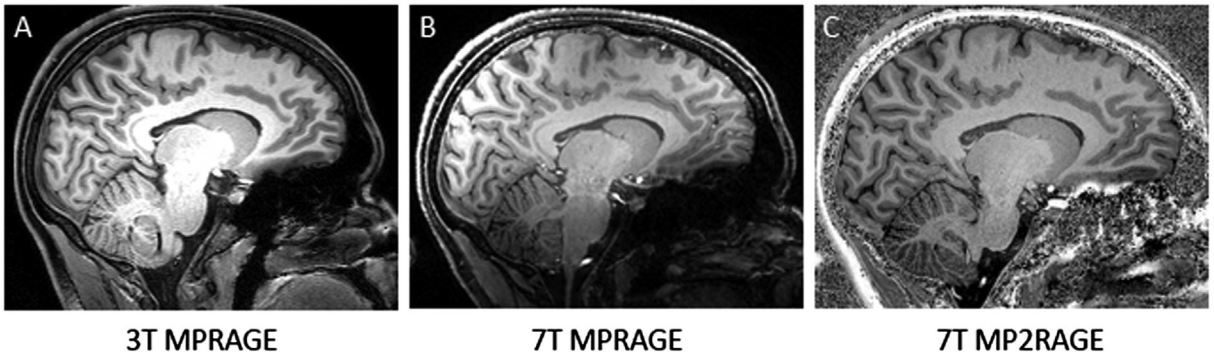

Fig. 1. Overview of a structural image of the same subject obtained with (A) 3 T MPRAGE, (B) 7 T MPRAGE and (C) 7 T MP2RAGE. 3 T is considered as standard for structural imaging so far and delivers overall good image quality. 7 T MPRAGE exhibits a strong bias field, giving low signal intensities in temporal and basal regions. 7 T MP2RAGE sequence tries to account for this bias field and delivers good contrast properties between gray and white matter. However, hyperintensities are visible in inferior parts of the brain.