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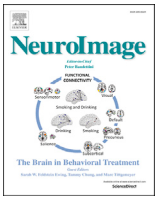

Human Connectome Project-style resting-state functional MRI at 7 Tesla using radiofrequency parallel transmission

Xiaoping Wu[a,*], Edward J. Auerbach[a], An T. Vu[b], Steen Moeller[a], Pierre-François Van de Moortele[a], Essa Yacoub[a], Kâmil Uğurbil[a]

[a] Center for Magnetic Resonance Research, Radiology, Medical School, University of Minnesota, Minneapolis, MN, United States
[b] Center for Imaging of Neurodegenerative Diseases, VA Healthcare System, San Francisco, CA, United States

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ABSTRACT

We investigate the utility of radiofrequency (RF) parallel transmission (pTx) for whole-brain resting-state functional MRI (rfMRI) acquisition at 7 Tesla (7T). To this end, Human Connectome Project (HCP)-style data acquisitions were chosen as a showcase example. Five healthy subjects were scanned in pTx and single-channel transmit (1Tx) modes. The pTx data were acquired using a prototype 16-channel transmit system and a commercially available Nova 8-channel transmit 32-channel receive RF head coil. Additionally, pTx single-spoke multiband (MB) pulses were designed to image sagittal slices. HCP-style 7T rfMRI data (1.6-mm isotropic resolution, 5-fold slice and 2-fold in-plane acceleration, 3600 image volumes and ~ 1-h scan) were acquired with pTx and the results were compared to those acquired with the original 7T HCP rfMRI protocol. The use of pTx significantly improved flip-angle uniformity across the brain, with coefficient of variation (i.e., std/mean) of whole-brain flip-angle distribution reduced on average by ~39%. This in turn yielded ~17% increase in group temporal SNR (tSNR) as averaged across the entire brain and ~10% increase in group functional contrast-to-noise ratio (fCNR) as averaged across the grayordinate space (including cortical surfaces and subcortical voxels). Furthermore, when placing a seed in either the posterior parietal lobe or putamen to estimate seed-based dense connectome, the increase in fCNR was observed to translate into stronger correlation of the seed with the rest of the grayordinate space. We have demonstrated the utility of pTx for slice-accelerated high-resolution whole-brain rfMRI at 7T; as compared to current state-of-the-art, the use of pTx improves flip-angle uniformity, increases tSNR, enhances fCNR and strengthens functional connectivity estimation.

1. Introduction

There has been a growing interest in pushing the spatiotemporal resolutions when using magnetic resonance (MR) neuroimaging to study human brain's organization and function. Most notably, increasing efforts aimed at generating descriptions of the connections among gray matter locations in the human brain at the millimeter scale are being launched following the approaches used in the Human Connectome Project (HCP) initiative of the National Institutes of Health in the United States. Two MR methods provide the core technologies in the HCP to deduce this connectivity (Glasser et al., 2016a; Uğurbil et al., 2013). The first is resting-state functional MR imaging (rfMRI), which uses correlations in spontaneous temporal fluctuations in a functional MRI (fMRI) time series to extract 'functional connectivity' (Biswal et al., 1995; Essen et al., 2013; Glasser et al., 2016b; Smith et al., 2013a, 2013b; Uğurbil et al., 2013) the second is diffusion imaging (dMRI), which provides information on 'structural connectivity' between gray matter regions (Aggarwal et al., 2010; Jbabdi and Johansen-Berg, 2011; McNab et al., 2013; Mori and Zhang, 2006; Setsompop et al., 2013; Sotiropoulos et al., 2013).

The original HCP produced a database of high-quality, freely and publicly shared, MR-based neuroimaging data (Glasser et al., 2016b; Uğurbil et al., 2013; Van Essen et al., 2013) on 1200 subjects at 3 Tesla (3T). In addition, 7 Tesla (7T) data were obtained on 184 of the original 3T subjects. Both the rfMRI and dMRI components of this effort at 7T were obtained with a higher spatial resolution and demonstrated advantages over the 3T data in inferring the brain's connectivity based on rfMRI (Vu et al., 2017) and dMRI (Sotiropoulos et al., 2016; Vu et al., 2015). However, 7T data were in many ways suboptimal because, at the time, it was only possible to perform such a large scale 7T study with a single-channel radiofrequency (RF) transmit head coil operating in a

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* Corresponding author. Center for Magnetic Resonance Research, University of Minnesota, 2021 6th Street SE, Minneapolis, MN, 55455, USA.
E-mail address: wuxxx184@umn.edu (X. Wu).

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Circularly Polarized (CP) mode.

It is well recognized that the transmit B_1 (B_1^+) field generated by a single-channel circumscribing RF head coil suffers from large inhomogeneities across the brain, exhibiting relatively high values in the middle of the brain, but low values in the periphery (Van De Moortele et al., 2005; Vaughan et al., 2001) and lower brain regions such as the cerebellum and inferior temporal lobes (e.g. reviews (Ugurbil, 2014; Uğurbil, 2018) and references therein). Such B_1^+ inhomogeneities lead to undesirable flip-angle nonuniformity, which in turn results in spatial variations in signal-to-noise ratio (SNR) and image contrast. In the HCP, this B_1^+ inhomogeneity was only partially mitigated by using passive RF shimming with dielectric padding (Vu et al., 2017, 2015), mainly to increase image signals in lower brain regions.

In addition, whole brain 7T data, like those obtained in the HCP, can suffer limitations in acceleration because of power deposition (i.e. Specific Absorption Rate (SAR)). The HCP relies on accelerated brain coverage using simultaneous multi-slice (SMS) imaging with multiband (MB) RF pulses and EPI-based image acquisition (SMS/MB-EPI) (e.g. (Glasser et al., 2016b; Setsompop et al., 2013; Uğurbil et al., 2013), and references therein). With this technique, power deposition increases linearly with the slice acceleration factor (i.e. MB factor) when acceleration is employed to acquire MB-fold higher number of volumes (shorter TRs) within a given period of data acquisition time.

The two afore-mentioned transmit limitations significantly disadvantage whole-brain studies at ultrahigh magnetic fields (7T or higher). Following our previous work with dMRI (Wu et al., 2018), we propose that these limitations can be simultaneously tackled with parallel transmission (pTx) techniques (Guérin et al., 2015b; Poser et al., 2014; Ugurbil, 2010; Wu et al., 2013b, 2016, 2018) in order to facilitate rfMRI at 7T. As such, in this paper we demonstrate the utility and advantages of pTx using the 7T HCP-style whole-brain acquisition (i.e., an acquisition similar to that of the HCP 7T rfMRI protocol, covering the whole-brain rapidly using slice-acceleration, 1.6-mm isotropic resolution, 1-sec TR and ~1-h scan time). We present pTx data using the commercially available Nova 8-channel transmit 32-channel receive (Nova 8Tx32Rx) head coil (Nova Medical, Inc., MA, USA) and compared the results to those of data acquisition using the single-transmit (1Tx) configuration of the same coil (i.e., Nova 1Tx32Rx coil) as employed in the 7T HCP protocol; thus, the receive coils employed in the comparison were identical, facilitating the comparison. Our results demonstrate that pTx can significantly improve flip-angle uniformity across the entire brain, which in turn increases the temporal signal-to-noise ratio (tSNR) and functional contrast-to-noise ratio (fCNR), leading to better estimation of brain's functional connectivity.

2. Methods

We conducted human experiments on a 7T MR scanner (Siemens, Erlangen, Germany) equipped with whole-body gradients (70 mT/m maximum amplitude and 200 T/m/s maximum slew rate), which can be operated in 1Tx and pTx modes. In the pTx mode, the MR system can independently drive 16 transmit channels with a 1-kW RF power amplifier each. In the 1Tx mode, the system can drive a 1Tx RF coil with a combined 8-kW RF amplifier. In both modes, the system is capable of receiving MR signals through 32 receive channels.

Human brain images were collected in five healthy subjects (3 males and 2 females, 20–72 years old) who signed a consent form approved by the local Institutional Review Board. Each subject was scanned twice: once in the pTx mode using the Nova 8Tx32Rx head coil and once in the 1Tx mode using the Nova 1Tx32Rx head coil. For pTx acquisition, 8 out of 16 transmit channels were utilized for the 8Tx-only Nova coil. Additionally, to ensure RF safety, the Nova 8Tx32Rx coil was used in the "protected" mode in which total RF power delivery (measured as sum of forward minus reflected power across all of the 8 transmit channels in use) was monitored in real time to be within the power limits specified by the coil manufacturer. In this study, the power limits at the coil plug were set to 11 W for long-term (6 min) and 22 W for short-term (10 s) RF exposures. For 1Tx acquisition, the Nova 1Tx32Rx coil was used with dielectric padding as in the 7T HCP protocol to improve B_1^+ in lower brain regions.

2.1. *Parallel transmit multiband pulse design*

In this study, we designed pTx MB pulses with single spokes (corresponding to RF phase and amplitude shimming) for rfMRI acquisition. In particular, these were band-specific pTx MB pulses which were formed by the sum of single-band pTx pulses, with each single-band pulse having its band-specific phase and amplitude "shim" setting. Because of this, these band-specific pTx MB pulses require fully independent amplitude and phase modulation functions to be played out for each channel during the pulse (Wu et al., 2013b, 2016a).

To increase the time efficiency in B_1^+ mapping and pulse sequence preparation, we followed the slab-wise design framework (Wu et al., 2016a) and calculated band-specific RF shim values (i.e. RF amplitude and phase modulations) based on a small number of contiguous, relatively thick B1+ mapping slices (which are defined as B1+ mapping slabs hereafter) instead of on the many relatively thin image slices to be acquired. Furthermore, we designed pTx MB pulses to image sagittal slices in order to capitalize on the coil geometry of azimuthally distributed transmit elements and promote the transmit performance in terms of flip-angle homogenization and SAR reduction (Wu et al., 2016b). Calculation of RF shim sets for pTx pulses was performed in Matlab (The Mathworks Inc., Natick, MA, USA).

Multi-channel B_1^+ maps covering the entire brain were first obtained at 3-mm isotropic resolution and then manipulated in the slice direction to be compatible with the generalized slab-wise design framework (Wu et al., 2016a) given the targeted MB factor and slice thickness to be used for data acquisition. Specifically, the B_1^+ maps were acquired within 60 contiguous sagittal slabs (each 3 mm in thickness) spanning 180 mm in the left-right dimension. For each slab, a single set of 8-channel B_1^+ maps were measured using a hybrid B_1^+ mapping technique, which has been demonstrated to be capable of providing accurate B_1^+ maps for pTx methods at 7T (Schmitter et al., 2014) and beyond (Wu et al., 2010). Briefly, this method combines a single absolute volumetric B_1^+ map (obtained in the large-tip-angle regime by transmitting with all channels) together with a series of relative multi-slice B_1^+ maps obtained in the small-tip-angle regime by transmitting one channel at a time. The single absolute B_1^+ map was obtained using the actual flip-angle imaging (AFI) (Yarnykh, 2007) with a 3D gradient-recalled-echo (GRE) sequence while the series of relative B_1^+ maps was acquired using a multi-slice GRE sequence. A CP-like-mode RF phase shimming (Schmitter et al., 2012) was applied on top of the vendor-provided "CP-mode" to increase the B_1^+ uniformity across the entire brain including the cerebellum. The reconstructed B_1^+ maps were down-sampled in the slice direction to create another set of B_1^+ maps with 4.8-mm slice thickness. The central part of this set of B_1^+ maps, defining 30 contiguous 4.8-mm sagittal slabs and spanning 144 mm in the left-right dimension, was chosen for the subsequent calculation of RF shim values. The choice of 4.8-mm slab thickness and 30 slabs was to match the MB factor of 5 and the resolution of 1.6 mm to be used for image acquisition. Relevant imaging parameters utilized in the acquisitions are reported in the Supporting Materials.

A single set of 8-channel band-specific RF shim values was calculated for each B_1^+ mapping slab, leading to a total of 30 RF shim sets. All RF shim sets were optimized jointly by solving a regularized magnitude least squares problem based on a two-step procedure for increased robustness (as described in detail in (Wu et al., 2018)).

To improve transmit performance, the calculation of RF shim values considered brain-extracted B1+ maps serving as the ROI. To define the ROI, a brain mask was created by acquiring a 0.7-mm, T_1-weighted (T1w) whole-head image with the MPRAGE sequence (Mugler and Brookeman, 1990) (see Supporting Materials for relevant imaging parameters) and by applying the FSL's brain extraction tool (BET) (Smith, 2002) to extract