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Whole brain, high resolution spin-echo resting state fMRI using PINS multiplexing at 7 T

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ABSTRACT

This article demonstrates the application of spin-echo EPI for resting state fMRI at 7 T. A short repetition time of 1860 ms was made possible by the use of slice multiplexing which permitted whole brain coverage at high spatial resolution (84 slices of 1.6 mm thickness). Radiofrequency power deposition was kept within regulatory limits by use of the power independent of number of slices (PINS) technique. A high in-plane spatial resolution of 1.5 mm was obtained, while image distortion was ameliorated by the use of in-plane parallel imaging techniques. Data from six subjects were obtained with a measurement time of just over 15 min per subject. A group level independent component (IC) analysis revealed 24 non-artefactual resting state networks, including those commonly found in standard acquisitions, as well as plausible networks for a broad range of regions. Signal was measured from regions commonly rendered inaccessible due to signal voids in gradient echo acquisitions. Dual regression was used to obtain spatial IC maps at the single subject level revealing exquisite localisation to grey matter that is consistent with a high degree of T_2-weighting in the acquisition sequence. This technique hence holds great promise for both resting state and activation studies at 7 T.

Introduction

Early in the history of BOLD fMRI, it was shown that T_2-weighted imaging should emphasise functional signal changes in the microvasculature, based on the finding that the contribution of extravascular dephasing around larger post capillary vessels is largely eliminated in T_2-weighted compared to T_2^*-weighted fMRI (Boxerman et al., 1995; Ogawa et al., 1993). Consequently, the use of T_2-weighted fMRI is desirable for the sake of a higher spatial specificity of BOLD activation. Owing to its high sensitivity, ready availability and (in relation to pure spin echo sequences) low radiofrequency power deposition SE-EPI is the most promising candidate sequence, but several alternatives have also been tested [FSE (Constable et al., 1994), RASER (Chamberlain et al., 2007), nb-S2-SSFP (Barth et al., 2010), HASTE (Poser and Norris, 2007), STE (Goerke et al., 2007), bSSFP (Miller et al., 2003; Scheffler et al., 2001)]. Unfortunately, the application of a sufficiently fast, whole brain SE-EPI protocol faces several practical limitations that have impeded the common use of T_2-weighting for fMRI:

i. In order to obtain the best possible sensitivity for SE-EPI one needs to measure the signal at an echo time corresponding to T_2 of grey matter which ranges from 60 to 80 ms depending on the specific magnetic field strength. This leads to a significantly longer TE than for GE imaging and consequently to a longer measurement time due to the lower efficiency of the sequence.
ii. The improvement in spatial specificity comes at the expense of functional sensitivity and is also due to reduced large vein effects. The drop in sensitivity of SE-EPI based fMRI has been shown to be significant (about a factor of 3 at 3 T) compared to its GE counterpart (Jochimsen et al., 2004; Norris et al., 2002). To compensate for (part of) the low sensitivity high field strengths have been advocated (Lee et al., 1999; Yacoub et al., 2003).
iii. The elimination of the static averaging contribution to the BOLD signal through the use of a spin-echo leaves contributions from both the well-localised extravascular dynamic averaging contribution originating from the capillary bed and smaller vessels, and from the intravascular compartment. At 3 T the gain in spatial specificity is hence limited (Parkes et al., 2005), and a further argument for the use of ultra high field strengths such as 7 T and

Abbreviations: IC, independent component; PINS, power independent of number of slices; RSN, resting state network.

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above is the virtual disappearance of the intravascular compartment owing to the short T_2 of venous blood at these field strengths (Lee et al., 1999; Yacoub et al., 2003).

iv. Last, but not least, the refocusing pulses may lead to very high SAR levels at field strengths of 7 T or above that either prohibit whole brain coverage or lead to restrictively long volume TRs. This SAR restriction unfortunately pertains at just the field strengths where the greatest benefit from spin-echo BOLD could be expected.

Due to these restrictions a whole brain protocol at 7 T with acceptable volume acquisition times and a sufficient spatial resolution to benefit from the higher SE specificity has hitherto proven impossible to realise. Recently, the development of multiplexed acquisition for EPI opened the possibility to speed up 2D multi-slice acquisitions considerably (Moeller et al., 2010) which has the potential to dramatically improve the efficiency of the sequence and hence reduce volume acquisition times. However, the SAR level of the multiplexed RF pulses increases linearly with the acceleration factor, which in combination with the requirement for short repetition times leads to prohibitively high SAR levels. In this study we implemented PINS RF pulses (Norris et al., 2011) for excitation and refocusing to overcome the above mentioned experimental limitations. We show that this enables the implementation of a whole brain SE-EPI protocol at 7 T with a spatial resolution of $1.5\times1.5\times1.6$ mm^3 within a volume acquisition time of less than 2 s while remaining within regulatory SAR levels. We use this technique to obtain resting state data from healthy subjects at 7 T.

Methods

Acquisition

Six right-handed subjects (5 male) were scanned after informed consent was given according to the guidelines of the local ethics committee. 2D SE-EPI scans were obtained using a 7 T MR scanner (Magnetom, Siemens Healthcare, Erlangen, Germany) equipped with a 32 channel head coil (Nova Medical, Wilmington, USA). Before acquiring multiplexed PINS resting state data, five volumes of non-multiplexed reference data were acquired, the average of which was used to calculate the reconstruction kernel (see: Reconstruction and registration). With the exception of the RF pulses used and the volume TR, the parameters of these two protocols were identical: TE 53 ms, sagittal orientation, phase encoding direction AP, matrix 160×160, voxel size 1.5×1.5 mm^2, 1.6 mm slice thickness with a 25% gap, flip angle 90°, PE-GRAPPA factor 3, bandwidth 1562 Hz/pixel, 40.3 ms readout train. Non-selective fat suppression was applied.

For the reference data conventional sinc RF pulses with the same bandwidth and duration as the PINS pulses mentioned below were used. The whole head was covered by 84 slices which led to a volume TR of 7430 ms. After the reference scan, the RF pulses were replaced by PINS pulses that allow multiple slices to simultaneously be excited/refocused with a considerable reduction in SAR compared to standard RF multiplexing techniques (Norris et al., 2011). PINS pulses consist of a series of RF hard pulses interleaved with slice selection gradient blips. The time integral of an individual blip is chosen such that it dephases the signal by 2π over the desired slice spacing thus creating a periodic slice profile. The amplitude of each of the hard pulses can be determined by a Fourier series expansion of the desired slice profile. Whereas periodicity may seem to imply an infinite number of slices, this is limited in practice by the extent of the subject's head or the transmit/receive volume(s) of the coil(s). Compared to the original single slice pulse there is an increase in SAR because part of the pulse duration is spent on gradients and not RF. This increase is however of a much lower magnitude than the increase in power deposition of a conventional multiplexed (summed) pulse which is proportional to the number of slices. Due to slew-rate limitations, PINS pulses have a relatively low bandwidth-time product (BWTP). To compensate for this we used RF pulse lengths of 7.68 ms for all RF pulses (excitation and refocusing, PINS and conventional pulse types) in order to achieve the desired slice thickness, allowing 35 sub-pulses to be used for a BWTP of 1.33. The multiplexed PINS acquisition used 21 stacks of slices with an inter-slice spacing of 42 mm. Consequently, the four-fold slice multiplexed acceleration reduced the volume TR to 1860 ms, allowing the acquisition of 500 volumes of high resolution SE resting state data in just over 15 min without exceeding SAR regulations.

Structural scans were acquired using MP2RAGE (Marques et al., 2010). Parameters were: matrix 320×320, 192 slices, voxel size $0.75\times0.75\times0.75$ mm^3, flip angles 4° and 5°, inversion times 900 and 3200, TE 2.04 ms, TR 5000, bandwidth 240 Hz/pixel, PE-GRAPPA factor 2. For two subjects (2 and 4) structural MP-RAGE data were already available from a different study (3 T Siemens Trio scanner, 32 channel head coil, matrix 256×256, 192 slices, TI 1100, TR 2300, flip angle 8°, bandwidth 130 Hz/pixel).

Reconstruction and registration

Both the 84 slice reference data and the 21 stack PINS data were first reconstructed in the phase encode direction using a 7×6 GRAPPA kernel (Griswold et al., 2002). Subsequently, the collapsed slices were disentangled using the SENSE-GRAPPA method (Blaimer et al., 2006) using a 5×4 kernel. Resting state data were realigned using SPM8 (http://www.fil.ion.ucl.ac.uk/spm/). We applied a distortion correction co-registration algorithm to map the EPI to the MP2RAGE data for each subject (Studholme et al., 2000; Visser et al., 2010). Based on normalised mutual information of the average EPI volume and the MP2RAGE this routine simultaneously estimated both the rigid body transformation parameters and the non-linear transformation in the phase-encode direction of the EPI data. In order to perform a group ICA this transformation was followed by registration to the MNI-152 T_1 template using FSL-FLIRT (Jenkinson et al., 2002). An example of a single volume before and after distortion correction is shown in Fig. 1.

Resting state analysis

Spatial smoothing was applied to the registered resting state data using a 5 mm kernel. Temporal drift was removed with a high-pass filter with a 100 s cut off. Group ICA was carried out with the multi-session temporal concatenation option of MELODIC v3.1 (Beckmann et al., 2005) with 70 components, a number similar to those used in previous resting state studies (Feinberg et al., 2010; Kiviniemi et al., 2009).

ICs from the group ICA which were identified as resting state networks (RSNs) are presented in figures in the Results section as overlays on the T1 weighted MNI-152 standard brain. The coordinates are in MNI space and images are shown in radiological convention. The most representative slices in three directions were chosen by either placing them on the z-score's centre-of-mass for ICs with a single or dominant cluster, or on the voxel with the peak z-score for ICs that consisted of distributed clusters where the centre-of-mass was in empty slices in between. The threshold for all ICs was set at 4.

Artefactual components were identified by examining each component's frequency spectrum (predominant RSN power should be concentrated below 0.1 Hz) and spatial location (ICs should be found in grey matter). RSN interpretation was achieved using previous group ICA studies with similar model orders (Kiviniemi et al., 2009; Varoquaux et al., 2010) and the Jülich histological (Eickhoff et al., 2007) and Harvard–Oxford cortical structural atlases (http://www.cma.mgh.harvard.edu/).

The components in Fig. 5 do not belong to the commonly reported RSNs, but also did not show any signs of artefacts. To interpret these the NeuroSynth database (Yarkoni et al., 2011) was consulted to