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Rapid whole-brain resting-state fMRI at 3 T: Efficiency-optimized three-dimensional EPI versus repetition time-matched simultaneous-multi-slice EPI

Rüdiger Stirnberg [a,*], Willem Huijbers [a,b], Daniel Brenner [a], Benedikt A. Poser [c], Monique Breteler [a], Tony Stöcker [a,d]

[a] German Center for Neurodegenerative Diseases (DZNE), Bonn, Germany
[b] Jheronimus Academy of Data Science, Cognitive Science and Artificial Intelligence, Tilburg University, The Netherlands
[c] Faculty of Psychology and Neuroscience, Maastricht University, Maastricht, The Netherlands
[d] Department of Physics and Astronomy, University of Bonn, Bonn, Germany

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ABSTRACT

State-of-the-art simultaneous-multi-slice (SMS-)EPI and 3D-EPI share several properties that benefit functional MRI acquisition. Both sequences employ equivalent parallel imaging undersampling with controlled aliasing to achieve high temporal sampling rates. As a volumetric imaging sequence, 3D-EPI offers additional means of acceleration complementary to 2D-CAIPIRINHA sampling, such as fast water excitation and elliptical sampling. We performed an application-oriented comparison between a tailored, six-fold CAIPIRINHA-accelerated 3D-EPI protocol at 530 ms temporal and 2.4 mm isotropic spatial resolution and an SMS-EPI protocol with identical spatial and temporal resolution for whole-brain resting-state fMRI at 3 T. The latter required eight-fold slice acceleration to compensate for the lack of elliptical sampling and fast water excitation. Both sequences used vendor-supplied on-line image reconstruction. We acquired test/retest resting-state fMRI scans in ten volunteers, with simultaneous acquisition of cardiac and respiration data, subsequently used for optional physiological noise removal (nuisance regression). We found that the 3D-EPI protocol has significantly increased temporal signal-to-noise ratio throughout the brain as compared to the SMS-EPI protocol, especially when employing motion and nuisance regression. Both sequence types reliably identified known functional networks with stronger functional connectivity values for the 3D-EPI protocol. We conclude that the more time-efficient 3D-EPI primarily benefits from reduced parallel imaging noise due to a higher, actual *k*-space sampling density compared to SMS-EPI. The resultant BOLD sensitivity increase makes 3D-EPI a valuable alternative to SMS-EPI for whole-brain fMRI at 3 T, with voxel sizes well below 3 mm isotropic and sampling rates high enough to separate dominant cardiac signals from BOLD signals in the frequency domain.

1. Introduction

Recent advances in undersampled multiband magnetic resonance imaging (MRI) (Larkman et al., 2001) and increasing availability of state-of-the-art simultaneous-multi-slice echo-planar imaging (SMS-EPI) (Setsompop et al., 2012) has made application of three- to eight-fold slice-accelerated whole-brain diffusion MRI and functional MRI (fMRI) feasible on a routine basis (Breteler et al., 2014; Miller et al., 2016; Smith et al., 2013; Sotiropoulos et al., 2013; Uğurbil et al., 2013). As opposed to spin-echo-based diffusion MRI, which benefits from the "snap shot" character of SMS-EPI, gradient-echo-based fMRI does not suffer from severe sub-millimeter motion artifacts, if image acquisition is distributed across multiple shots. Three-dimensional echo planar imaging (3D-EPI) (Poser et al., 2010) with controlled aliasing in volumetric imaging (2D-CAIPIRINHA) (Breuer et al., 2006) has therefore been suggested (e.g. (Narsude et al., 2013; Narsude et al., 2014b; Poser et al., 2013, 2014; Stirnberg et al., 2016b)) as a potential alternative to SMS-EPI with blipped controlled aliasing in parallel imaging (blipped-CAIPI) (Setsompop et al., 2012). Particularly at ultra-high fields 3D-EPI has the potential to achieve high acceleration factors at high spatial resolutions without exceeding specific-absorption-rate (SAR) or radiofrequency (RF) peak power limits (Poser et al., 2010; Stirnberg et al., 2013). This is due

* Corresponding author. Sigmund-Freud-Str. 27, D-53127, Bonn, Germany.
E-mail address: ruediger.stirnberg@dzne.de (R. Stirnberg).

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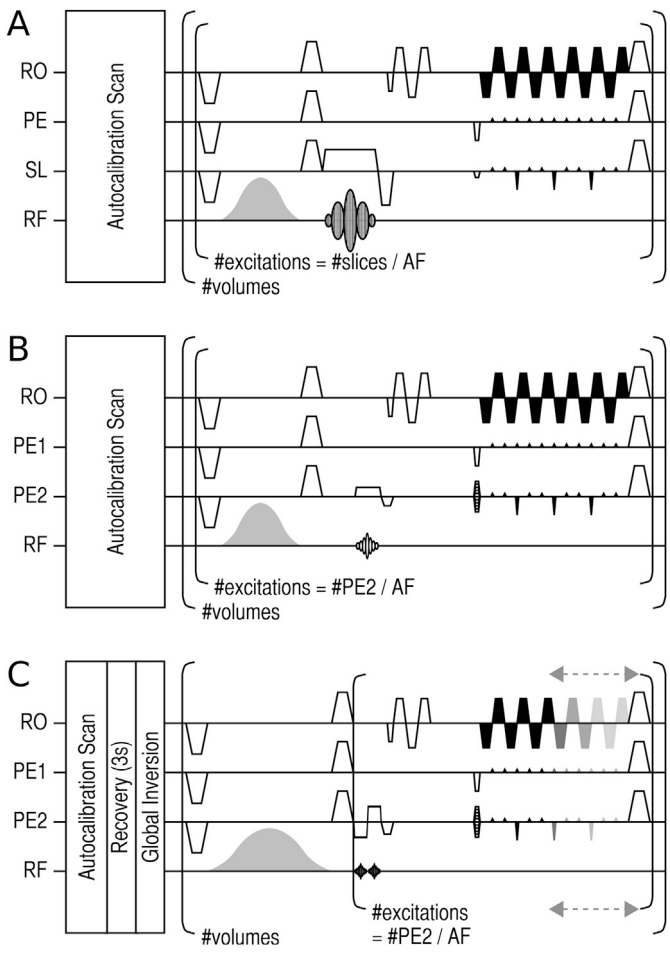

Fig. 1. Sequence diagrams of a generic SMS-EPI (A, multiband excitation), a corresponding 3D-EPI (B, slab-selective excitation) and the efficiency-optimized 3D-EPI (C, slab-selective water excitation). For each volume acquisition, the inner loop (i.e. optional CHESS fat-saturation, excitation, phase correction scans, EPI readout and spoiler gradients) runs several times, which defines the minimum volume TR. The number of excitations per volume is defined by the final number of reconstructed slices (#slices) or PE2 steps (#PE2) divided by the acceleration factor, AF (slice acceleration factor or PE2 undersampling factor, respectively). The Gaussian CHESS RF pulses in (A) and (B) and the adiabatic SPAIR RF pulse in (C) (gray) are fat selective. The EPI color gradient and the dashed arrows in (C) indicate that the ETL, and hence the TR across excitations, is variable.

to much simpler "singleband" spatially- or frequency-selective excitation pulses (Stirnberg et al., 2016a) or composite pulses that even allow for relatively simple parallel transmission field homogenization (Tse et al., 2016).

3D-EPI and SMS-EPI share several properties. For instance, both suffer from typical, susceptibility-induced geometric distortions only along the primary phase encode (PE) direction, as opposed to single-shot echo-volumar imaging (EVI) (Mansfield et al., 1989). As a matter of fact, blipped-CAIPI SMS-EPI and 2D-CAIPIRINHA 3D-EPI are equivalent under a generalized 3D Fourier description (Zahneisen et al., 2014) and can be reconstructed with identical g-factor penalties (Zahneisen et al., 2015). A thorough proof-of-concept characterization of SMS-EPI and 3D-EPI across a range of matching sequence parameters, in particular with regard to physiological noise, is of great scientific value. However, a stringent comparison is not as trivial in practice. Even if matching pulse sequence and on-line image reconstruction implementations were available, certain time-critical sequence aspects, such as the excitation pulse duration, cannot reasonably be equalized without unfairly penalizing one sequence type. Furthermore, 3D-EPI exclusively offers complementary acceleration techniques not based on parallel imaging principles (Poser et al., 2010; Stirnberg et al., 2014, 2016a), which are impossible to account for in such a hypothetical comparison.

This work, instead, aims at an application-oriented comparison of SMS-EPI and 3D-EPI at 3 T. The use of readily available on-line image reconstruction is of particular importance for actual feasibility and high-throughput utilization, e.g. for clinical or population-based studies (Breteler et al., 2014; Miller et al., 2016). The SMS- and 3D-EPI protocols investigated here are individually optimized for fast whole-brain fMRI with equal spatial and temporal resolution and otherwise – to the greatest possible extend – matching parameters. As a precondition, the imaging rate shall be fast enough to preclude aliasing of high cardiac frequencies (60–100 beats per minute) into typically considered BOLD frequencies (0.01–0.08 Hz).

2. Methods

All experiments were performed on a 3 T MAGNETOM Prisma scanner (Siemens Healthcare, Erlangen, Germany, software baseline VE11C) equipped with a nominal 80 mT/m and 200 T/m/s gradient system and a 64 channel head/neck receive array, of which the 52 head elements were utilized.

2.1. Custom 3D-EPI sequence

A time-optimized 3D-EPI sequence was developed in-house, which allowed for the introduction and combination of several dedicated techniques for enhancement of the sampling efficiency, as explained below.

2.1.1. 2D-CAIPIRINHA

Following several recent publications (Narsude et al., 2016, 2013; Poser et al., 2013; Zahneisen et al., 2015), we implemented an echo-planar 2D-CAIPIRINHA sampling scheme that minimizes the number of excitations per volume repetition time (TR). Following excitation, the *k*-space trajectory traverses as many secondary PE locations (PE2) as possible under the constraint of a constant bandwidth along the primary PE direction (PE1) and a virtually infinite bandwidth along PE2 (steady progression along PE1, as opposed to single-shot EVI or 3D-EPI with reduced number of segments without 2D-CAIPIRINHA (Narsude et al., 2014a)). Analogous to blipped-CAIPI SMS-EPI (Setsompop et al., 2012), this requires blipped gradients along both PE1 and PE2, as illustrated by the sequence diagrams in Fig. 1 (A,B). The inset in Fig. 2(F) demonstrates such a *k*-space sampling scheme on the example of a $R = 1 \times 6^{(2)}$ CAIPIRINHA pattern, where the superscript denotes the CAIPIRINHA shift in units of the PE2 increment (Breuer et al., 2006). For image reconstruction we utilize a generic, vendor-provided 2D-GRAPPA (Griswold et al., 2002) implementation compatible with 2D-CAIPIRINHA sampling, which we refer to as CAIPIRINHA reconstruction.

2.1.2. Variable echo train lengths

The sampling scheme is extended by two elliptical sampling options that restrict the actually sampled (PE1,PE2) *k*-space points to either an "elliptical" or "semi-elliptical" subset, whereby the radius is determined by the nominal desired image resolution (Bernstein et al., 2001). Such 2D *k*-space masking implies that the complete image is defined along two PE directions; a corresponding technique is thus, to the best of our knowledge, not available to SMS-EPI. Applied to 3D-EPI, skipping of *k*-space points outside the elliptical mask results in variable echo train lengths (vETL) across excitations, which can be used to increase imaging speed (Stirnberg et al., 2014). The fraction of *k*-space outside a full elliptical mask corresponds to $1 - \pi(0.5)^2 \approx 21\%$ of the total rectilinear *k*-space volume. Accordingly, "elliptical" and "semi-elliptical" sampling can theoretically save up to 20% and 10% readout time, respectively. Skipping only points at the end of a given EPI echo train results in a variable TR across excitations (cf. Fig. 2 B), whereas skipping also points at the beginning of the echo train additionally results in variable TE (cf. Fig. 2