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Reduction of across-run variability of temporal SNR in accelerated EPI time-series data through FLEET-based robust autocalibration

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ABSTRACT

Temporal signal-to-noise ratio (tSNR) is a key metric for assessing the ability to detect brain activation in fMRI data. A recent study has shown substantial variation of tSNR between multiple runs of accelerated EPI acquisitions reconstructed with the GRAPPA method using protocols commonly used for fMRI experiments. Across-run changes in the location of high-tSNR regions could lead to misinterpretation of the observed brain activation patterns, reduced sensitivity of the fMRI studies, and biased results. We compared conventional EPI autocalibration (ACS) methods with the recently-introduced FLEET ACS method, measuring their tSNR variability, as well as spatial overlap and displacement of high-tSNR clusters across runs in datasets acquired from human subjects at 7T and 3T. FLEET ACS reconstructed data had higher tSNR levels, as previously reported, as well as better temporal consistency and larger overlap of the high-tSNR clusters across runs compared with reconstructions using conventional multi-shot (ms) EPI ACS data. tSNR variability across two different runs of the same protocol using ms-EPI ACS data was about two times larger than for the protocol using FLEET ACS for acceleration factors (R) 2 and 3, and one and half times larger for R=4. The level of across-run tSNR consistency for data reconstructed with FLEET ACS was similar to within-run tSNR consistency. The displacement of high-tSNR clusters across two runs (inter-cluster distance) decreased from ~8 mm in the time-series reconstructed using conventional ms-EPI ACS data to ~4 mm for images reconstructed using FLEET ACS. However, the performance gap between conventional ms-EPI ACS and FLEET ACS narrowed with increasing parallel imaging acceleration factor. Overall, the FLEET ACS method provides a simple solution to the problem of varying tSNR across runs, and therefore helps ensure that an assumption of fMRI analysis—that tSNR is largely consistent across runs—is met for accelerated acquisitions.

Introduction

Temporal signal-to-noise ratio (tSNR) provides a crucial metric for assessing ability of an fMRI acquisition to detect subtle neuronally-driven changes in the measured time-series data. The detectability of a signal fluctuation of interest can be characterized by the functional contrast-to-noise ratio (fCNR), which is a joint function of both the tSNR and the percent signal change of the fluctuation of interest: fCNR = tSNR•ΔS/S (Krüger et al., 2001; Wald, 2012; Wald and Polimeni, 2015). While the percent signal change (ΔS/S) induced by local brain activation in fMRI measurements using the blood oxygenation level-dependent (BOLD) contrast depends only on the efficacy of the stimulation and the neurovascular coupling and on the TE value (since $\Delta S/S = 1 - \exp(TE\ \Delta R_2^*)$), the tSNR provides a convenient metric that characterizes the detection power of the fMRI measurement in a way that is independent of the specifics of the stimulation, neuronal activation, and local physiology. Therefore, tSNR is a practically useful metric that can be employed when optimizing the sensitivity of the functional acquisition. There are several sources of noise captured by the tSNR metric that may affect fMRI signal. Physiological noise (e.g., respiratory changes and cardiac pulsation), instrumental noise (thermal noise and low frequency drifts due to the scanner or hardware instabilities), as well as noise originating from spontaneous neuronal activity have different relative influence on the fMRI signal fluctuations (Bianciardi et al., 2009). Because tSNR is also a function of the static image signal-to-noise ratio (SNR_0), it is affected by acquisition parameters such as the receive coil, flip angle, TE and voxel size. The relative contribution of thermal and physiological noise depending on

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these parameters has been investigated in different tissues and at different magnetic field strengths and receive coil combinations (Bodurka et al., 2007; Triantafyllou et al., 2016, 2011, 2005).

Single-shot echo-planar imaging (EPI) has become the imaging technique of choice for functional, diffusion, and perfusion MRI due to its ability to quickly and repeatedly image the entire brain. Parallel imaging (PI) techniques (Griswold et al., 2002; Pruessmann et al., 1999; Sodickson and Manning, 1997) allow decreased echo spacing and readout time in EPI acquisitions, therefore reducing geometric distortion artifacts, signal losses and T_2^* blurring (de Zwart et al., 2006; Griswold et al., 1999). Since the severity of these artifacts increases with the magnetic field strength, PI acceleration methods are especially beneficial for high-field fMRI leading to improved data quality and higher spatial resolution (de Zwart et al., 2002; Setsompop et al., 2016). The two most commonly used PI methods, sensitivity encoding (SENSE) (Pruessmann et al., 1999) and generalized autocalibrating partially parallel acquisitions (GRAPPA) (Griswold et al., 2002), undersample the k-space data during the acquisition by skipping encoding steps, thereby shortening the total readout time, then estimate the fully-sampled dataset using a small amount of calibration data. For anatomical imaging techniques (such as MPRAGE) the PI reconstruction can be "autocalibrated" by acquiring a small amount of fully-sampled autocalibration signal (ACS) data during the acquisition (consisting of a set of additional k-space lines) which can be used to estimate coil sensitivities or derive GRAPPA kernel weights to reconstruct the undersampled data. However, for accelerated fMRI acquisitions where the under-sampled image data measurement is repeated many times during the time series, a fully sampled pre-scan can be acquired once per time-series to serve as calibration data, with the assumption that the calibration data remains valid throughout the time series and thus changes related to subject motion over time are negligible.

Functional imaging studies often consist of multiple runs of the same fMRI protocol performed with varying paradigms (such as different tasks) or the same paradigm repeated multiple times to increase sensitivity of the measurements. In conventional fMRI analysis it is typically implicitly assumed that the tSNR is largely consistent across runs, and therefore runs are often either simply concatenated or contrasted using straightforward fixed-effects analyses. However, recent work has shown that tSNR may indeed vary dramatically between multiple runs of accelerated single-shot EPI acquisitions reconstructed with the GRAPPA method, which is commonly used for fMRI acquisitions (Cheng, 2012). Large differences in the spatial distribution of tSNR values across multiple runs, such as varying location of the high-tSNR regions where the detection sensitivity is the highest, will cause false positives and negatives (if an activation is located in a high-tSNR region in one run and in a low-tSNR region in the next one) leading to misinterpretation of the brain activation patterns therefore reducing the accuracy of fMRI studies.

For accelerated EPI reconstructions, ACS data for GRAPPA kernel calibration are conventionally acquired as multi-shot segmented EPI (ms-EPI), with the number of segments equal to the acceleration factor (R) of the data acquisition. This is conventionally done on a consecutive-slice manner which allows for longitudinal magnetization recovery before proceeding to the next segment. Namely the first interleave is acquired for all the slices before acquiring the second interleave. Thus, any two interleaves are acquired a time TR apart, which can lead to artifacts related to the subject's breathing and head motion during the TR period. Since the ACS data are used to calculate the GRAPPA kernel applied to the time-series images, errors introduced by motion or breathing may result in lower tSNR in a subset of the slices. In conventional slice-interleaved acquisitions (where slices are acquired first stepping through the odd-numbered slices and then the even), this ACS data artifact is propagated to the reconstructed images as an "alternating" tSNR level across the adjacent slices. If the tSNR map is reformatted into another plane, alternating high/low tSNR stripes are readily seen (Polimeni et al., 2016). This spatially varying tSNR pattern is therefore likely to change depending on the timing of head motion or respiration relative to the ACS acquisition and thus is expected to change across runs.

An alternative solution is to use the fast low-angle shot (FLASH) (Haase et al., 1986) method to acquire ACS data for the accelerated EPI reconstruction. FLASH ACS for accelerated EPI has been proposed (Griswold et al., 2006), and a non-interleaved version in which the data for each slice is acquired in full before moving onto the next slice has been recently demonstrated to reduce g-factor penalties in EPI reconstructions (Talagala et al., 2016). However, while it may improve tSNR consistency across runs it does not provide matching geometric distortion between the ACS data and accelerated image data, and therefore may only be appropriate in cases where the EPI distortion is small.

A recent study has employed the Fast Low-angle Excitation Echo-planar Technique (FLEET) (Chapman et al., 1987) for acquiring ACS data to calibrate GRAPPA kernels for accelerated EPI reconstructions; the FLEET acquisition is simply a reordering of the acquisition of the multi-shot EPI segments that acquires the complete set of segments within a slice before proceeding to acquire the next slice, and has been proposed as an acquisition method for fMRI (Guilfoyle and Hrabe, 2006; Kang et al., 2015; Menon et al., 1997). This acquisition approach minimizes the time interval between the acquisition of all the segments of one slice, which, when applied to acquiring accelerated EPI ACS data, minimizes sensitivity to dynamic changes occurring during the ACS acquisition (such as subject motion and respiration) to increase the robustness of the ACS data and, consequently, the PI calibration (Polimeni et al., 2016). The resulting reduction in longitudinal recovery time necessitates lower flip angles to achieve equal magnetization across segments; empirically this loss of signal in the ACS data has not prevented the FLEET ACS data from providing high-quality EPI reconstructions, even for high-resolution acquisitions. This new FLEET ACS method has been shown to improve tSNR of the acquisition and eliminate the "slice-alternating" tSNR artifact in accelerated EPI by providing robustness to subject motion and respiration related artifacts (Polimeni et al., 2016). In this work we hypothesize that FLEET may additionally remove the aforementioned inconsistency of tSNR across multiple accelerated EPI runs.

In this work we investigated the effect of autocalibration acquisition strategy on tSNR variation between multiple runs of accelerated EPI acquisitions, and tested whether FLEET ACS could reduce this variability while maintaining high-quality image reconstructions. To characterize the performance of different autocalibration methods, we employed an across-run tSNR consistency measure as well as examined changes in the spatial distribution of high-tSNR voxels across the runs.

Methods

Five healthy volunteers (3 F/2 M, mean age 26 ± 4 y.o.) were scanned on a whole-body 7T scanner (Siemens Healthcare, Erlangen, Germany) using a set of seven single-shot gradient-echo EPI protocols – three with FLEET *ACS*: acceleration factor R=2,3,4, and the number of ACS lines set to 46, 90, 76, respectively; four with conventional ACS, including: a single-shot EPI ACS acquisition for R=2 and 48 ACS lines (*ss-EPI ACS*), and standard segmented multi-shot EPI for R=2,3,4, and 94, 90, and 88 ACS lines respectively (*ms-EPI ACS*). Protocol parameters were: TE/TR=25/2000 ms, FOV=192 mm, matrix=96×96, 39 slices, spatial resolution 2.0×2.0 mm, slice thickness 2.0 mm, flip angle 67°, bandwidth 2264 Hz/pix, echo spacing 0.53–0.57 ms (depending on R), 4 dummy scans, no partial Fourier, acquisition time approximately 2 min 10 s. For FLEET ACS protocols the excitation flip angle was 10° (with 5 preparation pulses). Additionally, three healthy subjects (2 F/1 M, mean age 26 ± 2 y.o.) were scanned on a 3T scanner (MAGNETOM Tim-Trio Siemens Healthcare, Erlangen, Germany) with a set of seven protocols matching the parameters used in 7T, except for: