Rapid full-brain fMRI with multi-shot 3D EPI accelerated with UNFOLD and GRAPPA

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Introduction:

Brain responses to cognitive stimuli will result in rapid dynamic BOLD signal modulations. Therefore, images acquired with high temporal resolution and full brain coverage are preferable for fMRI studies. A cascade of brain signal changes is typically observed in complex mental exercises where neural recruitment occurs in both parallel and serial fashion. Currently multi-slice single-shot 2D EPI is used for most fMRI studies. In this work we propose a multi-shot 3D EPI sequence instead, based on a standard 2D EPI sequence modified such that the third dimension of the excited volume slab is spatially encoded with a second phase-encoding gradient. Thus the entire volume is excited at each TR. Signal changes related to neuronal activity may be detected more faithfully with this 3D method as we avoid the signal loss in slice gaps common in multi-slice 2D EPI. Further, effective SNR is greater in multi-shot 3D-EPI, as each TR excites a whole 3D volume, although the output image is more T1-weighted compared to 2D-EPI [1]. Modern cognitive imaging asks for whole brain coverage, reasonable spatial resolution, and high temporal resolution. In an effort to achieve these goals with multi-shot 3D-EPI, we implemented: *i*) UNFOLD [2](in the slice encoding direction) and *ii*) Parallel imaging (in both the 3D slice and phase encoding directions). Below we demonstrate the result on healthy volunteer subjects using two fMRI paradigms: *a*) an event related complex cognitive paradigm where events lasted for a time period of up to twenty TRs and *b*) a simple visuospatial-motor task in a random-length block design. Activation patterns acquired with full kt-space coverage were compared to patterns collected with this new 3D EPI UNFOLD-GRAPPA technique.

Methods:

Experiments were performed with an 8-channel InVivo head coil on a 3T GE SIGNA machine with gradients constraints Gmax=40mT/m, slew rate S=140T/ms.

Imaging parameters: FOV=192x192x150mm^3, matrix=64x64x50, resolution=3mm isotropic, flip angle=15^o, spatial-spectral 2D RF pulse, 100Khz readout bandwidth, 3D encoding direction: left-right, EPI-readout direction: anterior-posterior, phase encoding (EPI-blip) direction: head-foot. Sagittal orientation was chosen to accommodate GRAPPA with the coil arrangements. Three different acquisitions were performed with the following parameters:

***a*)** Full k-space coverage: TE/TR=30ms/60ms, EPI ETL=64, TAQ/3D vol=3s. matrix size=64x64x50. ***b*)** 2x UNFOLD and 2x GRAPPA[3] applied along the 3D encoding direction. TE/TR=30ms/60ms, EPI ETL=64, TAQ/3D vol=1s. matrix size=64x64x17. ***c*)** 2x UNFOLD and 2x GRAPPA applied along the 3D encoding direction and 2x GRAPPA applied along phase encoding direction. TE/TR=30ms/48ms, EPI ETL= 40, TAQ/3D volume=0.82s. matrix size=64x40x17. For the UNFOLD-GRAPPA acquisition in the 3D encoding plane 8 full resolution reference slices were acquired, resulting in a total of ~3x acceleration in that direction.

Paradigms: • Visuospatial-motor task where subjects were exposed to visual quadrants with high-contrast random noise patterns and asked to focus on a center dot. A finger motion scheme was exerted in the left and in the right hand when the visual wedge was active in the left upper quadrant and in the right lower quadrant, respectively. Block lengths of stimulating quadrants varied between 5s and 15s. Noise pattern changed at a frequency of 5Hz

• Audio-visual mental arithmetic paradigm: Subjects were exposed to simple multiplication problems and offered consecutive incorrect solutions. They indicated by button press if the consistently incorrect product was (a) *close* to their (presumably correct) mental solution, (b) too *big* or (c) too *small*. The task was self-paced. Stimulus events lasted between 4s to 8s while the inter-stimulus interval was kept at 2s. Total scan time for each method was 430 seconds.

Image Processing: All images were reconstructed off-line using published UNFOLD and GRAPPA routines [4]. First, the 18 kz slices were expanded to 40 using UNFOLD, followed by GRAPPA in the alternate directions. Data processing was performed using the SPM8 software. For the visual-motor task, *T*-score thresholds were kept at $p<0.001$ uncorrected. Stimulus onset vector was convolved with the canonical HRF. For the multiplication task, a FIR window length of 16s was chosen for a train length of 20 bins for 2D GRAPPA+UNFOLD and 6 bins for full data set.

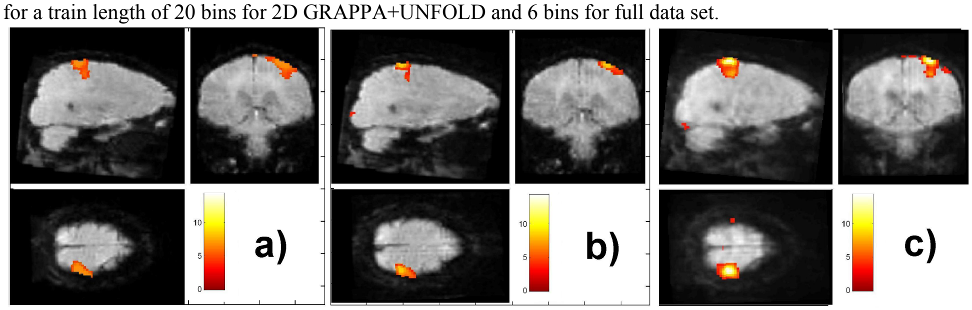
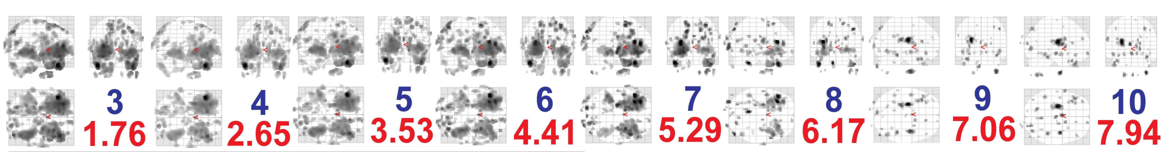


Figure 1-Brain activation patterns obtained from the following imaging modalities: **a)** full 3D-EPI (*left*) **b)** UNFOLD + GRAPPA along 3D slice encoding direction (*center*). **c)** UNFOLD + GRAPPA along 3D slice encoding direction and GRAPPA along phase encoding direction (right). Activation patterns were similar but t-scores increased from left to right.

Results: Figure 1 shows mean activation patterns corresponding to the visual-motor task for *a*) full, *b*) UNFOLD+1D GRAPPA and *c*) UNFOLD+2D GRAPPA. As expected t-scores increased as we increased the time resolution and thus the number of measurements included in the analysis, even though the paradigm is not periodic.

Figure 2 shows FIR bins for 2D GRAPA+UNFOLD and Full data sets. Time resolution of the full data set is not sufficient to capture the rapid dynamic changes in this complex cognitive task. However, the increased resolution in 2D GRAPA+UNFOLD method gives overall more informative results.



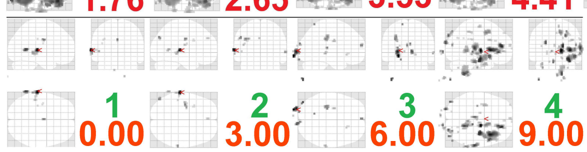


Figure 2- FIR bins for **a)** UNFOLD + GRAPPA along 3D slice encoding direction and GRAPPA along phase encoding direction (*top*) **b)** full 3D-EPI (*bottom*). Blue numbers indicate bins and red numbers indicate time in seconds.

Discussion: UNFOLD was shown [2] to produce an SNR comparable to the full data acquisition. The increase in temporal resolution outweighed the SNR loss due to parallel imaging acquisition and captured short-lived signal changes that remained hidden to the slow full data acquisition.

Conclusions: Multi-shot 3D EPI with UNFOLD and parallel imaging acquisition at a volume TR of 0.82sec was successfully applied to two different fMRI paradigms. Temporal decoding of neural activity improved in spite of a loss in SNR.

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References: **1.**Goerke et.al. NMR in Biom. 2005,18:534-542 **2.**Madore et al. MRM 1999;42:813-828 **3.** Griswold et al. MRM. 2002;47:1202–1210. **4.** NCIGT Fast Imaging Library