Improved BOLD detection at 3T using High-Resolution GRAPPA EPI fMRI

D. Mintzopoulos[1,2], L. G. Astrakas[1,2], G. C. Wiggins[3], L. L. Wald[3], B. R. Rosen[3], and A. A. Tzika[1,2]

[1]NMR Surgical Laboratory, Department of Surgery, and Shriners Burn Institute, Massachusetts General Hospital, Boston, MA, United States, [2]Athinoula A. Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Boston, MA, United States, [3]Athinoula A. Martinos Center for Biomedical Imaging and Dept. of Radiology, Massachusetts General Hospital, Boston, MA, United States

Introduction– Parallel imaging techniques enable whole-brain fMRI at increased resolution (temporal, spatial, or a combination of both). Penalties of using parallel imaging methods include reduced image SNR and, in general, noise that is spatially dependent/correlated. Gains from using parallel imaging include reduced susceptibility artifacts and improved BOLD fMRI resulting from higher spatial resolution, at optimal TE, and thus by avoiding partial voluming effects. Here, we present results from a motor (hand-squeezing) BOLD fMRI experiment that volunteers performed with GRAPPA EPI at 3× acceleration (or, equivalently, k-space reduction factor) and high spatial resolution and with a no-GRAPPA "standard" EPI sequence at lower spatial resolution. GRAPPA was preferred over SENSE as it is seen to perform more robustly [1-3] and to have better noise distributional properties [4].

Materials and methods– Healthy volunteers (N=5) performed a hand-squeezing motor task at three different levels of their own maximum force (15%, 45% and 60%). Maximum force was determined using a dynamometer. A simple block design was used, alternating three action (A) and rest (R) epochs, each epoch 30 s. During the action epoch subjects compressed and released continuously at 1Hz rate exercise gel balls. Subjects performed the experiment both at high spatial resolution (HR) using GRAPPA (TR/TE=3000/31.1 ms, GRAPPA factor=3, voxel size (1.6mm)2×3.0 mm, 128×128 acquisition matrix/200mm×200mm FOV, 48 slices (5% skip) covering the entire brain with a tilted axial orientation, 85 PE reference lines for GRAPPA calibration) and at lower spatial resolution (LR) (voxel size 3.13mm in-plane, 5mm through-plane, 2.3kHz bandwidth per pixel), without GRAPPA. Single subject analysis was performed at native space (fMRI series were not normalized to stereotactic space) in order to avoid the confound of spatial normalization.

Results– We compared the HR and LR raw images, and the functional activation results. We found a significant increase in percent BOLD signal when using the high-resolution GRAPPA protocol (Table 1). We calculated two different measures of SNR, (a) spatial image SNR (sSNR), estimating the noise from the intensity histogram from a background region of interest (ROI), and (b) temporal SNR (tSNR) using the first resting-state epoch. For the SNR calculation, images were not motion-corrected to ensure that the distributional properties of noise were not artificially altered. With said values of TE, voxel size and BW/px, the theoretical ratio sSNR(LR)/sSNR(HR) equals 2.10. The calculated sSNR(HR) with GRAPPA is actually better than $(2.10^{-1})\times$sSNR(*LR*) (Figure 1), with the caveat that the background ROI method inherently fails to account for regions with significant spatial noise correlation, due to GRAPPA unfolding operations. The tSNR figures conform to the expected values. For example, gray matter ROIs from three axial slices from three different volunteers resulted in tSNRs of 107±55, 111±57, and 101±38. tSNRs from using the GRAPPA protocol were lower (as expected): 44±18, 49±17, and 41±15, resulting in a relative temporal SNR ratio (LR/HR) of 2.38±0.41.

Table 1

Effort Level	BOLD (%) ratio [(a)]	P-value[(b)]
15%	1.66 ± 0.59 *	<0.1 (0.067)
45%	1.79 ± 0.49 **	<0.05 (0.023)
60%	1.67 ± 0.50 **	<0.05 (0.039)

(a) BOLD ratio defined and calculated as the mean BOLD signal across subjects using the high resolution GRAPPA, divided with the BOLD signal across subjects using the low resolution, no GRAPPA, protocol
(b) Compared to the null effect, ratio=1; (N=5 in each group)

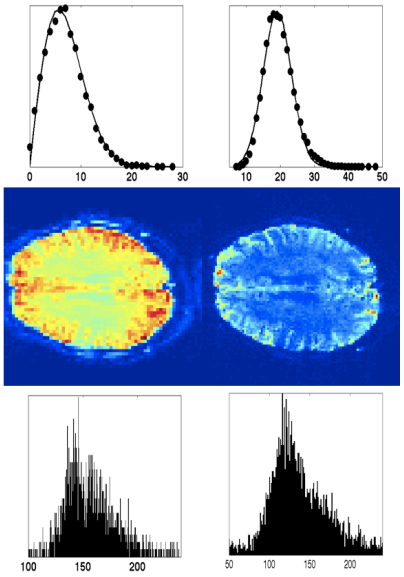

Figure 1. Image SNR comparisons of the non-GRAPPA and GRAPPA EPI. Typical SNR calculations. Non GRAPPA EPI data are arranged along the left column, and GRAPPA EPI data are arranged along the right column. **Top row, left,** typical noise histogram of non GRAPPA EPI, fitted by a Rayleigh distribution with width $\sigma = 5.7$ (Note that the horizontal scale always depicts intensity in arbitrary units). **Top row, right,** typical noise histogram of GRAPPA EPI, calculated in the image domain and fitted by a central chi-square distribution [9] with width $\sigma = 5.5$. **Middle row, left,** voxel-wise SNR image of a representative axial slice, non-GRAPPA EPI (maximum image value: SNR=250). **Middle row, right,** voxel-wise SNR of a representative axial slice, GRAPPA EPI (maximum image value: SNR=484)**. Bottom row, left,** histogram of the non GRAPPA EPI image in SNR units, scaled to SNR=250. **Bottom row, right,** histogram of the GRAPPA EPI image in SNR units, scaled to a maximum value of SNR=484.

Discussion– Our results are in agreement with previous studies using GRAPPA for visual fMRI ([5]) and SENSE [6] that found that better overall SNR than expected, and, together with improvement in spatial resolution, that BOLD detection and statistical power were not adversely affected. Also in agreement with our results, the reduction of slice thickness and use of pMRI has resulted in significant BOLD gain in the medial temporal lobe [7]. A contradictory study compared the effects of parallel fMRI (p-fMRI) and non-parallel fMRI keeping the spatial resolution fixed, and reported loss of SNR and BOLD signal when using GRAPPA and SENSE [8], however the difference indicated a trend but failed to reach significance ($0.05<P<0.1$) when the comparison was performed at the same TE, and only reached statistical significance when the comparison was performed between p-fMRI at TE shorter than the TE of the non-parallel fMRI, with a subsequent loss of T2*/BOLD sensitivity. In summary, detected BOLD signal values were consistently and significantly higher with the high-resolution GRAPPA sequence versus the no-GRAPPA sequence. Since it is impossible to attain such high-resolution unless severely limiting the field of view and/or increasing TE beyond the optimal range for BOLD detection, we conclude that the benefits of GRAPPA in fMRI may outweigh its disadvantages due to voxel-wise SNR loss.

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