IMPROVEMENT OF TASK-BASED AND RESTING-STATE FMRI USING GRAPPA ACCELERATED EPI WITH A FLASH BASED REFERENCE SCAN

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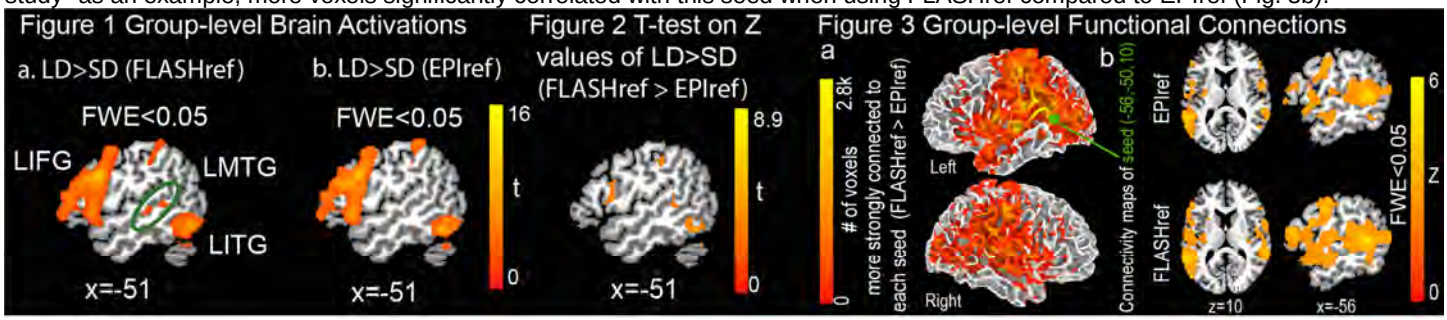
Target audience: fMRI researchers using EPI with GRAPPA parallel acquisition.

Introduction: GRAPPA[1], a primary accelerated parallel acquisition technique (PAT), is frequently used with EPI in current fMRI protocols to reduce EPI distortions and to increase the time resolution. Previously, we reported that the temporal SNR (tSNR) of GRAPPA EPI data is more uniform and higher when using a PAT reference scan collected with a FLASH, rather than an EPI acquisition scheme[2]. Here we investigated how these two PAT reference acquisition schemes affect the sensitivity to detect brain activations in task-based fMRI using a traditional lexical decision paradigm[3] and to detect functional connections in resting-state fMRI.

Method: *Design:* 11 right-handed native English-speakers participated in this study approved by NIH IRB. In a randomized block design, all subjects performed two tasks: lexical decision (LD), in which subjects judged whether or not visually presented orthographic stimuli represent a real word; and symbolic decision (SD), in which subjects judged whether or not strings of symbols represent an assigned target. 7 of these subjects did a 10-minute resting-state session with eyes opened. *Acquisition and reconstruction:* Images were collected on a 3T MRI scanner (Siemens, Skyra) using a 20 channel brain receiver array in sagittal planes with 2D gradient echo EPI, TR = 2 s, TE = 30 ms, matrix = 64 X 64 X 35, spatial resolution = 3.5 X 3.5 X 4 mm, 4 dummy scans, GRAPPA acceleration factor R = 2 (PATX2). Two sets of 36-line PAT reference data were collected using EPI and FLASH acquisition schemes. The same raw EPI data were reconstructed using either EPI (EPIref) or FLASH (FLASHref) reference data to generate two separate image series using software provided by the manufacturer. *Processing:* EPIref and FLASHref data were analyzed in the same way. Preprocessing was implemented in a standard way. *Task-based*: GLM analysis was applied at the individual subject level. At the group level, a paired Student's t-test on beta values was used in both EPIref and FLASHref data to draw random-effect statistical inferences for LD>SD (Fig. 1). Another group-level paired Student's t-test on z-transformed individual t-statistics for LD>SD was used to check the difference in functional sensitivity between EPIref and FLASHref (Fig. 2)[4]. For each subject, we examined the difference between EPIref and FLASHref in cluster sizes and peak t values of significantly and positively activated regions. *Resting-state:* At the group level, 3dGroupInCorr in AFNI[5] was used to generate the functional connectivity map at a given seed. To systematically evaluate these two methods, using each voxel in the brain as a seed, we calculated the number of voxels that were significantly and positively correlated to this seed in both EPIref and FLASHref data (Fig. 3b) and saved the difference of this number of voxels between EPIref and FLASHref back to this voxel examined (Fig. 3a). Family wise error (FWE) <0.05 was used to correct for multiple comparisons for all tests. Only positive values were considered here for simplicity. In addition, the average tSNRs were computed for EPIref and FLASHref data.

Results: *Task-based:* At the group level, when using FLASHref, we found significant activations for LD>SD in the left inferior frontal (LIFG), the middle temporal (LMTG) and the inferior temporal (LITG) gyri, as expected for a lexical decision task[6] (Fig. 1a). When using EPIref, the smaller cluster, LMTG in EPIref data was not detected as its cluster size was lower than the threshold (Fig. 1b). Z-values of LD>SD were significantly higher for all three regions in FLASHref data than in EPIref data (Fig. 2), indicating that using FLASHref increased the sensitivity to detect brain activations in all locations although its benefit was not obvious in the LIFG and ITG with large effect sizes. The sensitivity also increased at the individual subject level as we found higher cluster sizes (31%) and peak t values (18%) in all three regions for each subject when using FLASHref rather than EPIref. *tSNRs*: Consistent with our previous findings[2], the average tSNRs increased when using FLASHref compared to EPIref and the increases were 21-59% within these three clusters. *Resting state*: When FLASHref was used rather than EPIref, stronger functional connections were found in voxels (when used as seeds) all over the brain (Fig. 3a, see Method for how this map was generated). Using a posterior MTG seed defined in an independent study[7] as an example, more voxels significantly correlated with this seed when using FLASHref compared to EPIref (Fig. 3b).



Discussion: In this study, we found that the sensitivity to detect brain activations increased when using a FLASH instead of EPI based reference scan for GRAPPA accelerated EPI. It is attributed to the enhancement of tSNR when using FLASHref compared to EPIref. As both cluster sizes and t values increased for each subject, using FLASHref would be beneficial to case studies. At the group level, since the current prevailing group-level analysis only accounts for individual betas but not variances within each subject, such an increase in sensitivity may not be essential for identifying strongly activated regions but could be critical in detecting activated regions with small effect sizes. On the other hand, the improved tSNR represented a reduction in the temporal variance attributed to noises, resulting in a more accurate estimation of correlation coefficients. Therefore, using FLASHref instead of EPIref brought direct benefits to the group-level resting-state results. Our results emphasize the need for careful selection of the reference acquisition scheme when using a GRAPPA based EPI fMRI protocol.

References: 1) Griswold et al., MRM 47:1202 (2002). **2)** Talagala et al., ISMRM, 2658 (2013). **3)** Kiehl et al., HBM, 7(4):225-233 (1999). **4**) Preibisch et al., JMRI 27(3): 590-598 (2008). **5)** Cox, Computers and Biomedical Research, 29:162-173 (1996). **6)** Cabeza and Nyberg, JoCN 12(1): 1-47 (2000). **7)** Power et al., NeuroImage 59(3): 2142-2154 (2012).