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Advanced Echo-planar Parallel Imaging with Gradient Harmonization (AEPIG): an optimization strategy for fast high resolution fMRI

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Synopsis (100 words, without titles)

Motivation: Sub-millimeter resolution fMRI with large coverage of brain is limited by relatively long acquisition times. Shorter TRs with very high GRAPPA factors>8 are challenged by image artifacts.

Goal: We aim to develop, optimize, and validate highly accelerated Cartesian EPI protocols for efficient whole-brain layer-fMRI.

Approach: AEPIG (Advanced Echo-planar Parallel Imaging with Gradient Harmonization): an approach for mitigating GRAPPA artifacts by optimizing EPI trajectory accuracy.

Results: We find that AEPIG allows acceleration up to a factor of 20. Further acceleration is limited by superlinear g-factor noise amplification.

Impact: AEPIG makes it possible to perform whole brain layer-fMRI while maintaining common TRs.

Purpose

Whole-brain fMRI at mesoscale resolutions has the potential to capture the laminar functional connectome and neural information flow across brain hierarchies (Koiso 2023). However, the broader application for whole-brain layer-fMRI (100-200 slices) is limited by long TRs. Parallel imaging acquisition of mesoscale fMRI is usually limited to undersampling factors (R) of 6-9 (Koiso 2023, Yun 2022, Sharoh 2019, Chai 2024).
Higher acceleration factors for EPI have been discussed in context with g-factor noise amplification (Poser 2018, Wall 2023) but empirical results of R>8 seem to be rather limited by phase-related image artifacts (Fig. 1A), not by thermal noise.

Previous ISMRM abstracts suggested that parallel imaging amplifies artifacts due to EPI trajectory problems. I.e. any erroneous EPI ghosting can compromise GRAPPA unaliasing performance (Huber 2024).

We want to mitigate these artifacts to overcome previous acceleration limits to achieve robust protocols with R=16-20 (inspired by previous studies (Poser 2013)). We call this approach AEPIG: Advanced Echo-planar Parallel Imaging with Gradient Harmonization. Finally, we seek to validate these protocols in speed-constrained fMRI settings of popular cognitive neuroscience tasks: resting-state and autobiographical memory vs. math.

Methods

The AEPIG approach includes optimizations in acquisition and data preprocessing. Only complex-valued images from the vendor GRAPPA image reconstruction were used.

Ramp-Sampling:
Ramp-sampling can challenge EPI phase correction (odd-even correction) (Huber 2024). We compared large FOV with and without ramp-sampling and their impact on EPI artifacts that challenge higher R factors (4 sessions) (Fig. 2A).

Short-term eddy currents:
With vendor-provided service tuneup procedures, we explored the impact of short-term eddy currents on EPI image phase integrity (Fig. 2B).

Dual-Polarity Calibration:
Remaining EPI odd-even artifacts are aimed to be mitigated with a dual-polarity readout approach (Fig. 3, Stirnberg 2024). Instead of sliding-window image averaging, we update opposing polarities with an artifact model adapted from (VanDerZwaag 2009).

Experimental procedures:
We scanned 6 participants with conventional EPI and CAIPIRINHA with R=1-20. Setup: SIEMENS 7T, 32ch Nova coil, 3D-EPI skipped-CAIPI sequence (Stirnberg 2021), 0.8mm isotropic voxels. Full scan protocol: https://layerfmri.page.link/AEPIG_protocol.

Cognitive neuroscience task:
AEPIG's feasibility is tested with an auto-biographical memory task (Leelaarporn 2024) including memory-finding task-blocks terminated with self-paced button-presses, followed by a period of 'retrieving' the memory.

Furthermore, we collected low-resolution multi-echo and single-echo R=21 datasets in 3 participants.

Results

Fig. 2A shows how ramp-sampling at high resolutions can cause faint artifacts in high-resolution fMRI. While ramp-sampling increases the readout efficiency, the accompanying aliasing artifacts might limit acceleration.

Fig. 2B depicts measured gradients of a desired trapezoidal 'L'-shape. Here, the x-gradient exhibits some uncorrected short term (0.14ms) eddy currents. These eddy currents can cause low spatial frequency artifacts (aka Fuzzy Ripples). As part of the AEPIG approach, we minimized these trajectory imperfections in two ways. 1.) modifying the short-term eddy current compensation, 2.) switching to a read gradient axis (to scanner z-axis) with least short term eddy currents (Fig. 2B).

Fig. 3 demonstrates retrospective image improvement using a dual-polarity calibration approach as part of AEPIG.

Fig. 4 shows how AEPIG allows effective mitigation of phase interference artifacts up to R=20. However, at R=20, thermal noise amplification challenges signal quality in the center of the brain. The highest tSNR efficiency is achieved with R=16 and R=12 for cortical periphery and central brain regions, respectively.

Fig. 5A shows the feasibility of AEPIG using R=16 for whole-brain activation maps at TRs of 2.7s with reliable detection sensitivity during an autobiographical memory task.

While high-resolution whole-brain layer-fMRI specifically benefits from AEPIG, multi-echo fMRI is also often challenged by longer TRs. Thus, we also applied AEPIG to the conventional 2mm whole brain resting-state fMRI. Fig. 5C shows how the fast TR of AEPIG allows distinctions of resting-state network separation, as expected (LeVan 2018, Raatikainen 2017, Greicius 2003).

Discussion and summary

We proposed an optimization procedure, AEPIG, that allows us to increase the achievable acceleration by means of optimizing EPI gradient waveforms and mitigating remaining artifacts retrospectively. We find that this approach enables substantially more aggressive GRAPPA acceleration without typical artifacts. This method can address one of the biggest limitations of the whole-brain layer-fMRI, the long TRs. We note that high undersampling factors as used

here are likely less feasible for partial brain coverage. RF coils with higher channel counts (Feinberg 2023) might allow further acceleration.

Acknowledgements (no work count limit)

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Conflict of interest statement

The work presented here may be partly specific to industrial design choices of SIEMENS Healthineers' UHF scanners. This vendor is used in 83% of all human layer-fMRI papers (source: www.layerfmri.com/papers).
Michael Koehler is an employee of SIEMENS Healthineers. David Feinberg is an employee of Advanced MRI Technologies, LLC.

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5 Figures (500 characters per caption)

Abstract figures:

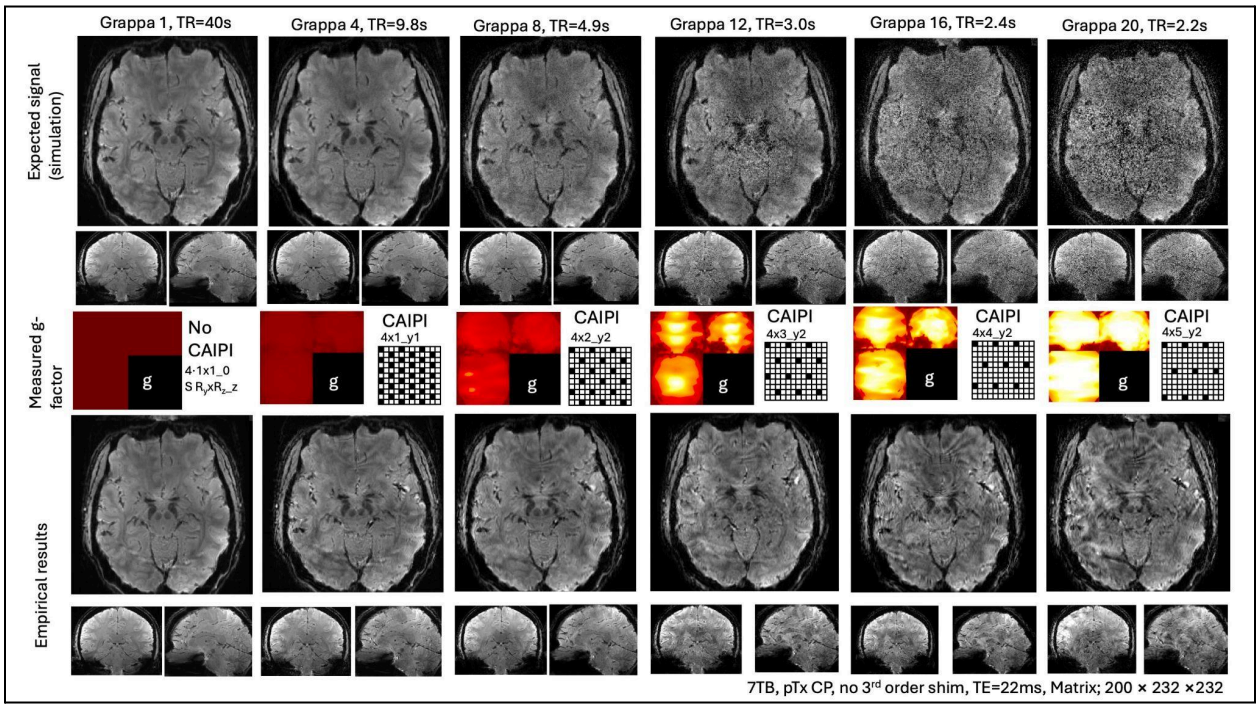

Fig. 1: Expected and experimentally measured data quality of whole brain 0.8mm fMRI.
The top row shows simulation results using measured g-factor maps, assuming that the signal at 0.8mm resolution is only limited by thermal noise.
The bottom row depicts empirically measured EPI data. It can be seen that GRAPPA >8 is unusable due to EPI phase-related artifacts rather than g-factor induced thermal noise amplification.

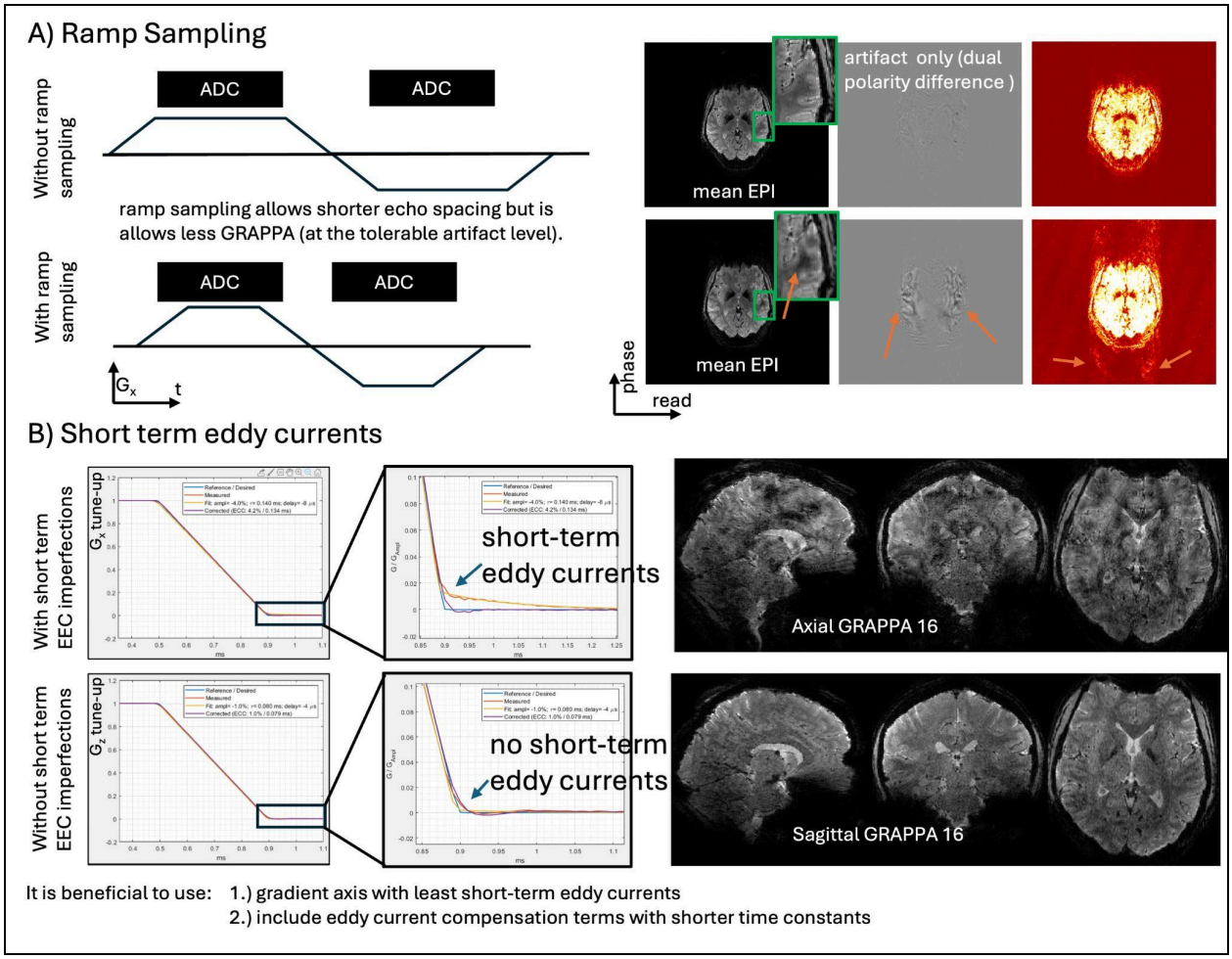

Fig. 2: Acquisition strategies to remove artifacts of large R

Panel A) in the top row shows the impact of ramp-sampling on EPI phase artifacts. While pushing gradients to their limits with high res fMRI, EPI phase correction works better without ramp-sampling, at the cost of longer echo spacing.

Panel B) in the bottom row shows the effect of short term eddy currents using the vendor's tuneup and modified eddy current compensation. Corresponding EPI data at aggressive R are shown on the right (top: readout along left-right, bottom: readout along head-feet direction).

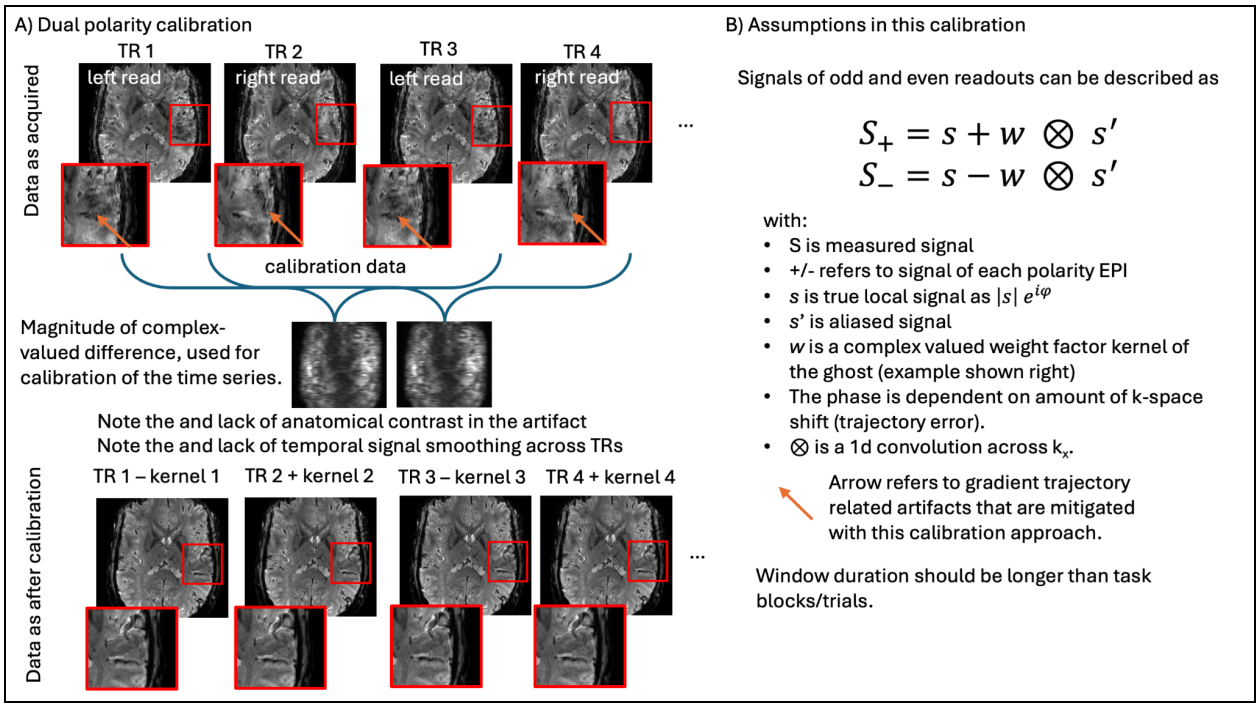

Fig. 3: Reconstruction strategies to remove artifacts of large R

A): retrospective data processing. All data were acquired using alternating amplitudes of frequency encoding gradients. With this, the readout amplitudes are inverted in every other TR. Such conventional EPI images exhibit Fuzzy ripple artifacts that are amplified with R (orange arrows).

B): the simplified signal model of the dual-polarity calibration. Each triplet of TRs is used to generate an error field for subsequent artifact correction.

Unlike previously proposed mitigation methods (Huber 2024), this approach does not result in temporal signal smoothing across TRs.

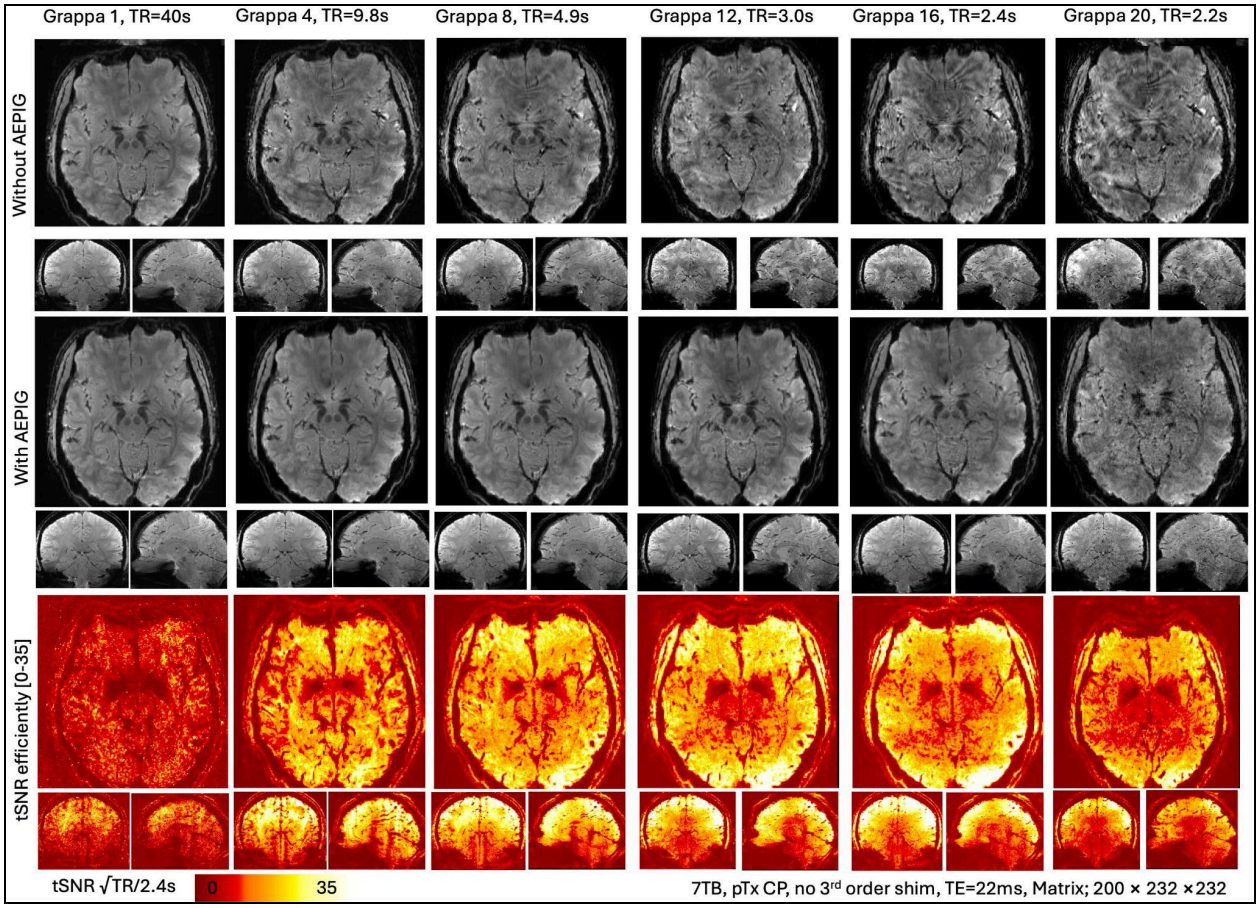

Fig. 4: Improvement of data quality with AEPIG

For increasing acceleration factors (left to right), temporal mean images are shown using conventional GRAPPA EPI (top, simulated as in Fig. 1) and AEPIG (middle, measured) and the respective AEPIG tSNR efficiency (bottom). The same sampling patterns and g-factors apply as in Fig. 1.

It can be seen that AEPIG maintains good image integrity up to higher R acceleration parameters with peak tSNR at R=16. For even higher acceleration factors (GAPPA 20 in last column), the salt-pepper looking thermal noise amplification starts to dominate.

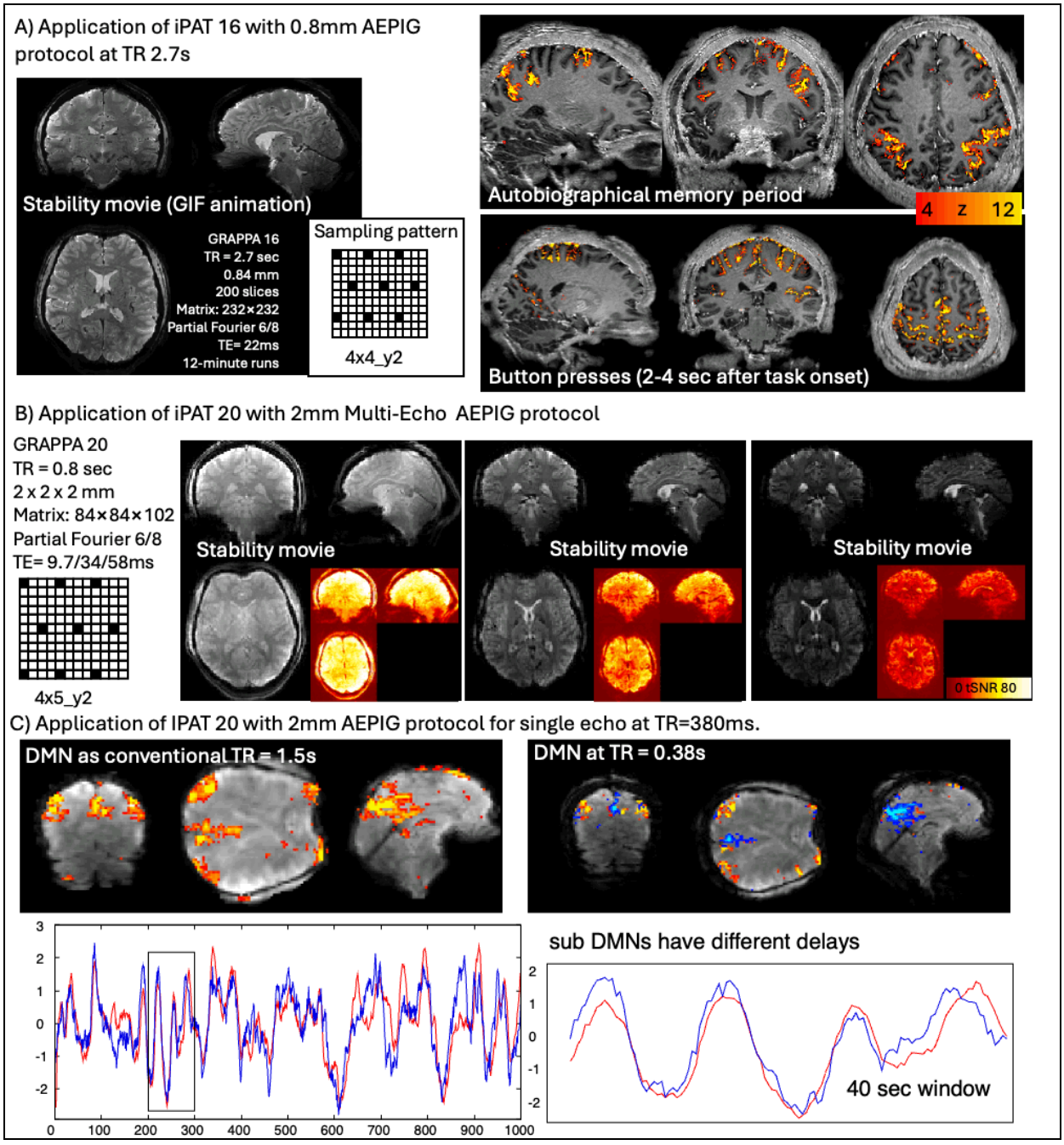

Fig. 5: Applications of AEPIG imaging for layer-fMRI and multi-echo fMRI

A) Whole brain 2.7s TR layer-fMRI imaging during an autobiographical memory and math task. The fast acquisition allows separation of individual trial sub-periods with and without button presses that are as close as 2s.

B-C) Fast conventional 2mm resolution multi-echo fMRI with R=20. The time series movie (gif animation) shows the signal stability. These fast samplings allow for subnetwork subdivision, which is less robust at longer TRs.