

# The Influence of Bold-fMRI (GRE-EPI) on MEGA-PRESS Measurements of GABA Concentrations

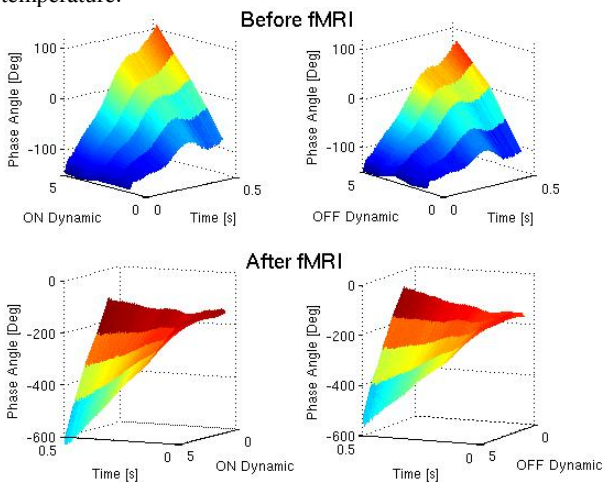
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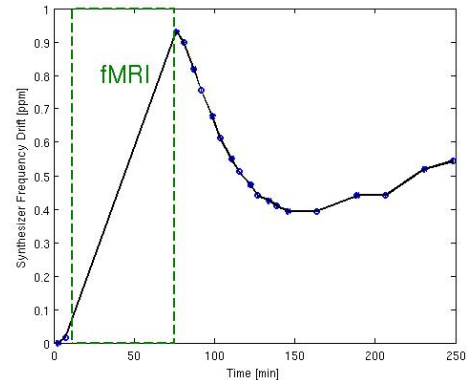
**Purpose:** In many recent experiments BOLD-fMRI has been combined with quantitative measurements of GABA-concentrations in order to elucidate the correlation between positive or negative BOLD and GABA and Glutamate concentrations in connection with a range of diseases affecting the CNS. For reasons of experimental design, GABA MRS [1] is in many cases performed subsequent to the fMRI data-acquisition. As the GABA-measurements are performed as an extended and consecutive sequence of alternating on- and off-resonance acquisitions lasting between 10-25 minutes, the quality of the GABA-measurements heavily depend on the short term stability of the MR-scanner. Thus our aim was to determine the possibly deleterious effects a BOLD-fMRI (GRE-EPI) experiment had on the stability of MEGA-PRESS [2] measurements, and we have performed careful investigations of the drift in synthesizer frequency. In addition, we determined if there were any drift in the phase, and also if any systematic phase differences between the sequential OFF- and ON-dynamics could be observed. All measurements were performed both before and after GRE-EPI.

**Materials and Methods:** The experiments were performed using a 2.00 L spherical phantom (containing 1.510 mM GABA, 0.200 mM NiCl<sub>2</sub>, and 6.000 mM creatine, from Sigma-Aldrich, in saline; pH was adjusted to 7.4 and the temperature was 22 °C) using a Philips 3.0 Tesla system equipped with a 12-channel phased array head coil. A water-suppressed MEGA-PRESS sequence (TR 3.2 s, TE 68 ms) was used with the editing pulses placed at 1.90 ppm ('ON-dynamics') and at 7.46 ppm ('OFF-dynamics') with a voxel (3x3x3 cm<sup>3</sup>) placed in the center of the phantom. Each MEGA-PRESS measurement resulted in a sequence of OFF- and ON-dynamics, where each dynamic consisted of 8 phase cycles and 1024 sample points. Directly after each completed MEGA-PRESS measurement, a shorter 2-dynamic unsuppressed water MEGA-PRESS measurement was performed within the same voxel. The protocol used in the data acquisition consisted of a single MEGA-PRESS measurement (10-dynamics) followed by a one-hour GRE-EPI sequence causing internal heating of the gradients (Single-Shot GRE-EPI, TR 2.0 s, TE 40 ms, 1800 dynamics), then six 10-dynamic MEGA-PRESS measurements, and finally three 40-dynamic MEGA-PRESS measurements. The synthesizer frequency was determined by the scanner software prior to the MEGA-PRESS measurements (in the preparation phase). The 10-dynamic measurement that was acquired first was used as reference before GRE-EPI and the first of the six 10-dynamic measurements was used as reference after the GRE-EPI experiment. Moreover, the phases were computed for each individual dynamics (including all ON and OFF).

**Results:** The synthesizer frequency increased very rapidly during the GRE-EPI sequence (1 ppm/h at 3 T; see Fig.1), presumably as a consequence of heating of the passive shim rods near the gradient coil. Directly after the GRE-EPI sequence, a gradual reduction of the synthesizer frequency was observed for about one hour suggesting cooling of the system to normal temperature.



**Fig. 2** The phases from the 5 ON-dynamics and 5 OFF-dynamics from the MEGA-PRESS measurements performed before and directly after the fMRI measurement. (N.B. The Dynamic and Time axes are reversed in the post-fMRI figures.)



**Fig. 1** The drift in synthesizer frequency before, during and after an fMRI measurement. The blue dots correspond to the MEGA-PRESS measurements.

The phase of the complex FID for the ON- and OFF-dynamics are presented in Fig.2. Directly after the one-hour GRE-EPI measurement, a very large drift in the phase was observed. This we interpreted as being a direct result of the induced system drift.

**Discussion:** The stability of the MR-scanner was severely affected by the one-hour GRE-EPI sequence for approximately one hour. Moreover, the phantom measurements showed that it is highly recommended to phase the ON- and OFF-dynamics from a MEGA-PRESS measurement individually and separately as a consequence of the large frequency drift that may be present in the MR-scanner after by for example a BOLD-fMRI experiment (such as GRE-EPI).

**Conclusions:** The large and undesired influence of EPI-induced gradient heating on quantitative GABA-concentration measurements needs to be corrected for using a procedure taking both the frequency- and phase-drift in each individual dynamic into account.

## References:

1. Mullins, P.G., et al., Current practice in the use of MEGA-PRESS spectroscopy for the detection of GABA, *NeuroImage* (2013), <http://dx.doi.org/10.1016/j.neuroimage.2012.12.004>
2. Mescher, M., Tannus, A., Johnson, M.O., Garwood, M., 1996. Solvent Suppression Using Selective Echo Dephasing. *J. Magn. Reson. Ser. A* 123 (2), 226-229.