Single Shot T_2*-sensitive Spectroscopic Imaging increases fMRI Sensitivity: Preliminary Evidence from Visual and Olfactory Activation

S. Posse, S. Wiese, C. Kessler[#], D. Gembris, U. Weiss, M. Peyerl[§], M.L. Grosse-Ruyken, B. Elghawaghi, T. Richards[‡], S. Dager[‡]
Institute of Medicine, Research Center Jülich GmbH, D-52425 Jülich, Germany;§:Siemens Medical Systems, Erlangen, Germany; #: Dept. of Psychiatry, University of Düsseldorf, Germany; ‡: Depts. of Radiology and Bioengineering, Univ. of Washington, Seattle, WA, USA

Introduction: BOLD contrast fMRI suffers from a number of limitations: (a) lack of quantitation, in part due to poorly characterized signal contributions from microvasculature, from large blood vessels and from CSF, (b) loss of sensitivity in brain regions with macroscopic susceptibility inhomogeneities, (c) physiological noise (d) in-flow sensitivity for short repetition times (TR).
Quantitative measurements of water relaxation changes during neuronal activation may help to better characterize BOLD-contrast mechanisms (1,2) and to improve sensitivity in situations where T_2*-values differ between brain regions (3). Further, distinction of T_2*-relaxation and other factors (e.g. inflow, hardware instabilities) can be achieved. We previously presented a fast T_2*-sensitive Proton-Echo-Planar-Spectroscopic-Imaging (PEPSI) method to assess functional changes in water spectra during visual stimulation (4). However, the technique was limited to single slice and had poor temporal resolution of 4.5 s.
For this study we developed a single-shot multi-slice spectroscopic imaging technique based on PEPSI (4) which we termed Turbo-PEPSI, utilizing a high gradient switching rate. We quantitatively measured T_2* signal relaxation during visual and olfactory stimulation, combined with ECG-gating to reduce physiological noise (5).

Materials and Methods: Measurements on 4 healthy male subjects (age range between 20 and 30 years) were performed on a Vision 1.5 Tesla, whole body scanner (Siemens Medical Systems, Erlangen, Germany) equipped with the standard quadrature head coil and 25 mT/m gradients, capable of a rise time of 300 µs. Wide angle visual stimulation was achieved by home-made LED goggles flashing red light at 8 Hz. For olfactory stimulation, rotten yeast (40g per 200 ml of water) was applied to the nostril using a home-made olfactometer. Multiple odor aliquots of 3 s duration and separated by 3 s rest intervals were delivered with a flow rate of 50 ml/s.
The Turbo-PEPSI pulse sequence incorporates lipid suppression and acquires 12 echo-planar-images (matrix size: 64 x 32 pixels, pixel size: 3 x 6 mm^2) with echo times (TE) ranging from 12 to 228 ms from a single FID ($\alpha = 90^o$). Phase encoding is refocused between images to encode the same k-space trajectory in all images. Multislice-slice image data sets in axial or oblique orientation were obtained with a slice thickness of 3 or 6 mm and with a temporal resolution of 250 ms per slice. The total number of acquired images (max. 2048) was dependent on TR and the number of slices due to limitations of the data transfer rate.
Visual activation was measured using TR = 3 s, 15 s baseline and subsequent 3 cycles of 12 s stimulation and 18 s baseline condition without ECG-gating. Olfactory activation was measured with ECG-gating using TR = 3 s, 18 s baseline, 24 s of stimulation, 24 s of baseline, 24 s stimulation and 15 s of baseline. For comparison, the same paradigms were performed using conventional EPI (TE: 66 ms) using the same image resolution, TR and readout bandwidth.
Reconstructed magnitude images were fitted with single exponential lineshapes of the form: $S = S_o e^{(-TE/T_2^*)}$. The range of fitted echo times was varied to assess signal characteristics at different echo times. Functional activation in the resulting images was detected by correlation with a delayed boxcar reference vector. Activated regions were confirmed by ROI analysis using the Stimulate software package (5).

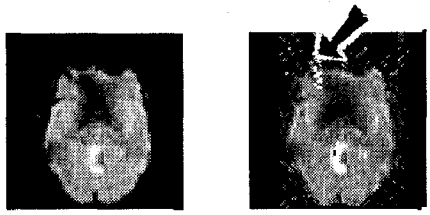
Results: With Turbo-PEPSI strong functional activation was detected in primary visual cortex with T_2* changes of up to 20 % in those areas. Stimulus related changes in S_o were measured in parts of the sagital sinus. By contrast, the extent and correlation coefficients of functional activation were much smaller with EPI than with Turbo-PEPSI. The maximum functional contrast was obtained with fitting the first 6 echoes. There was no significant functional activation when fitting the last 6 echoes. Olfactory stimulation produced significant signal changes in the orbitofrontal cortex, which is tightly connected to primary olfactory cortex, and in parts of temporal cortex. However, there was no observable activation of the amygdala. In orbitofrontal cortex two adjacent areas with different signal response characteristics were found: One area showed positive and the other showed negative signal changes. By contrast, functional contrast was much smaller in EPI scans, which was only slightly improved by ECG-gating.

Discussion: Functional mapping with Turbo-PEPSI increases functional contrast as compared to conventional EPI methods. The improved sensitivity was particularly advantageous for measuring olfactory activation, which is difficult to detect with conventional techniques. In addition, Turbo-PEPSI offers comparable data acquisition speed to conventional EPI, as well as several distinct advantages: absolute quantification of T_2*-changes, characterization of different BOLD-effect signal contributions, reduced sensitivity to spatial variations in T_2^*, feasibility of ECG-gating at short TR. With previous ECG-gated techniques it was necessary to adjust for signal instabilities due to heart rate variations and due to regionally varying T_1-values (7). This approach to quantitative functional imaging of brain activation requires further characterization to define limitations of the technique, but preliminary results are promising.

References

1. Kirsch, JE et al, *Radiology* **193**, Suppl., Abstract 93, 1994.
2.Kiselev,VG, S.Posse, *Abstr. Proc. ISMRM* 1998 (submitted)
3. Clare, S et al., *MAGMA* **5** (2), Suppl., Abstract 329, 1997.
4. Posse, S. et al., *Abstracts Proc. ISMRM,* **376,** 1997.
5. Posse, S et al., *Abstracts Proc. ISMRM,* 1837, 1996.
6. Cox, R.W., *Comput. Biomed. Res.*, **29**, 162, 1996
7. Guimaraes, A et al., MRiM 1995

Figure 1 Correlation maps (cc_{min} = 0.7) in axial slices of left orbitofrontal cortex activation (arrow) overlayed on the first image of the time series. EPI (left), Turbo-PEPSI-T_2* (right).



Acknowledgements
This work was supported by the EU grant BIOMED II PL 950870. We gratefully acknowledge F.Schneider (University of Düsseldorf) for suggestions regarding the olfactory stimuli. We thank V. Kiselev for help with data interpretation and N.J. Shah for helpful comments regarding pulse sequence programming.