Time-dependent Analysis of Functional Connectivity Using Low Frequency BOLD Fluctuations (LFBF) in Visual Areas

J. G. Hirsch[1], M. J. Lowe[2], C. Rossmanith[3], A. Gass[1,3]

[1]Dept. of Neuroradiology, University Hospital Basel, Basel, Switzerland, [2]Division of Radiology, The Cleveland Clinic Foundation, Cleveland, OH, United States, [3]Dept. of Neurology, University Hospital Mannheim, Mannheim, Germany

Introduction: Low frequency BOLD fluctuations (LFBF) are supposed to reflect slow oscillations of neuronal activity [1], and have been observed with fMRI [2, 3] as well as with other techniques [4]. LFBF are characterized by high spatiotemporal correlations in functionally connected brain regions. Synchrony is assumed as major condition in current evaluation strategies of LFBF analysis in primary functional networks [5, 6]. We extended the functional connectivity MRI (fcMRI) analysis into the time domain and investigated the time-dependent cross-correlation function [7]. This study extends the previous work by focussing specifically on the visual cortex and, in particular, smaller phase offset differences observed in functional subunits. Preliminary studies in 6 normal subjects show a more detailed differentiation of functional areas with respect to the time dependence of the cross-correlation function.

Materials/Methods: Activation in visual areas was identified by using a flickering checkerboard block-design paradigm, alternating 4 active and 5 blocks of rest à 32 s; foveal and periferal areas, resp., were stimulated. T2*w timeseries were acquired on a 1.5T system (Siemens AVANTO) in 20 slices (th=5mm, gap 1mm) with sequence parameters TR/TE=2000/50ms, flip angle=90°, fov=240x240 mm^2, mat=64x64. For the resting-state fcMR study (eyes closed), 4200 measurements were acquired in 2 slices (th=5mm, gap 1mm), covering areas of the visual cortices; TR/TE=200/50 ms, flip angle=30°. Corresponding T1w slices were acquired for anatomical reference.

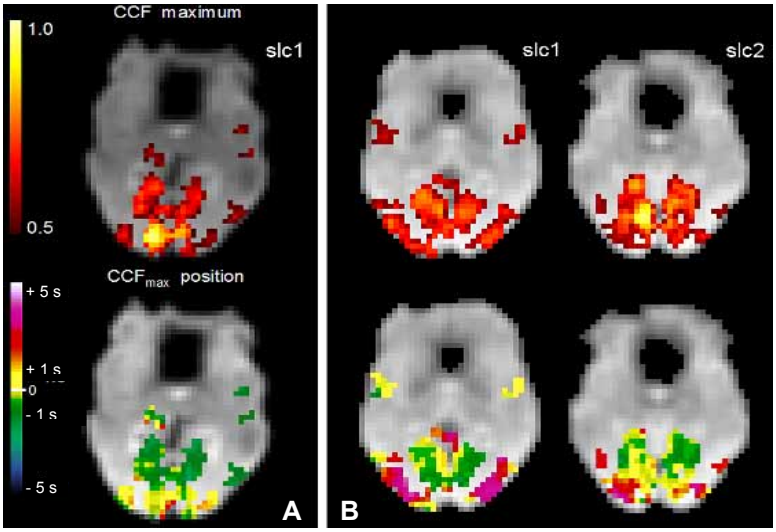
T2*w images were Hamming-filtered and digitally lowpass-filtered (<0.1Hz) to remove temporal fluctuations arising from cardiac and respiratory-related physiological noise [3]. For cross-correlation function (CCF) estimation, reference ROIs (3x3 pixels) were positioned in the visual cortex (occipital V1, ventral V3/V4, occiparietal V5). Connectivity maps were calculated showing the CCF's maximum (fig.1) within the time regime [–10s; +10s]. In addition, maps were generated coding the timeshift of the CCF's maximum in comparison to synchronous correlation (fig.2).

Results: Synchronous connectivity maps showed robust and reproducible results in regard to anatomic localisation when probing the "visual network". Analysis of the time-dependent CCF revealed increased areas showing timeshifted, highly correlated patterns. In the visual cortex (refROI in occipital V1) synchronous and delayed correlations (up to +3 s) exist to lateral V5/MT and lateral superior regions, resp., whereas timeshifted (0.5 – 2.5 s in advance) correlations to anterior parts of the visual cortex (anterior V1 or V3/V4). These findings were consistent within data subsets of 2048 measurements and across subjects. Patterns varied in size of correlated areas and amount of timeshift among the studies. Additional correlation patterns apart from visual areas have not been observed.

Discussion/Conclusion: It was demonstrated that the cross-correlation function might reveal meaningful information when the time dependence of LFBF correlations are taken into account. In a preliminary study similar patterns were observed with respect to localization and timing characteristics in correlated areas, however, quantitative measures varied, which might result from the experiment's restriction to 2 slices and varying anatomy among subjects.

As LFBF arise from underlying basal neuronal activity, a different hemodynamic coupling might cause the observed timeshifted correlations. Furthermore, the visual cortices belong to different vascular territories supplied by the middle and posterior cerebral arteries. Future studies will include block-design fMRI scans to more precisely identify functional subdivisions of the visual system as well as LFBF studies in continuously activated state.

References: [1] Leopold, D, *Cereb Cortex* 13:422, 2003. [2] Biswal B, *MRM* 34:537, 1995. [3] Lowe, MJ et al., *Magn Res Med* 37:723, 1997. [4] Hudetz AG et al., *J Cereb Blood Flow Metab* 12:491, 1992. [5] Lowe, MJ et al., *NeuroImage* 7:119, 1998. [6] Cordes D et al., *Am J Neuroradiol* 22:1326, 2001. [7] Hirsch, J et al., Proc ISMRM 13th Scientific Meeting, #179, 2005.



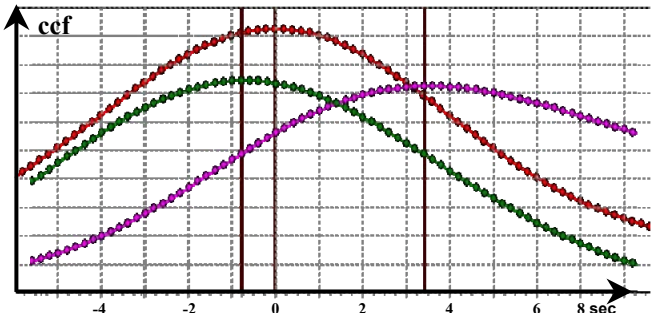


Fig.1: Resting-state (eyes closed) fcMRI studies in 2 normal subjects and time-dependent cross-correlation evaluation of LFBF. Maps of the CCF's maximum in time regime [-5s; 5s], and position of CCF's maximum on time axis.

Fig.2: Plot of time-dependent cross-correlation functions in study B; reference ROI in calcarine sulcus V1 (slc2), areas with advanced timeshift in anterior and superior adjacent regions (green), lateral areas with delayed cross-correlation (violet).