Periventricular Areas Anti-Correlate with Visual Cortex in High Resolution Resting-State fMRI at 7T

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Introduction: In previous work, anti-correlation between the default mode network and an extended dorsal attention system has been observed in fMRI data at rest [1]. We observed fMRI signal fluctuations in periventricular areas, which anti-correlate with spontaneous activity in the visual cortex (VC) at rest. Aim of this work was to investigate the modulation with behavior, the localization and the origin of this activity pattern.

Methods: To identify the regions anti-correlating with spontaneous-activity in the VC, we employed seed analysis, with the seed positioned in the VC. Two behavioral conditions (N. scans=115) were investigated: 1) "Fixation" = visual fixation on a central red fixation-dot positioned in a uniformly gray image; 2) "Eyes closed"= resting with the eyes-closed. A 360° rotating-wedge stimulation (retinotopy, N. scans=172) was employed as functional localizer for a region-of-interest in the VC (ROI_{VC}, $p<10^{-5}$, uncorrected for multiple-comparisons). Eight subjects (4m/4f, age 32±3y) participated in the IRB-approved study. GE-EPI SENSE-rate3 BOLD-fMRI was performed at 7T (GE-Medical-Systems) using 32 receive-only coil-elements and the following parameters: TE/TR=32ms/3s, F.A.=75°, N. slices=36, voxel-dim=1.25x1.25x2mm^3, slice-gap=0.2mm. To localize the spontaneous activity patterns, we repeated the fMRI-protocol on five subjects (3m/2f, age 33±4y) and also acquired a high-resolution multi-gradient-echo image (parameters: TR=1.9s; TE=14/28.5ms, FA=90°, voxel-dim=0.31x0.31x1mm^3, slice-gap=1.2mm; SENSE-rate=2). To investigate the origin of the activity pattern in periventricular areas, on three subjects (3m, age: 30±4y) we repeated the fMRI protocol acquiring multi-echo EPI images (TEs=12/28.2/44.4ms; TR=2s, FA=75°, N. slice=20, voxel-dim=2.5x2.5x2mm^3, slice-gap=2mm, SENSE-rate=3, N.scans=178 for resting conditions and 245 for retinotopy). We extracted T_2* and S_0 (S_0=S(TE=0)) by linear least square fitting of multi-echo data.

Pre-processing of fMRI-data included: slice-timing, motion-correction, co-registration between 4D-volumes, removal of effects related to the phase of physiologic cycles [2] and due to fluctuations of physiologic rates [3], conversion of fMRI signals to percentage signal-changes (SC, %) relative to baseline, low-pass filtering (cut-off frequency=0.073Hz). Global signal regression was not performed. Multiple-regression was then performed for the two conditions. The design matrix comprised third-degree polynomials modeling low frequency drifts, six motion-correction parameters, and the averaged time-series across ROI_{VC} (seed-timeseries), modeling spontaneous-activity in the VC. An ROI including the areas (mainly periventricular regions) anti-correlating with spontaneous-activity in the VC was defined during the eyes-closed condition ($p<0.05$, Bonferroni corrected, ROI_{AC}). The amplitude (% SC) of spontaneous-activity and motion in each voxel of ROI_{VC} and ROI_{AC} was measured as the standard-deviation of the signal explained by the seed-timeseries and by the motion-related regressors; the amplitude was then averaged within each ROI and across subjects.

Results: Positive-correlations with the seed-timeseries occurred widespread in the VC; negative-correlations were seen adjacent to and inside ventricular areas (Fig. 1, ependymal lining of the posterior and anterior horns of the lateral ventricles, glomus and choroid plexus of lateral ventricles, fourth ventricle). Behavior modulated the amplitude of spontaneous activity in the VC [4] and in ROI_{AC} ($p < 0.002$), but not the amplitude of motion-related effects (for a threshold $p < 0.05$, Fig. 2). Spontaneous activity in periventricular areas co-localized with large veins (Fig. 3). Negative correlations in periventricular areas persisted in T_2* images and were reversed in sign in S_0 images (Fig. 4, see black arrows). Considering that blood has shorter T_2* and T_1 than CSF, a decrease in T_2* and an increase in S_0 are expected for a blood volume increase in periventricular areas.

Conclusions: We found spontaneous-fMRI-activity in proximity of the ependymal vascularization of the ventricular system. This activity is modulated by behavioral state and is not an artifact due to head motion, or heartbeat/respiration. Periventricular fMRI-signal decreases were also reported during REM-sleep [5]. Our results are consistent with a blood volume increase of veins draining the inner parts of the brain (e.g. internal occipital veins for occipital areas), concurrent with increased fMRI signal in the VC.

References: [1] Fox MD, et al. (2005), *PNAS*, 102:9673:78. [2] Glover GH, et al. (2000), *Magn Reson Med*, 44: 162-7. [3] Bianciardi M, et al. (2009), *Magn Reson Imag*, 27:1019-29. [4] Bianciardi M, et al. (2009), *NeuroImage*, 45:160-8. [5] Hong, C.C., et al. (2009), *Hum Brain Mapp*, 30:1705-22.

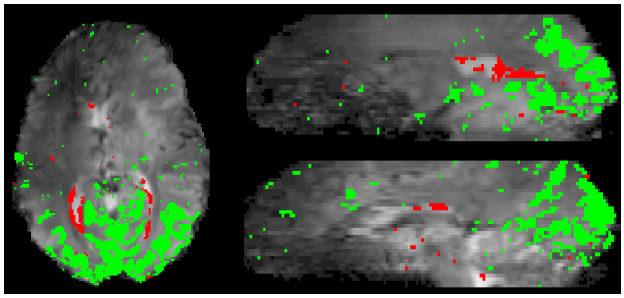

Fig. 1 Left, axial view and, right, sagittal views of the spatial distribution of signals correlating (green) and anti-correlating (red) with the seed-timeseries in the VC (example data-set, $p < 0.05$ Bonferroni corrected; same statistical threshold applied in Figs. 3-4).

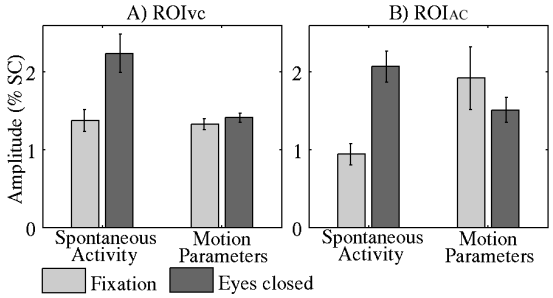

Fig. 2 The amplitude of spontaneous activity (group analysis) in both A) ROI_{VC} and B) ROI_{AC} in different behavioral conditions.

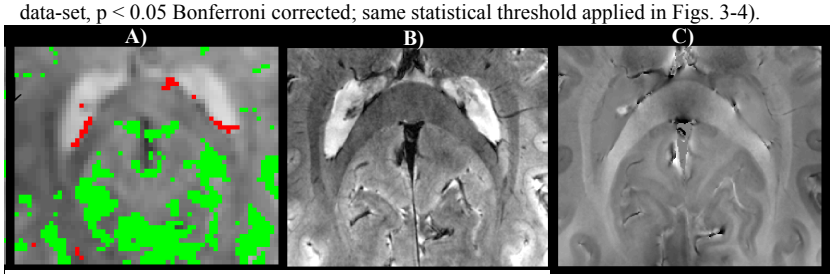

Fig. 3 For an example data-set, we show a zoomed view of: A) negative/positive correlation maps (red/green) with the seed-time series in the VC, and the anatomy of the lateral ventricles in high-resolution B) magnitude and C) phase images (TE = 28.5 ms).

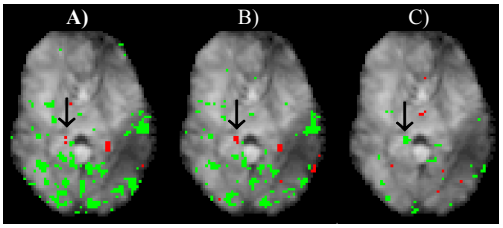

Fig. 4 Correlation maps (red/green = negative/positive) with the seed timeseries in the VC from the second echo (TE = 28.2ms). Images for an example data-set for A) third echo (TE = 44ms), B) T_2* and C) S_0 images.