Spontaneous fMRI activity reflects a dynamic image of brain state

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Purpose: It is still poorly understood if spontaneous fMRI activity (SA-fMRI) of the human brain represents ongoing sensory processing or homeostatic/cognitive functions that depend on brain state. For example, the reduction of SA in the visual system observed when opening the eyes in low ambient light conditions [1-2] may result from a change in sensory input or brain state, possibly including effects from arousal and oculo-motor activity. To investigate this, we measured the amplitude (AM) of SA-fMRI in the visual cortex (VC) in different behavioral and environmental conditions, affecting preferentially the brain attentive state (eyes open/closed [3]) and the visual input (presence/absence of light). We further studied the neuronal and oculo-motor correlates of changes in SA-fMRI, by measuring, in a separate experiment with the same subjects and conditions, the AM of spontaneous activity in magneto-encephalographic recordings (SA-MEG), and in electro-oculogram recordings (SA-EOG), respectively.

Method: ***Paradigm:*** Nine subjects (7m/2f, age 36.3±2.5) participated in the IRB-approved study. Four conditions (345 s each) were investigated: 1) "EO-fixation-light" = visual fixation on a dot positioned in the center of a uniform gray image (luminance = 60.0 cd/m^2), with dim room light (0.7 cd/m^2); 2) "EO-darkness"= resting with the eyes open in darkness (<0.05 cd/m^2); 3) "EC-darkness"= resting with the eyes closed in darkness (<0.05 cd/m^2); 4) "EC-light"= resting with the eyes-closed with a white image projected on the screen viewed by the subject (90.0 cd/m^2; the estimated luminance -primarily red light- perceived by the retina was ~ 9cd/m^2 [4]). The MRI and MEG scanner rooms were completely darkened in conditions 2)-4). ***fMRI-Data Acquisition and Analysis:*** GE-EPI SENSE-rate3 BOLD-fMRI was performed at 7T using 32-receive-only coil elements and parameters: TE/TR=32 ms/3 s; flip angle=80 deg; N. slices=42; voxel-size:1.25x1.25x2 mm^3. A 360 deg-rotating-wedge stimulation (516 s) was employed as functional localizer for a region of interest in the VC (ROI_{VC}, Fig.1A), $p<10^{-5}$, uncorrected for multiple comparisons). Pre-processing of fMRI data included slice-timing, motion correction, co-registration between different 4D-volumes, conversion of fMRI signal fluctuations to % signal changes relative to their time average, correction of instrumental and physiologic noise [5], and temporal low-pass filtering at f_C=0.073 Hz. SA-fMRI maps were generated by computing the correlation of the average timeseries in ROI_{VC} with the signal in each voxel. For each condition and subject, the AM of SA-fMRI was measured as the standard-deviation (S.D.) of the average timeseries in ROI_{VC}. ***MEG-EOG-Data Acquisition and Analysis:*** A whole-head SQUID magnetometer with 273 channels was employed for continuous MEG recording at 600 Hz. Eyelid- and eye-movements were recorded by two EOG Ag/AgCl electrodes, positioned at the left outer canthi and below the left eye, respectively. Pre-processing of MEG and EOG data included: band-pass filtering (0.5-70 Hz); downsampling to 200 Hz; signal scaling by the signal S.D. over time averaged across conditions. The spectral distribution of AM-MEG and AM-EOG for frequencies between 0 Hz and 70 Hz was calculated as the S.D. over time of the absolute value of the spectrogram computed over 3 s adjacent and non-overlapping windows. The spectral distribution of the AM was averaged across frequencies in the delta (0.5-4 Hz), theta (4.5-8 Hz), alpha (8.5-13 Hz), beta (13.5-30 Hz), and gamma (45-70 Hz) bands for MEG data, and across 4-30 Hz for EOG data. AM of SA-MEG and of SA-EOG was then averaged across occipital MEG channels and the two EOG channels, respectively.

Results and Discussion: SA-fMRI maps of localizer A) and the various resting conditions B)-E) are shown in Fig. 1 (single subject, p<0.01 Bonferroni corrected). For each condition, the spectral amplitude of the average fMRI signals in ROI_{VC}, prior to low-pass filtering, is shown in Fig. 1F (averaged across subjects). The spectral distribution of the AM of SA-MEG averaged across occipital channels and subjects is shown in Fig. 1G (frequency range 0-30 Hz shown only). With respect to EC-darkness: the group average AM (± S.E. across subjects) of SA-fMRI shows a state-dependent decrease with EO, either in darkness or in light/fixation conditions (** p < 0.01, Fig. 1H); a similar decrease was found for AM of SA-MEG in the theta, alpha, and beta band for the EO-fixation-light condition in agreement with previous work [3], but not for EO-darkness condition (** p < 0.01, * p < 0.03, Fig. 1I, mean ± S.E. across subjects); the AM of SA-EOG increased during EO conditions (p<0.01, results not shown), reflecting increased activity due to eyelid- and eye-movements. No significant reduction in AM of SA-fMRI, SA-MEG, or SA-EOG is seen with the presentation of light through the eyelids in the EC condition.

Conclusion: SA-fMRI reflects a dynamic image of the current brain state, and may not solely depend on sensory processing. Our results suggest that the level of spontaneous fMRI activity may depend on the level of arousal and oculo-motor activity.

References: [1] Bianciardi et al, NeuroImage, 45:160-68, 2009. [2] McAvoy et al, J Neurophysiol, 100:922-931, 2008. [3] Adrian, and Matthews, Brain 57: 355-385, 1934. [4] Moseley, Ophthal Physiol Opt, 8:229-30, 1998. [5] Bianciardi et al, Magn Reson Imag, 27:1019-29, 2009.

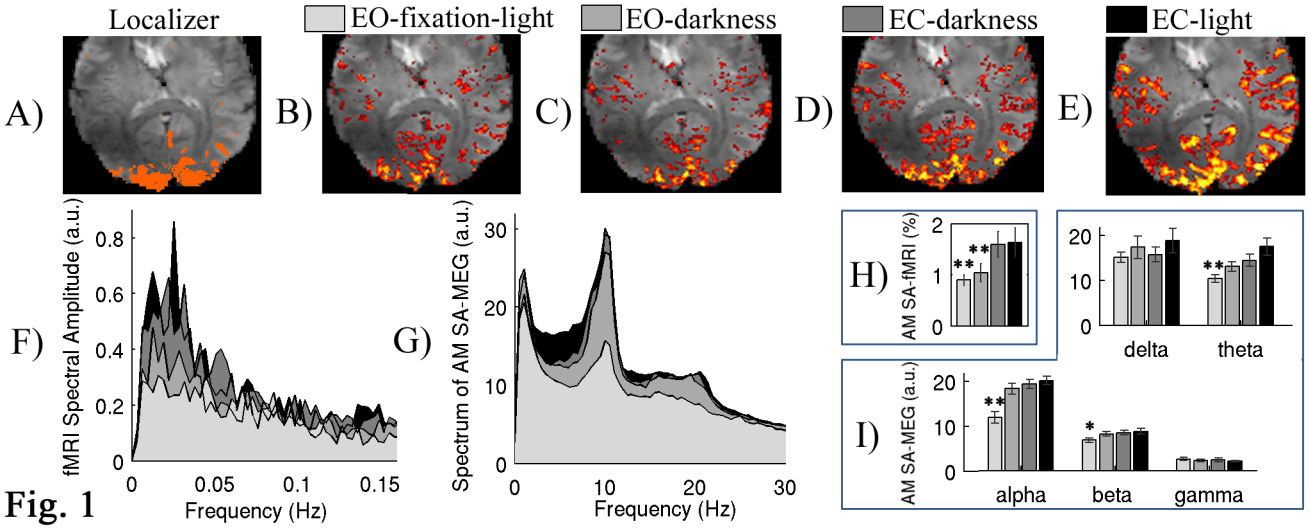

Fig. 1