State-dependent, widespread correlation of neural and fMRI endogenous fluctuations in the awake monkey

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Introduction. Even in the absence of sensory stimulation, mapping the spatial correlation of fMRI fluctuations gives rise to organized patterns in the brain, and is thought to reflect functional connectivity [1-3]. While the basis of the fMRI correlations is unclear, recent work has demonstrated that spontaneous hemodynamic fluctuations are correlated with electrophysiological signals in the brain [4-6], and therefore may reflect neural signaling. Of particular note are fluctuations in gamma range local field potential power and multiunit activity, whose correlation with BOLD fluctuations in the anesthetized monkey is spread over a large portion of the visual cortex [6]. In the present study, we explore the spatiotemporal correlation of fMRI signal and electrophysiological signals in occipital, parietal, and frontal sites in the brain.

Methods. Endogenous fluctuations in the brain were evaluated by simultaneously measuring electrophysiological and fMRI signals in the awake monkey. Resting state data were collected in a 4.7T vertical bore primate scanner (Bruker Biospec 47/60). MR-compatible multicontact electrodes (NeuroNexus Technologies) were implanted in the primary visual cortex in three monkeys, as well as in the parietal (area 7A), and frontal lobes (area 6) in one monkey. Fluctuations in local field potential power were measured during fMRI scanning using a specialized amplifier placed inside the magnetic bore (Brain Products, GmbH). Functional imaging was conducted following the IV administration of monocrystalline iron oxide nanoparticles (MION), providing a measurement of regional cerebral blood volume (rCBV) with good signal to noise ratio. The monkeys' eyes were monitored with a video camera during the scan.

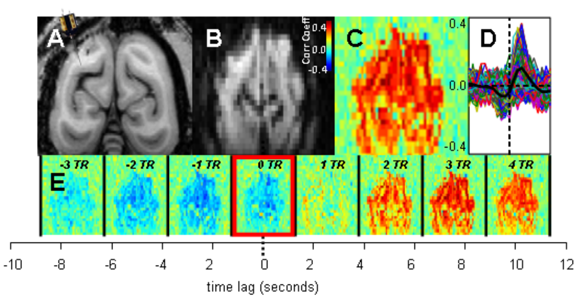

Figure 1. Cross correlation of spontaneous gamma LFP power and fMRI time course in coronal slice containing the electrode. **A**. Multicontact electrode superimposed on recording site in V1 of a macaque monkey. **B**. EPI image from a sequence collected simultaneously with neurophysiological recordings. **C**. Functional map of correlation in the spontaneous fluctuations in the gamma range (40-80 Hz) power of the LFP signal and the MION fMRI time course. **D**. Cross correlation time course of all voxels in C. **E**. Evolution of cross correlation map, as a function of lag between the electrophysiology and MION fMRI signals. MION correlation signals are inverted in C-E for clarity, since increased MION volume leads to decreased signal.

Results. Endogenous fluctuations of the gamma LFP power and fMRI signals were strongly correlated, not just in the region of the electrode but across a large portion of the brain. Gamma frequency power showed widespread correlation with endogenous rCBV fluctuations throughout the cerebral cortex. Cross correlations functions typically showed positive peaks at lags of 6-8 s and negative correlation before lag = 0 (see **Figure 1**).

The widespread correlation of the gamma LFP power was present for frontal and parietal sites, as well as for the V1 site. Based on scoring of a video of the monkey's face during data collection, the correlation was significantly stronger during periods when the monkeys eyes were closed than when they were open (**Figure 2**). Other portions of the LFP spectrum were more variable in their correlation with the fMRI signal. Alpha-range power modulations were frequently negatively correlated with the rCBV fluctuations.

Discussion. These findings demonstrate that a significant portion of the variance of resting state activity is correlated with underlying neural activity, and that the relationship between fMRI and neural signals changes as a function of behavioral state. The widespread correspondence between endogenous gamma and fMRI fluctuations is linked to the behavioral state, and is likely therefore to reflect ascending neuromodulation of the cerebral cortex. Specifically, the *correlation* between these variables that is not fixed, but changes with behavioral state, a finding with implications for the understanding of neurovascular coupling.

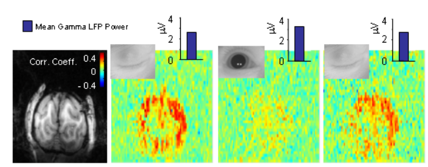

Figure 2. Influence of eye closure on the correlation with gamma LFP power. Monkeys were seated in total darkness. Three panels correspond to sequential periods during which the monkey's eyes were predominantly closed, open, and closed. Note that there is a slight increase in gamma LFP power in the eyes open condition, when the correlation is lowest.

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