Eigenvector centrality mapping based on low-frequency phase alignment

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Introduction. Our brain acts like a small world network much like the World Wide Web (WWW). Therefore, techniques known from internet search engines such as Google's PageRank that specifically exploit small world properties of the WWW can be assumed to work well for analyzing brain data. We have recently proposed a variant of Google's PageRank called ``eigenvector centrality mapping'' (ECM) as a new analysis method for fMRI data (Lohmann et al, 2010). In ECM, each voxel receives a rank describing its centrality (hubness) within the brain. Centrality measures depend on a metric describing similarity between time series. In our previous study, we had used ECM based on spectral coherence which assesses linear dependence between time series as a function of temporal frequencies. However, this measure ignores phase shifts between time series so that time series may receive high coherence values even though they are separated by large phase shifts. In the present work, we specifically focus on such phase shifts and investigate whether changes in brain state may produce phase adjustments such that fMRI time series become more closely aligned in time. We re-evaluated rs-fMRI data of 22 subjects who were scanned in two sessions comparing a hungry versus a sated state and computed ECM based on a phase alignment measure. We found regionally specific and statistically significant changes in phase centrality between the two scans.

Methods. We re-evaluated data described in Lohmann el al. (2010). Functional MRI/EPI data were acquired of 22 normal volunteers on a 3T MRI scanner (Siemens Trio) using TR=2.3sec, TE=30ms, (3 mm)^2 in-plane resolution, 3mm slice thickness, 1mm gap between slices. The subjects were asked to attend two scanning sessions, in one of which they were asked to refrain from eating after 6pm of the previous day. During both sessions, we acquired resting state data for 6.5 minutes during which subjects were asked to fixate on a fixation point. All data sets were initially registered to an AC/PC coordinate system and resampled to an isotropic voxel grid with a resolution of (3 mm)^3. We manually defined a mask containing about 40,000 voxels covering the entire cerebrum. We then computed a similarity matrix containing pairwise similarities between fMRI time series within this mask. The entries of its principal eigenvector are a measure of node centrality (Lohmann et al, 2010). We have previously used spectral coherence as a similarity measure. It is defined as follows (Priestley, 1981). Let X,Y be two time series centered around zero. Their cross-correlation function is defined as $c_{xy}(k) = E(X_{t+k},Y_t)$, and the corresponding cross-spectral density at frequency ω is $f_{xy}(\omega) = \mathrm{Sum}_k\ W(k)\ c_{xy}(k)\ \exp(-2\pi i\omega\ k)$ with some weighting function W(k). The real part of $f_{xy}(\omega)$ is the cospectrum (denoted as C) and the imaginary part is the quadrature spectrum (denoted as Q). Spectral coherence is defined as $\psi(\omega) = \mathrm{sqrt}\{(C^2+Q^2)/(f_{xx}(\omega)f_{yy}(\omega))\}$. The corresponding phase angle is given by $\phi = \arctan [Q/C]$ in $[-\pi,\pi]$. For the purpose of centrality mapping, we define a measure of phase alignment as $s(\omega) = 1 - |\phi/\pi|$ so that s(ω) is a value between 0 and 1 with '1' denoting complete synchrony (lack of a phase shift) at frequency ω. The results reported below are based on this measure so that voxels that receive high ECM ranks are closely aligned in time with many other voxels. However, one should note that phase measurements are only meaningful for coherent time series. Therefore, we defined a second measure t(ω) in which phase alignment is multiplied by spectral coherence, i.e. $t(\omega) = s(\omega)\ \psi(\omega)$, and we re-computed ECMs accordingly. The results obtained using s(ω) and t(ω) were very similar so that we may assume that phase alignment and not just spectral coherence played a significant role. We computed phase alignment at ω=1/10, 1/20, 1/30 Hz, and applied paired t-tests contrasting the resulting phase centrality maps of the hungry versus the sated state.

Results and Discussion. The most pronounced differences in phase centrality were found at 1/20 Hz (fig 1). Specifically, we found that phase centrality increased significantly during the hungry state in precuneus and the right anterior insula/frontal operculum (AI/FO), whereas it was stronger in the middle temporal gyrus (MTG) and the left orbito-frontal region (OF) during the sated state. Results are corrected for multiple comparison at the cluster level using $p< 0.05$. The AI/FO belongs to the gustatory cortex and is therefore relevant to food intake, like the MTG which was found by Santel et al (2006) in a similar context. Precuneus was already reported and discussed in our previous study (Lohmann et al, 2010), and the orbito-frontal cortex is well known to play a crucial role in reward-dependent decision making in men.

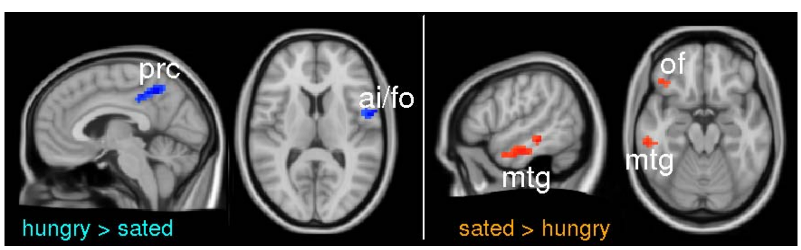

Figure 1: Contrasts between hungry and sated states.

Conclusions. We found regionally specific and statistically significant changes in phase centrality in the low frequency domain between two scans. We attribute these differences to changes in brain state produced by feelings of hunger versus satiety. Our findings suggest that brain states manifest themselves not only in patterns of spectral coherence but also in phase alignment. This may indicate an important mechanism of functional integration closely related to the concept of phase synchrony recently investigated in fMRI data by Kitzbichler et al., 2009 and Chang et al., 2010. Future work will be directed at further exploring this avenue.

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