Transient synchronising sub-networks within large scale networks

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Introduction: We have previously demonstrated that spontaneous brain activity can be detected with fMRI using paradigm free mapping (PFM) a model free analysis method capable of characterising spontaneous BOLD events¹. However the problem with studying spontaneous events is that it is difficult to interpret them since they relate to an undirected task. In recent years, fMRI has shown that highly focal areas of the brain relate to specific tasks, for instance the parcellation of the motor cortex into areas responsible for the control of individual fingers. If similar patterns of activation could be detected by PFM then we could interpret the functional significance of the activity underlying the spontaneous events. Here we use PFM and temporal independent component analysis (tICA) to identify patterns of brain activity and connectivity associated with spontaneous events.

<u>Aim</u>: To identify consistent patterns of activation associated with spontaneous events observed in fMRI data.

Methods: Twelve subjects were scanned using a 7T Philips Achieva system (volume transmit and 32-channel receive coil) using a gradient echo EPI acquisition (TE/TR 25/2000ms, 2mm isotropic resolution) and physiological data recorded using a respiratory belt and VCG. Two experiments consisted of 5 minutes of rest, 6 minutes of task (unilateral finger tap exercise or 2-back working memory task) and a subsequent 6 minutes of rest. Data were realigned and corrected for slice timing (SPM5), physiological noise was removed using RETROICOR, data were smoothed with a 4mm FWHM Gaussian kernel and drift was removed by subtraction of a 3rd order polynomial. Data were separated into three periods: rest 1 (1<t<240s), task (360<t<600s) and rest 2 (780<t<1020s). PFM was applied to each data set to identify BOLD events without prior knowledge of their timing. For each subject, each of the four rest periods were temporally concatenated, and the identified events convolved with a HRF. Standard masks² of the nodes of the motor network (MN), fronto-parietal network (FPN) and default mode network (DMN) were used to define ROIs in the concatenated data. The timecourses from these ROIs were used to produce network-specific voxel-by-time matrices. Note that masking to ROIs reduced the ratio of the number of signals to time points, thus making subsequent tICA more stable. PCA was used to reduce the dimensionality to 15, tICA was then applied using fastICA³ resulting in temporally independent signals and associated weights which comprise spatial maps of the 10 temporally independent components. These maps were transformed into MNI space using FLIRT.

Results: Figure 1 depicts a voxel-by-time matrix from the MN for a single

PULTICATION OF A single subject for the MN.



subject for the first rest period; and shows temporal and spatial clustering of spontaneous events within the network nodes. This effect was apparent in all subjects and networks. Figure 2A shows three tICA maps for the MN, the beige overlay depicts the mask, red indicates an IC positive weight and blue indicates a negative IC weight. The three maps show consistent shape and structure with areas of high weighting following the cortical structure. The positive and negative weights within a single map depict opposing responses to the same event within a single large scale network. Figure 2B and 2C show similar tICA maps for the left FPN and the DMN, again with consistent structure. Note that some components show the same polarity of response across the network (left) whilst others show opposing polarities in different nodes (centre, right).

Discussion: Using PFM, network masks and tICA, the events found by PFM have been shown to represent BOLD responses that are clustered spatially within network nodes (figure 2). The tICA maps show that spontaneous events do not necessarily involve whole networks, or whole network nodes, but rather clusters of voxels which act in concert, forming transiently synchronising sub-networks related to the spontaneous events. The alignment of these regions with the cortex suggests that these foci are likely to relate to functional regions that have been found in task driven fMRI studies. The positive and negative responses within the same network show that different areas of a single network can respond in opposition to one another within a single BOLD event. This opposition could arise due to combined functional activation and deactivation of a region, or due to vascular constraints. The fact that particular regions of the brain consistently participate in concerted activity involving different transiently synchronising sub-networks suggests that pattern spatio-temporal recognition methods might be applied to relate this spontaneous activity to function *post hoc*. Thus pattern recognition methods might allow resting state datasets to be compressed, whilst retaining information at an appropriate spatial and temporal time scale, to make them amenable to neuroscientific interpretation. **References:** 1. Petridou et al, HBM 2012. 2. Hyvarinen, IEEE 1999; 3 (10): 626-34. 3. Filippini et al, PNAS 2009; 17 (106):

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