Network-level comparisons of functional connectivity differences between cognitive tasks

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Introduction: The field of brain imaging has taken a large interest in examining networks and connectivity patterns between brain regions, rather than just modulated activity in unimodal regions. Several networks have been identified using fMRI in both the 'resting' state and the 'task-positive' state. On switching states, resting state networks (e.g. Default Mode Network; DMN) give way to task-relevent networks. Whilst the basic findings are robust, many variations in post-processing can elucidate different aspects of the underlying connectivity. Specifically, care must be taken to remove effects of physiological fluctuations unrelated to neural changes. In addition to collecting physiological information (heart rate and respiration), task-specific functional connectivity can be preprocessed using a condition-specific weighting function to further remove physiological effects, as they will be largely uncorrelated with task changes [1]. However, direct examination and comparison of condition-specific connectivity matrices is challenging due to the large number of elements, especially in cognitive paradigms with a large number of regions interacting. In this work, we present a network information-based analysis approach to compare two condition-specific functional connectivity matrices. This approach is demonstrated by application to a two-condition task designed to elicit functional networks related to interpretation and processing of either abstract (e.g. dream) or concrete (e.g. house) words. Furthermore, to gain the SNR needed for subtle classification metrics, a 7T MRI system was used.

Methods Data Acquisition: Four healthy subjects participated in the study. The paradigm had previously been optimised for condition-specific network comparison (rather than detection of individual regional activity differences) on previous data collected elsewhere at 3T [2]. Three words appeared for three seconds: the one at the top was the 'test' word and the other two were presented below side-by-side. The participant had to make a decision as to which of the two bottom words was closer to the 'test' word in meaning. They made a button press (right hand, 2nd or 3rd digit) to indicate either the word on the left or right. The screen showed fixation for 7 seconds after each set of words. The words alternated pseudo-randomly between either abstract or concrete nouns. All sets of three words were similar such that there was no 'correct' answer. A total of 96 trials was presented in blocks of 16 each with a 90s rest between blocks. Echo-planar images were acquired using a 7T Philips Achieva system (2s TR, 25ms TE, 36 slices, 2.4 mm^3 voxels, 80x80 FOV, SENSE factor 2). A parcellated shimming procedure was used to ensure homogenous B0 for whole-brain coverage. An anatomical MRI was also collected for coregistration to MNI coordinates.

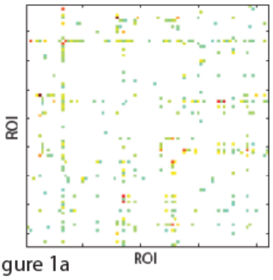
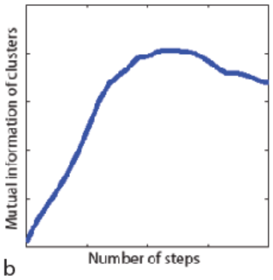


Figure 1a



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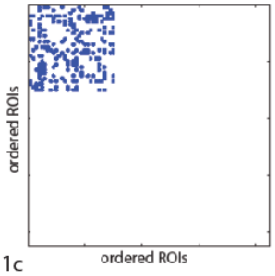

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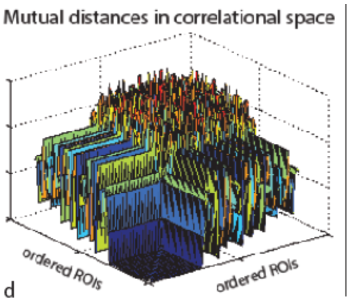

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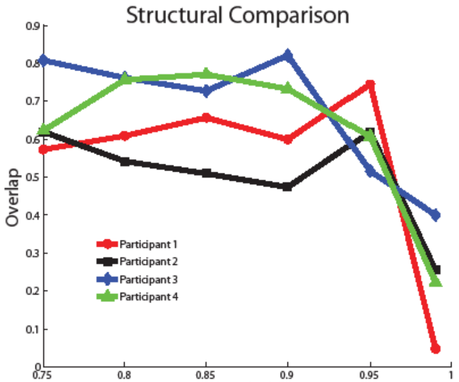
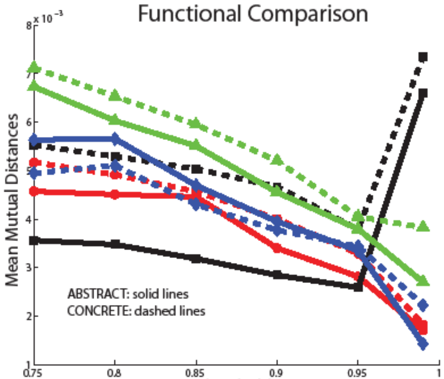


Figure 2a



2b

Methods Data Analysis: Data were corrected for motion and slice timing, and normalized. Data were segmented into 116 regions defined by Automated Ananatomical Labelling (AAL) [2], and voxels within each region averaged together. A temporal weighting coefficient was created based on task timing convolved with the canonical haemodynamic response. Correlation between the temporally-weighted time series for each region was computed for a 116x116 connectivity matrix, one for each of abstract and concrete trial types. The connectivity matrix for the rest period was also computed and subtracted from both task-based matrices. Each matrix was then thresholded for the top (0.75, 0.8, 0.85, 0.9, 0.95 and 0.99) percentile of positive correlations (Fig 1a). The remaining nodes (matrix elements) and their connectivity values were examined in the Dynamical Simplex Evolution (DSE) algorithm, which iteratively calculates the mutual entropy of the resulting network at each step until the entropy reaches is minimal value, as this corresponds to the most organised structure of clusters on the given network [4] (Fig 1b, c). The output of DSE is mutual distances between nodes (which represent how likely nodes are to be within the same cluster) (Fig 1d). By choosing an appropriate threshold for the mutual distances, clusters are extracted from an initially 'non-organised' network. Clusters are then examined both for which nodes are extracted (structural) and how they are connected (functional). For the thresholded mutual distances matrix for each condition, we define the 'overlap' by the square-root of the element-wise matrix multiplication. The mean mutual distances as a function of distance threshold are computed to examine functional differences.

Results: A single cluster within DSE was found for both abstract and concrete word trial types, with similar brain regions involved to create this cluster ($p<0.05$). Figure 2a shows the 'overlap' of nodes for each subject as a function of mutual distance threshold, indicating high overlap of individual nodes involved (out of maximum value 1). However, Figure 2b shows functionally significant differences ($p<0.05$) within each subject comparing the abstract (solid) with concrete (dashed) mean mutual distances between nodes, indicating the same brain areas are involved in different ways or to different extents between task conditions.

Discussion and Conclusion: This novel analysis of connectivity patterns can be widely applied to any comparison of tasks (including comparing task to rest). Temporally weighting the fMRI BOLD signal prior to correlation, as well as comparing between task conditions, both help to remove effects of physiological noise, even at high field (7T) where these artefacts are stronger. Rather than focussing on a pre-defined seed-based connectivity approach, this network (cluster) level analysis allows for examination of whole-brain changes with task. Each subject might complete this higher-cognitive-level task in different ways; thus, it is not expected that every subject would show the same pattern of brain activity or connectivity. Indeed, even though across subjects the mean mutual distances between tasks was not significant, they were significantly different within each subject, indicating they could be used for further classification of new data from that same subject.

References: [1] Dodel et al. 2005. *Phil. Trans. Royal Soc. London. Series B: Biol. Sci*. 360, 921-935 [2] Shinkareva et al. 2009; *NeuroImage*, V 47, Suppl. 1, Page S147 [3] Tzourio-Mazoyer et al., 2002. *NeuroImage 15*:273-289 [4] Gudkov et al, 2008 *PhyRevE* E78.