Temporally sensitive multi-voxel functional connectivity in fMRI?

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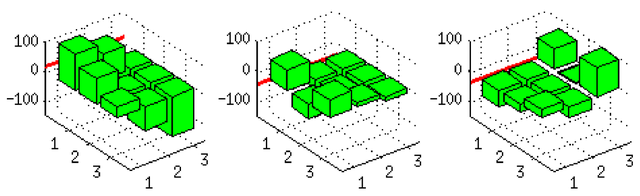
Introduction

The success of multi-voxel pattern analysis to discriminate fMRI tasks[1] suggests that fine-grained patterns of voxel activity can encode information in a local region.
We developed methods of multi-voxel resting state connectivity to explore the potential exchange of information encoded in fine-grained fMRI voxel patterns.
Such metrics might be useful in detection of subtle changes in disorders of connectivity, such as Alzheimer's Disease.

Methods

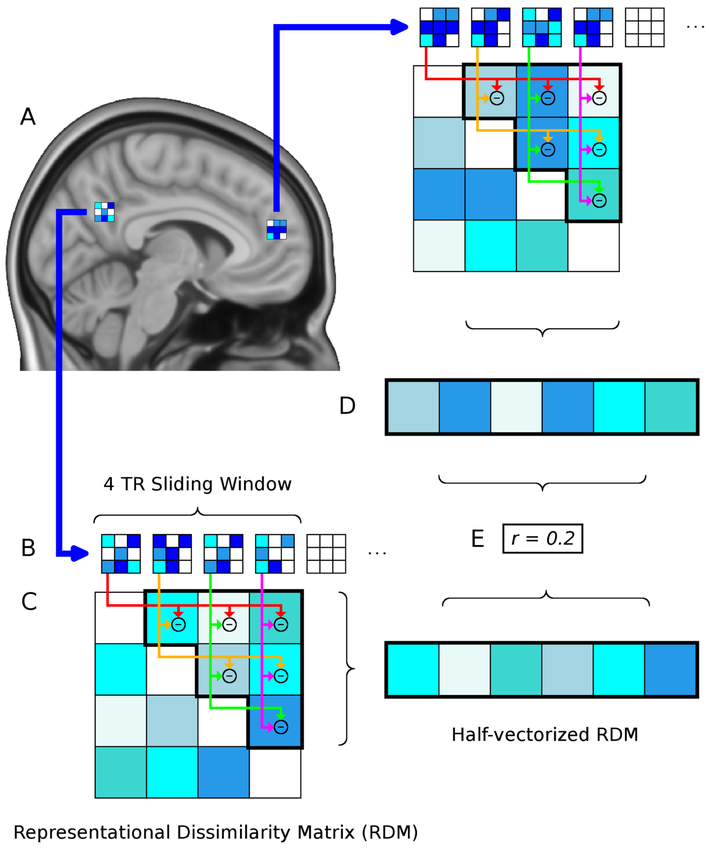
Multi-voxel Patterns of Residuals

Our analysis focused on residual voxel activity, after the local temporal and spatial means were removed, as shown here for 3 successive TRs of a 3 x 3 voxel grid in posterior medial wall (PMW). Standard functional connectivity (FC) correlates local spatial mean values, marked as a red line in the figures, which can be small compared to residual values.



Representational Dissimilarity Matrix Method

The first connectivity method (RDM Method) correlates representational dissimilarity matrices (RDMs) from seed and target regions.[2,3] Each RDM contains the differences of residuals at different lags within a sliding window, as shown below.



Lag-1 Spatial Correlation Similarity

The second method (Lag1 Method) correlates residuals between each time point to form a time series of successive spatial correlation similarity at each voxel.

Data Set

Resting state fMRI (5 min, 3mm iso, TR 2s) and T1 images were acquired from 19 subjects, (10 male) aged 28.6 ± 8.6 years old, on a 3T Siemens scanner.

Surrogate Data

Surrogate data sets were generated by 80 phase randomizations of the original fMRI series while maintaining Hermitian symmetry in the frequency domain.

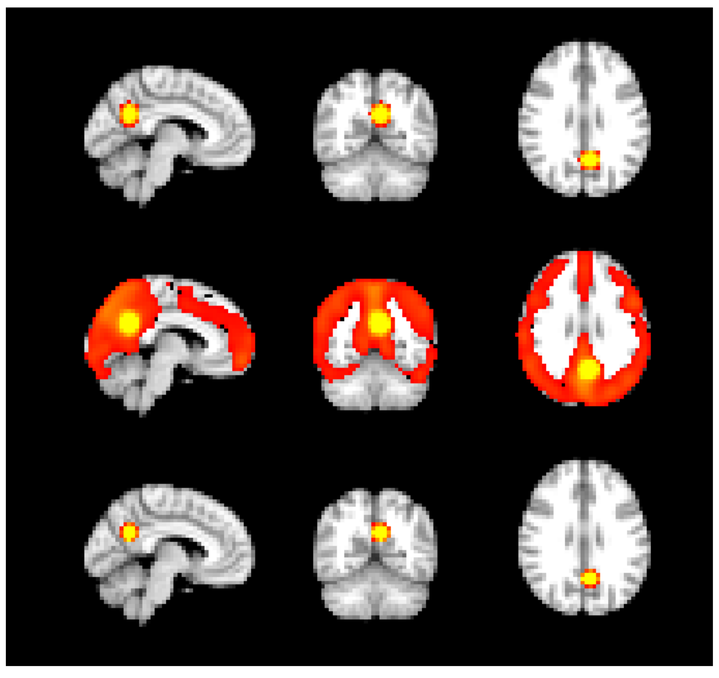
Statistical Analyses

Standard whole time-series FC, RDM, and Lag1 methods were run on the original and surrogate data, with the latter used to form null distributions of connectivity metrics. Connectivity maps were generated using a seed in the PMW (-6,-58,-28mm), and z-transformed prior to group analysis.[4] Metrics from the original data were thresholded above 95% of the null distribution values and corrected for multiple comparisons. Regional specificity was determined using Desikan atlas[5] parcellations generated by Freesurfer.[6]

Results

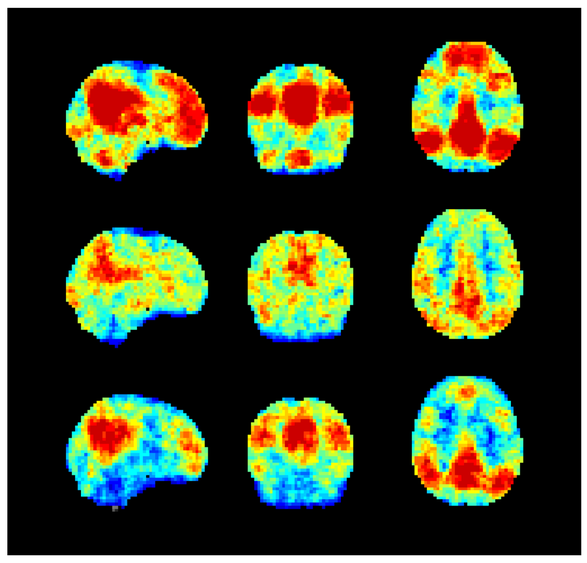
Surrogate Data

The figure below shows seed-localized connectivity maps of FC (top), RDM (middle), and Lag1 (bottom) methods, averaged over all subjects and randomizations. Colormaps indicate z-score range from 2 to 5. FC and Lag1 methods show elevated random connectivity in the seed region only. The RDM method shows wider areas of elevated random connectivity, suggesting that this method is less sensitive to phase changes between PWM and these areas .

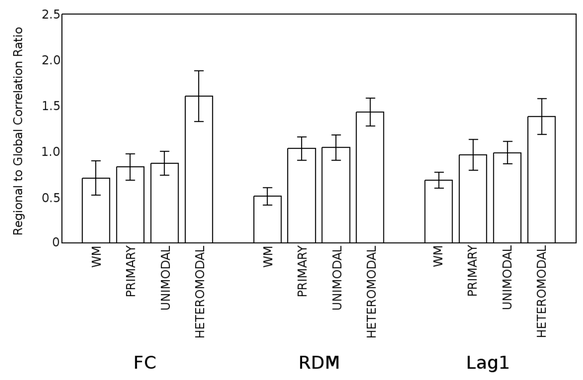


Regional Specificity

The figure below shows the voxelwise number of subjects exceeding the subject-specific thresholds set by the surrogate data, for FC (top), RDM (middle), and Lag1 (bottom) methods. Dark blue indicates no subjects and dark red indicates maximum (19) subjects.



Greater connectivity to PMW was significantly higher in heteromodal compared to unimodal, primary, and white matter (WM) regions for all methods, as shown in the figure below.



Conclusions

Methods based on residual activity (RDM and Lag1), show similar regional specificity of correlations to standard FC, suggesting that neurophysiological information is contained within local fine-grained voxel activity patterns.
The Lag1 method appears to be more sensitive to residual pattern changes compared with the RDM method, suggesting greater temporal sensitivity for this method.
Connectivity between residual pattern changes provides complementary information to FC and may be useful in enhancing fMRI detection of connectivity changes in neurological disorders.

References

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Acknowledgments

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