Spatial dynamics separates higher order from primary resting state networks

Ashish Anil Rao[1], Ek Tsoon Tan[2], Rakesh Mullick[1], and Suresh Emmanuel Joel[1]
[1]*General Electric Global Research, Bangalore, Karnataka, India,* [2]*General Electric Global Research, New York, United States*

Introduction: Independent component analysis (ICA) has been widely used to extract functional networks from resting state functional MRI (rs-fMRI) [1]. Spatial distribution of these networks has been used to study state of mind [2] traits [3] and diseases [4]. ICA has also been proposed to be used in clinical applications [5]. Understanding variability in the spatial distribution of the functional networks is crucial to interpret differences observed. Few studies have looked at inter-subject variability and fewer have looked at intra-subject variability (dynamics). Here we compare inter-subject and intra-subject variability in spatial distribution of ICA derived functional networks. Highly dynamic networks (variable within the same subject at different times) may be useful to study state of mind. Highly variable networks (variable across participants but stable within participants) may be useful to study traits and stable networks (both intra and inter-subject) can be used to study disease and progression of disease. We report the finding that higher order networks were consistent (across subjects) in their dynamic nature while primary networks were not. In general, higher order networks were found to be less dynamic than primary networks.

Methods: For each of 10 participants, 10 runs of resting state fMRI (7 minute long, TR/TE=2000/30 ms, FA = 75°, 3 mm isotropic voxel with 1 mm slice gap) were obtained using a GE Discovery 750 3T MR scanner. The 10 runs for the same participant were obtained over two sessions (five runs each session) separated by a day. A T1-weighted image was also acquired for normalization to atlas. The data were slice time corrected, motion corrected, coregistered, spatially transformed to MNI space, spatially smoothed and nuisance removed (by regressing motion parameters, global signal, top 90% of WM and CSF signal using PCA, COMPCOR, [6]) using SPM8 [7]. Group ICA with temporal concatenation was performed using a custom developed implementation of spatial ICA.19 out of 30 independent components (ICs) were manually selected as neurophysiologically relevant networks and were back-reconstructed to give individual spatial maps and timecourses. For each of the 19 networks, inter- and intra-subject reproducibility metrics were computed as follows. Inter-subject reproducibility: for each participant, the mean spatial map was computed. Pearson's correlation coefficient (PCC) between every pair among the 10 mean spatial maps was computed (45 pairs). The mean PCC was the inter-subject reproducibility. Intra-subject reproducibility: for each subject, the spatial map PCC between every pair among the 10 runs was computed, and the mean of the 45 PCCs was the reproducibility for that subject.

Results: The 19 neurophysiologically relevant networks (group level ICs) are shown in Fig 1. The intra- and inter-subject reproducibility for each of these networks is plotted in Fig 2. The inter-subject reproducibility for a particular network is a single number. The intra-subject reproducibility for a particular network is a vector of 10 numbers (corresponding to 10 subjects) and the median and inter-quartile range (IQR) are displayed.

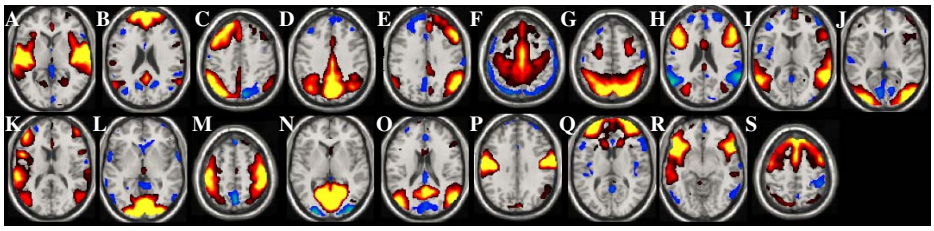

Fig 1: Neurophysiologically relevant networks chosen for spatial map reproducibility analysis. A-auditory, B-default mode network (DMN-3) (anterior), C-left executive control (LEC), D-DMN-2 (superior), E-right executive control (REC), F-sensorimotor (superior), G-dorsal attention system (DAS), H-ventral attention system (VAS), I-ventral stream, J-visual 3, K-language, L-visual 2, M-sensorimotor (hands), N-visual 1, O-DMN-1 (posterior), P-sensorimotor (face), Q-salience (inferior), R-insula, S-salience (superior)

Discussion & Conclusions: All ICA components' spatial maps had reasonably high inter and intra-subject reproducibility (clustered tightly around mean PCC of 0.6).

Networks found below the diagonal in Fig 2 are those with higher inter than intra-subject reproducibility. These include all primary networks (visual networks, auditory network, and sensorimotor networks) and some higher order networks such as DMN-2 and 3. Networks found above the diagonal in Fig 2 are those with higher intra than inter-subject reproducibility. These are only higher order networks such as executive control networks and DMN-1. These results agree with previous findings of network variability [8]. These results imply that some higher order networks (above diagonal) may be good markers for studying trait while primary networks found below diagonal may serve as good markers for state. Higher order networks (all DMNs, LEC, REC, Attention networks, language network, insula and salience networks) have significantly shorter (p=0.013) IQR in y-axis of Fig 2 than primary networks (visual, sensorimotor and auditory networks). This implies that the intra-subject reproducibility of higher order networks varied little between subjects, i.e. if a network is found to be dynamic (low intra-subject reproducibility) in one subject, it is likely to be dynamic in others. On the other hand, primary networks showed large inter-subject variability in dynamics, i.e. dynamic in one subject and non-dynamic in another.

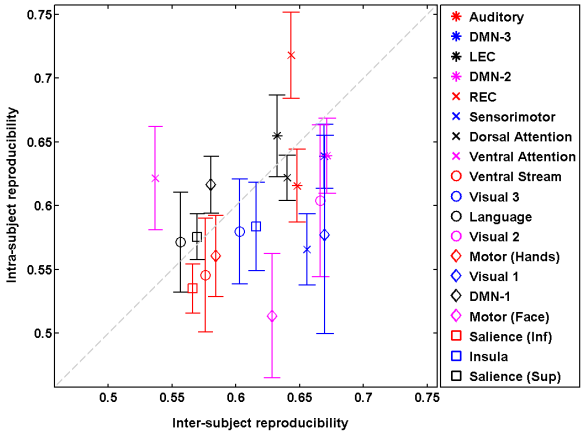

Fig 2: Plot of intra-subject vs. inter-subject reproducibility for the 19 networks of Fig 1. Inter-quartile range across subjects around the median is shown for intra-subject reproducibility for each network. .

References: [1] McKeown MJ et al., 1998, HBM, 6(3):160-88. [2] Chang C et al., 2010, Neuroimage 50(1), 81-98. [3] Mennes M. et al., 2010, Neuroimage, 50(4), 1690-1701. [4] Greicius M, 2008, Curr Opin Neurol., 21(4), 424-30. [5] Kollndorfer K et al., 2013, Front. Hum. Neurosci., 7(95). [6] Behzadi Y et al, 2007, NeuroImage, 37(1), 90–101. [7] Statistical Parametric Mapping, www.fil.ion.ucl.ac.uk/spm/ [8] Joel SE et al., 2011, 19th Annual Meeting of ISMRM.