Trends, seasonality, and persistence of resting-state fMRI over 185 weeks

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Target Audience Clinical MR researchers in the field of neuroimaging, who are interested in using resting state fMRI (rsfMRI) outcome measures as imaging biomarkers.

Purpose RsfMRI is used to noninvasively identify brain functional networks without explicit tasks[1]. Robust changes in resting state networks (RSNs) have been observed in neurological diseases[2, 3], and strong interest exists in identifying rsfMRI-based biomarkers suitable for monitoring clinical trials. In a previous study, we showed high intra-subject inter-session reproducibility of rsfMRI outcome measures over a time period relevant for clinical trials; using a longitudinal dataset reporting on a healthy adult subject scanned on a weekly basis over 128 weeks[4]. We sought to further the study and identify potential covariates-of-interest for clinical rsfMRI studies, by assessing the existence of temporal structure in three commonly used rsfMRI outcomes measures (spatial map similarity, temporal fluctuation magnitude, and between-network connectivity (BNC)).

Methods The dataset was acquired from a healthy volunteer (male; 40 yrs at the start of the study). A total of 158 sessions of data was acquired on a weekly basis, over 185 weeks. RsfMRI data of the subject was acquired using a multi-slice SENSE-EPI pulse sequence with TR/TE = 2000/30 ms, SENSE factor = 2, flip angle = 75°, 37 axial slices, nominal resolution = 3x3x3 mm^3, 1 mm gap, 16 channel neuro-vascular coil, number of dynamics per run = 200. The dataset was preprocessed, and independent component analysis was used to estimate RSNs. Spatial similarity of each week's component maps to the group mean map, as calculated using eta-squared (η^2)[5], was obtained as an outcome measure of RSN spatial maps. The magnitude of temporal signal fluctuations for each RSN was calculated as the quadratic mean (root mean square) of the back-reconstructed timecourses that were scaled to the original data to represent percent signal change. BNC, a measure of synchrony between networks, was computed for each session as the Pearson correlation coefficient of the RSN timecourses[6, 7]. Finally, timeseries analysis was performed on the timecourses of the three outcome measures, and existence of significant trend, annual periodicity, and persistence were tested and corrected for multiple comparisons.

Results Fourteen RSNs were identified. Time series analysis revealed significant linear trend, annual periodicity, and persistence in many RSNs, for all outcome measures. Such temporal structure was most prominent in spatial similarity (η^2) values, and the least in BNC values. Eleven out of 14 total RSNs showed significant linear trends. Of the 11 RSNs, ten showed positive trends, and Exec-R showed a negative trend. In comparison, only two (Vis-a and DMN-b) out of 14 RSNs showed significant trends in the temporal fluctuation magnitude. Twenty-nine out of 105 RSN pairs showed significant trends in the BNC measures. All trends observed for the temporal fluctuation magnitude and BNC measures were positive. Existence of significant linear trend in BNC measures was more pronounced in RSN pairs containing DMN-a or DMN-b networks, although significant trends were observed in various RSN pairs involving all categories of functional networks. Nine out of 14 total RSNs showed significant annual periodicity in the η^2. In comparison, only three (Vis-a, Attn-ven, and Attn-dor) out of 14 RSNs showed significant annual periodicity for temporal fluctuation magnitude measures, and none of the 105 RSN pairs showed significant annual periodicity for the BNC measures. Twelve out of 14 RSNs exhibited autocorrelation betweenthe η^2 values. In comparison, only three (Vis-a, DMN-b, and Sal) out of 14 RSNs displayed autocorrelation for temporal fluctuation magnitude measures, and 26 of the 105 RSN pairs exhibited autocorrelation structures for the BNC measurements.

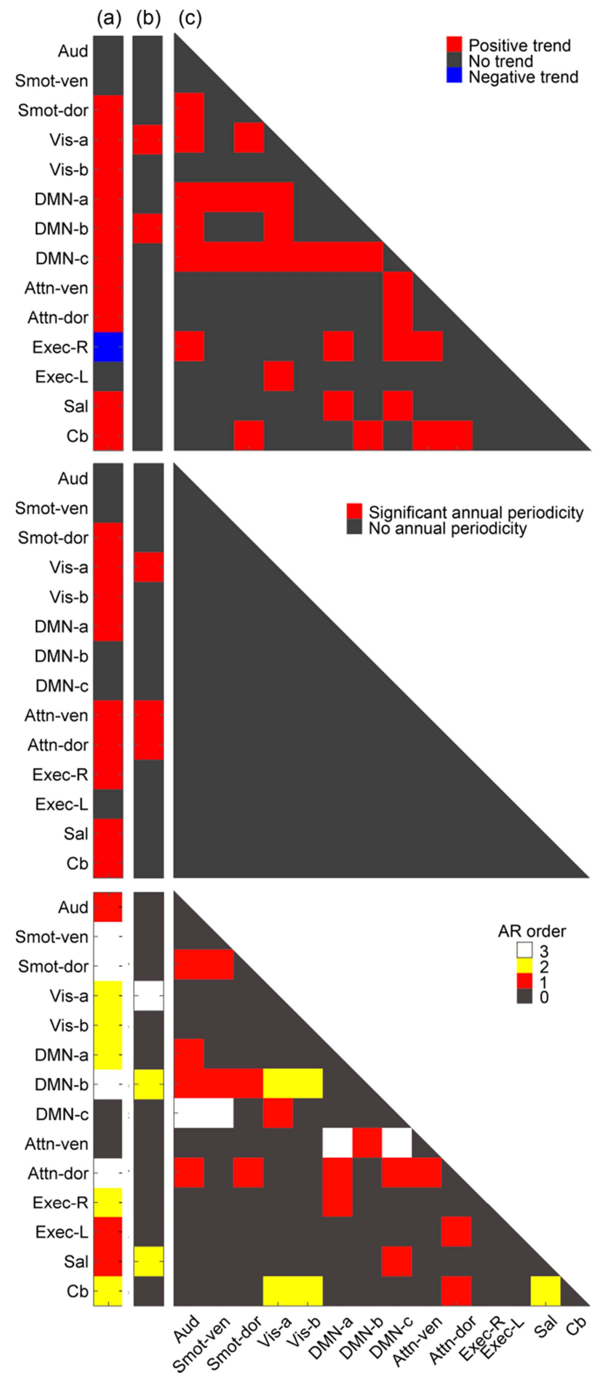

Figure 1. RSNs with significant temporal structures. TOP Existence of significant linear trends in three RSN outcome measures, namely the (a) spatial similarity (eta-squared, η^2), (b) temporal fluctuation magnitude, and (c) between-network connectivity MIDDLE Existence of significant annual periodicity in RSN outcome measures. BOTTOM Autoregressive (AR) orders (MA order not shown) of the estimated autoregressive-moving-average (ARMA) models for RSN outcome measures. (Aud: auditory, Smot: seonsorimotor, Vis: visual, DMN: default mode network, Attn: attention, Exec: executive, Sal: salience, Cb: cerebellar)

Discussion/Conclusion Time series analysis of the RSN timecourses, made possible by the unique longitudinal dataset, showed that temporal structure of the RSN outcome measures over extended period of time include properties such as linear trend, annual periodicity, and persistence. The study suggests that when RSN outcome measures are considered as imaging biomarkers for lengthy therapeutic interventions in chronic conditions, including the temporal structure parameters as covariates may yield more accurate results.

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