Noise-related variance of functional networks

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Introduction: Resting state functional connectivity has been a promising tool to characterize the integrity of brain functions from a network perspective. Recently, the time–frequency dynamics of the resting state MRI signal has been explored and it shows that the functional connectivity is not static[1], which might play a key role for the variability of constructed functional networks[2]. On the other hand, the noise, including scanner noise and physiological noise, can also contribute to the variance of functional networks. Because the correlation can be significantly underestimated when signal to noise ratio is low, it is essential to estimate the amplitude of intrinsic noise. With the hypothesis that the 'true' functional connectivity is only dependent on the cognitive state that may change slowly over time, we present a simple method to estimate the variance originated from residual noises in the MRI signal. Additionally, the variance from noise is compared with the total variance between networks from different time periods.

Theory: Noise has two different impacts on the correlation coefficient: underestimation of the value and increasing the variance. For signal x and y with noise η, the correlation is written as Eq. 1. It is easy to derive that the correlation coefficient, r, is underestimated from its true value, r_0 (Eq. 2). The level of underestimation is determined by the ratio of variance of noise to the variance of contaminated signal. On the other hand, the variance of correlation coefficient is also related to the variance of noise, in addition to the square root of number of sampling points, N (Eq. 3). Therefore, the variance of noise can be estimated if the variance of coefficient is known. A method similar to NEMA standard noise computation can be used to compute the variance of network[3]. The variance of network at different times is defined as the standard deviation of the elements in the network difference and divided by $\sqrt{2}$ (Eq. 4). The variance of network for one time period can be calculated in a similar way. For a time series of N points, two networks can be constructed from the subsets of even and odd points. The variance of network is subsequently derived from the difference of the two networks. Assuming the variance of coefficient varies little from different brain regions, the standard deviation of the correlation coefficient is approximated by variance of network for that time period.

$$r = \frac{\sum_{i=1}^{N}\left(x_i + \eta_i^x\right)\left(y_i + \eta_i^y\right)}{\sqrt{\sum_{i=1}^{N}\left(x_i + \eta_i^x\right)^2 \sum_{i=1}^{N}\left(y_i + \eta_i^y\right)^2}} \quad (1)$$

$$r = r_0\sqrt{1 - \frac{\sigma_x^2}{S_x^2 + \sigma_x^2}}\sqrt{1 - \frac{\sigma_y^2}{S_y^2 + \sigma_y^2}} \quad (2)$$

$$\sigma_r^2 = \frac{\sigma_x\sigma_y + S_x\sigma_y + S_y\sigma_x}{\sqrt{S_x^2 + \sigma_x^2}\sqrt{S_y^2 + \sigma_y^2}}\frac{1}{\sqrt{N}} \quad (3)$$

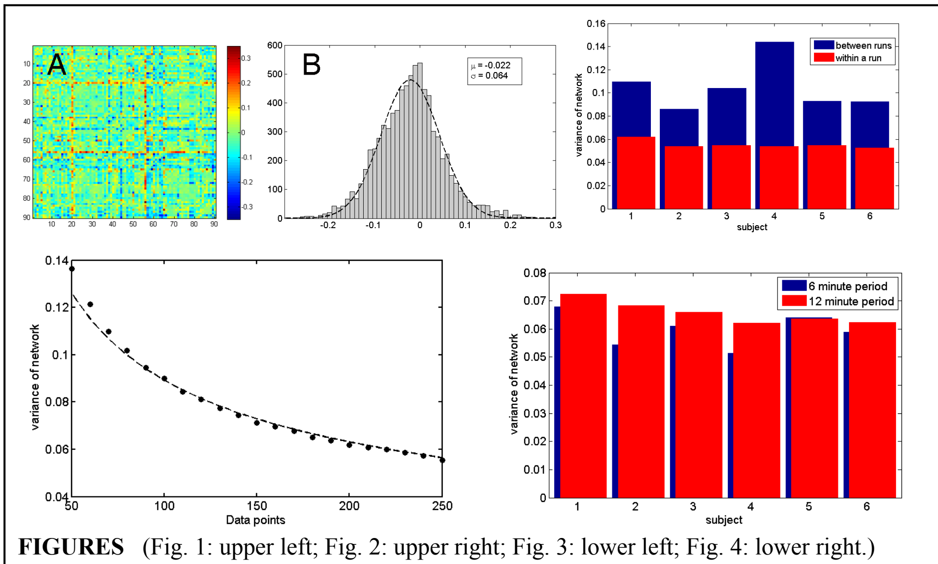
$$VON = \frac{std\left(net1 - net2\right)}{\sqrt{2}} \quad (4)$$

S and σ are variance of the signal and noise.

EQUATIONS

Methods: Six subjects were scanned on a Siemens TIM Trio 3 T scanner, at rest, for 12 minutes with EPI sequences (TR/TE = 1500/30 ms, 96×96 matrix, iPAT2), followed by high resolution (1 mm^3) anatomical scan with MP-RAGE sequence, and ended with resting scans for another 12 minutes with exactly the same parameters. The functional images were parcellated using automated anatomical labeling (AAL) with the help of anatomical image. After regressing out motion, white matter and CSF time signal, and band-pass filtered between 0.01 and 0.1 Hz, time courses were extracted from 90 ROIs for the cerebral cortex and averaged. The functional network was obtained as the correlation matrix for the 90 ROIs. For each run of resting scans, the variance of network was computed as described previously (effective TR = 3 s). For comparison purpose, the variance of network between runs was also computed using data from odd time points to match the same effective TR. For the data from run1 of each subject, the variance of network was also calculated for different number of time points from 50 to 250. In addition, for the same number of sampling points of 125, the variance of networks were calculated respectively from the same data using a segment of 6 minutes (effective TR = 3s) and 12 minutes (effective TR = 6 s).

Results: An example of the difference of the networks is shown in Fig. 1A with its histogram shown in Fig. 1B, which is close to a Gaussian distribution. The variance of network for run1 and that between two runs are shown in Fig. 2 for all six subjects. The variance between runs is nearly double the variance within a run. The dependence of variance of network on the number of sampling points is demonstrated in Fig. 3. As the sampling points increase, the average of variance of network over six subjects decreases and follows an inverse square root relation with the number of points N (dashed line), in good agreement with the prediction from Eq. 3. For the same number of sampling points, longer sampling period gives rise to slightly larger variance of network with 95% confidence interval of [0.004 0.015] from bootstrap testing (Fig. 4).



FIGURES (Fig. 1: upper left; Fig. 2: upper right; Fig. 3: lower left; Fig. 4: lower right.)

Discussion: Both Fig. 1B and Fig. 3 indicate that the proposed method is an effective and valid way to characterize the variance of functional networks. The results suggest that a substantial amount of variance of the functional network comes from the intrinsic noise that is not coupled with the coherences of different brain regions (Fig. 2). This noise can be effectively estimated based on the difference method. In our case, the constant term before $1/\sqrt{N}$ in Eq. 3 is ~ 0.95, resulting $S \sim 2\sigma$ assuming S and σ is equal for all functional nodes, that is equivalent to a 20% reduction of the correlation coefficient. The source of the residual noise is not clear from this study and needs further investigation including, but not limited to: scanner noise, cardiac, respiratory, and neurovascular noise.

References: 1. Chang, C. & Glover, G., NeuroImage (2010) 50:81–98. 2. Wang, J. et al., PLOS (2011) 6:e21976. 3. Cheng, H. et al., 10.1016/j.jneumeth.2011.09.021.