Research Ideas and Outcomes 3: e12641
doi: 10.3897/rio.3.e12641

Project Report

Noise paradoxically increases reliability metrics

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Reviewable v1

Received: 09 Mar 2017 | Published: 13 Mar 2017

Citation: Chen J, Bagga D (2017) Noise paradoxically increases reliability metrics. Research Ideas and Outcomes 3: e12641. https://doi.org/10.3897/rio.3.e12641

Abstract

Lower signal to noise ratio (SNR) of the scanning environment is generally considered to exert a negative impact on the inter-/intra-subject consistency of resting state functional connectivity (RSFC) metrics. Here, we show through simulations that this assumption is not always true - poor SNR may paradoxically increase reliability metrics of RSFC under certain circumstances, due to the reduced senstivity to dynamic changes in brain connectivity.

Keywords

test-retest reliability; resting state functional connectivity

Introduction

The reliability of a functional connectivity (FC) metric, typically quantified by its inter-scan variability, reflects the robustness of this metric as a potential biomarker for neuroscience and clinical applications. However, several studies have recently reported that resting state functional connectivity (RSFC) may undergo substantial changes across the course of a minute-long scan segment (Chang and Glover 2010, Hutchison et al. 2013, Preti et al. 2016), incurring the concern that variable inter-subject/session observations of RSFC may

stem from neuronal instead of noisy origins. Linked with emerging evidence that the strength of brain FC scales negatively with its variability (Thompson and Fransson 2015), it is possible that a noisier acquisition environment may yield more consistent observations by virtue of the lower sensitivity to subtle changes in RSFC, which are less stable across scan sessions in spite of neuronal origins. To test this hypothesis, we evaluated the variability of RSFC across subjects and segmented time windows of a scan session, using data simulated with different signal to noise (SNR) ratios. Our results suggest that poor SNR may lead to increased inter-/intra-subject consistency of RSFC, which to our knowledge, has rarely been discussed in existing literature concerning test-retest reproducibility of RSFC.

Methods

Real data: 10-min RS scans from 10 healthy subjects aged 36 +/- 12 yrs (4 females) were collected at 3T (GE Signa 750, 32 channel coil, Simultaneous MultiSlice (SMS) EPI with blipped CAIPI sequence (Setsompop et al. 2011), TR/TE= 350/30 ms, multiband acceleration factor of 6, CAIPI FOV shift factor of 3, flip angle = 40^o, 30 slices, voxel size 3.14*3.14*4 mm^3). Preprocessing steps included slice timing correction, removal of scanner drifts and physiological fluctuations synchronized with cardiac/respiratory cycles using RETROICOR (Glover et al. 2000), and normalization to the MNI template.

Simulated data with various SNR levels: Low-frequency bands (< 0.2 Hz) of the preprocessed real data were further de-noised by linearly projecting out several nuisance factors (including six motion parameters, RVHRCOR (Chang et al. 2009), white matter and CSF signals) filtered to the same band (< 0.2 Hz), and taken as the “true signal”, i.e., variable neural activity. Correlating structures > 0.2 Hz were destroyed by transforming the data into the Fourier domain and randomly scrambling phases of complex components > 0.2 Hz, as performed in (Chen et al. 2017). Since frequencies > 0.2 Hz of the simulated data demonstrate purely noise, the SNR of the data can be manipulated by tuning the cut-off frequency threshold of low-pass filtering. Datasets with four levels of SNR (having cutoff-frequency 0.2/0.4/0.8/1.4 Hz respectively) were produced for the ensuing analyses.

Reliability of RSFC at different SNR levels: To obtain multiple sessions of each subject, each subject’s scan was divided into 2, 3, or 4 evenly distributed but non-overlapping windows, within which linear Pearson correlation with respect to a posterior cingulate cortex (PCC) seed was calculated. Between-subject, within-subject variability, and the intra-class correlation (ICC(3,1)) (Koch 1982) of Fisherz-transformed correlation values were computed on each voxel’s basis. To examine whether noisier acquisitions stabilize faster, PCC centered RSFC was also estimated as a function of scan length. Specifically, for each subject, we fixed the scan onset as the starting point, gradually increased the scan length from 0s to 10 mins with the step size 7s (20 time points), and calculated the spatial correlation between the PCC correlation map generated with the current scan length and that obtained using the entire scan data.

Results

Fig. 1A shows the voxel-wise ICC values estimated with different SNR levels and window numbers. Regions within the default-mode network exhibit higher ICC values than rest brain voxels. As hypothesized, lower SNR data (higher cut-off frequency) results in diminished between-/within-subject variability, and elevated ICC values, as quantified in Fig. 1B. This trend is consistent across all window numbers, despite that ICC values are slightly lower for shorter window lengths due to reduced scan time per segment as well as increased session numbers.

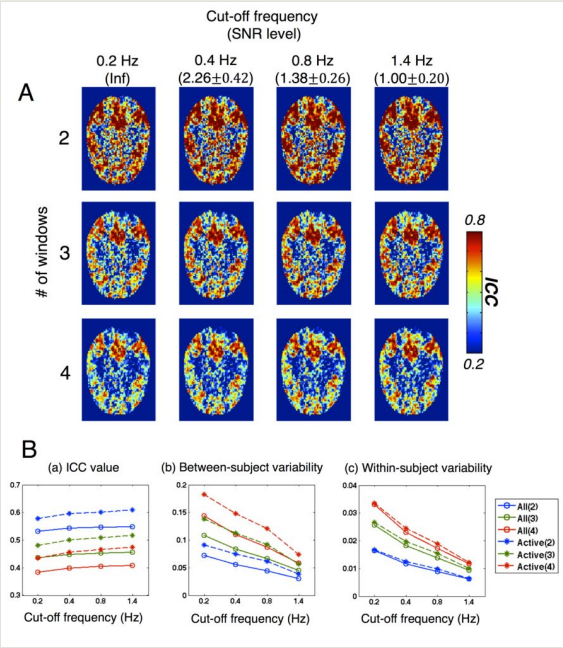

Figure 1.

A: The voxel-wise ICC values of RSFC with respect to a PCC seed under different SNR levels (SNR is defined as the ratio of the amplitude of fluctuations < 0.2 Hz to > 0.2 Hz, averaged across voxels in the slice, each column) and session numbers (by partitioning each subject's scan to multiple windows, each row). **B**: ICC values (a), between-subject (b) and inter-subject (c) variability averaged within all voxels of the displayed slice in A ('All', numbers in the parenthesis are the window number), and voxels significantly correlated with the PCC seed at the group level ('Active', evaluated across 10 subjects using the entire scan dataset filtered < 0.2 Hz, $p < 0.05$, uncorrected)

In accordance with observations above, RSFC estimated with lower SNR stabilizes faster than higher SNR data. The shortest scan length that well replicates PCC correlation obtained using the whole scan dataset (spatial correlation > 0.95) is on average 15s ($p = 0.04$ for 10 subjects) shorter for non-filtered data (<1.4 Hz) compared to the "true signal" (filtered < 0.2 Hz).

Conclusions

Through simulations, we have shown that lower SNR may lead to reduced variability across scan sessions due to mitigated sensitivity to time-varying changes of brain RSFC. By truncating a single subject's scan to multiple sub-sessions, the scan length estimated in the current project is shorter than the length recommended by recent reports (Birn et al. 2013). Since the dynamic brain network patterns tend to average out in longer scans, resulting in reduced inter-session variability, the impact of SNR on the reliability of longer scans remain unclear and warrant further investigations.

Acknowledgements

This work was completed during Brainhack Vienna 2016.

Author contributions

Chen J contributes to data analysis and writing; Bagga D contributes to discussion and writing.

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