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Characterizing the Effects of MR Image Quality Metrics on Intrinsic Connectivity Brain Networks: A Multivariate Approach

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Abstract

Motion-induced artifact detection has become a fixture in the assessment of functional magnetic resonance imaging (fMRI) quality control. However, the effects of other MR image quality (IQ) metrics on intrinsic connectivity brain networks are largely unexplored. Accordingly, we report herein the initial assessment of the effects of a comprehensive list of IQ metrics on resting state networks using a multivariate analysis of covariance (MANCOVA) approach based on high-order spatial independent component analysis (ICA). Three categories of MR IQ metrics were considered: (1) metrics for artifacts including the AFNI outlier ratio and quality index, framewise displacement, and ghost to signal ratio, (2) metrics for the temporal quality of MRI data including the temporal framewise change in global BOLD signals (DVARs), global correlation of time-series, and temporal signal to noise ratio, (3) metrics for the structural quality of MRI data including the entropy focus criterion, foreground-background energy ratio, full-width half maximum smoothness, and static signal to noise ratio. After FDR-correction for multiple comparisons, results showed significant effects of the static and temporal signal to noise ratios on the spatial map intensities of the basal ganglia, default-mode and cerebellar networks. AFNI outlier ratio, framewise displacement and DVARs exhibited significant effects on the BOLD power spectra of sensorimotor networks. The global correlation of time-series displayed wide-spread modulation of the spectral power in most networks. Further investigations of the effect of IQ metrics on the characteristics of intrinsic connectivity brain networks allow more accurate interpretation of the fMRI results.

I. INTRODUCTION

Neuroimaging data acquired using blood-oxygen-level-dependent (BOLD) functional magnetic resonance imaging (fMRI) are often contaminated with some types of artifacts or noise, which can affect interpretation of fMRI results [1]. Among the nuisance variables, motion artifacts are considered the main cause of degraded accuracy and post-hoc subject-level motion artifact detection in brain images has become a must for MRI quality control assurance [2]. However, in addition to noise stemming from the subject motion, other system noises can influence the image quality. Specifically, temporal noise can be present in the fMRI time series due to physiological fluctuations, thermal, scanner and device-related contributions (e.g., MRI hardware/software such as timing instabilities and drifts) [3].

There has been a great deal of research in recent years concerning identification and quantitative estimation of image quality (IQ) metrics for MRI quality control [4]. It has

become a common practice particularly in resting state studies, to monitor for some noises to retrospectively correct for their confounding effects post-acquisition [1]. However, the majority of previous findings on noise are (i) limited to specific noises particularly those that can be measured at the time of scan (e.g., head motion, physiological noise), and (ii) generally based on univariate statistical hypothesis testing that are applied on a voxel-by-voxel basis to fMRI time series. Accordingly, the effects of some IQ metrics on intrinsic connectivity brain network patterns remains unknown. The main objective of this study was to evaluate the effect of different noise measures on resting state networks to characterize the degree each IQ metric affecting the network features. We used the recently developed statistical framework based on high-dimensional independent component analysis (ICA) [5], where multivariate models were used first to identify important covariates, followed by univariate tests with a reduced design matrix to study the nature of the relationship between the selected metrics and ICA-based outcome measures. We focused on two ICA-based features, namely, the intensities of spatial maps related to the degree of activation within a network (i.e., intra-network connectivity), and the time course power spectra [5].

II. MATERIALS AND METHODS

A. Participants

Participants were eighteen right-handed healthy volunteers (10 females, 8 males, mean age 40.9 years, range 27–62) free of major medical or neurological illness. All study activities were approved by the Stanford School of Medicine Institutional Review Board and consent forms were collected prior to MRI scans.

B. Data Acquisition

Resting state fMRI scans were collected on a 3T GE Discovery MR750 scanner (GE Healthcare, Waukesha, WI) with a standard 8-channel head coil (8HR Brain, GE Healthcare, Waukesha, WI) at the Stanford University Lucas Center for Medical Imaging. The functional T2*-weighted images were acquired with a three-dimensional enhanced fast gradient echo (EFGRE3D) pulse sequence using the following scan parameters: repetition time, 2000 ms; echo time, 30 ms; flip angle, 76°; matrix size, 64 × 64; field of view, 22 cm; number of time frames, 360; 31 axial slices acquired in a sequential ascending order.

C. Data Analysis

A schematic diagram illustrating our analysis approach is shown in Fig. 1. First, IQ metrics were calculated from the raw images using the MRIQC package (<http://mriqc.readthedocs.io>). Among various metrics for MRI quality control, we focused on three categories of metrics implemented in the MRIQC package. Many overlap with the ones outlined in the quality assessment protocol of Human Connectomes Project [4].

1. Metrics for artifacts

- AFNI Outlier Ratio (AOR): The mean fraction of outliers in each volume using AFNI *3dToutcount* [6].

- AFNI Quality Index (AQI): The mean distance (i.e., 1 - spearman's ρ) between each fMRI volume and the median volume using AFNI *3dTqual* command [6].
- Framewise Displacement (FD): The sum of the absolute values of six realignment parameters at each timepoint t , after converting the rotational displacements from degrees to millimeters [2]:

$$FD_t = |\Delta d_{t,x}| + |\Delta d_{t,y}| + |\Delta d_{t,z}| + |\Delta \alpha_t| + |\Delta \beta_t| + |\Delta \gamma_t| \quad (1)$$

where $d_{t,x} = d_{(t-1)x} - d_{tx}$, and similarly for others.

- Ghost to Signal Ratio (GSR): The mean signal intensity (SI) in the areas of the image prone to ghosting (due to acquisition in a particular phase encoding direction x or y) relative to SI within the brain [7].

$$GSR = \frac{\mu(SI \text{ of ghost ROI}) - \mu(SI \text{ of non-ghostbackground ROI})}{\mu(SI \text{ of primary image ROI})} \quad (2)$$

2. Metrics for the temporal quality

- DVARS: D refers to temporal derivative of fMRI time courses, VARS refers to the variance of root mean square (RMS) over voxels [2]. It is calculated by *confounds.py* command in Nipype [8] as the RMS value of the differentiated BOLD timeseries (by backwards differences) within the brain mask at each timepoint.

$$DVARS_t = \sqrt{\frac{1}{N} \sum_i [x_{i,t} - x_{i,(t-1)}]^2} \quad (3)$$

- Global Correlation (GCOR): The average correlation between every voxel and ever other voxel over a given mask using AFNI *compute-gcor* command [9]:

$$GCOR_t = \frac{g_u^T g_u}{N} \quad (4)$$

where N is number of voxels, T is number of timepoints.

- Temporal Signal to Noise Ratio (tSNR): The ratio between mean signal intensity of time series x_j and its temporal standard deviation [10]:

$$tSNR = \frac{\mu}{\sqrt{\frac{1}{T} \sum_{i=1}^T [x_i - \mu]^2}} \quad (5)$$

3. Metrics for the structural quality

- Entropy Focus criterion (EFC): Shannon's entropy of voxel intensities normalized to the maximum possible entropy of the image [11]:

$$EFC = - \sum_{j=1}^N \frac{B_j}{B_{max}} \ln \left[\frac{B_j}{B_{max}} \right] \quad (6)$$

where N is number of voxels and B_j is the modulus of the complex value (i.e., "brightness") of the j th voxels. Shannon's entropy is used to summarize the principal directions distribution (e.g., ghosting and blurring induced by head motion).

- Foreground-Background Energy Ratio (FBER): The variance of voxels inside the brain divided by the variance of voxels outside the brain [4].
- Full-Width Half Maximum Smoothness (FWHM): Spatial distribution of the image intensity values in units of voxels. It is computed using the Gaussian width estimator filter implemented in AFNI *3dFWHMx*.
- Static Signal to Noise Ratio (SNR): The mean intensity within gray matter divided by the standard deviation of the values outside the brain [12].

Following IQ measurements, images were preprocessed using SPM12 (Wellcome Department of Imaging Neuroscience, London, UK). Preprocessing included realignment, unwrapping, slice-time correction, co-registration, spatial normalization with MNI template, and spatial smoothing. Group ICA was performed on preprocessed data using GIFT software package version 4.0b. We applied high-order ICA model of 75 independent components (ICs) with the infomax algorithm to achieve better parcellations of cortical and subcortical components [13]. To ensure the robustness of component estimation, ICA was repeated 20 times in ICASSO. GICA3 back-reconstruction based on PCA compression and projection was used to extract subject-specific spatial maps and their corresponding time courses.

The MANCOVA toolbox in GIFT [5] was utilized to evaluate the relationships between ICA measures and IQ metrics. The selected covariates in the design matrix included (1) IQ metrics for artifacts (AOR, AQI, FD, GSRx, GSRY), (2) IQ metrics for temporal quality of functional data (DVARs, GCOR, tSNR), and (3) IQ metrics for structural quality (EFC, FBER, FWHM, SNR). Participants' age and gender were also included. Log-normalizing transformations were applied to all continuous variables to correct for the skewness of data and improve symmetry as suggested in [5]. Multivariate analyses were performed first to

assess the extent to which each of the covariates explained variance in the data. Univariate analyses were subsequently performed to determine which spatial map voxels and spectral bins of the ICA derived intrinsic connectivity brain network were associated with different IQ metrics. Univariate tests were corrected for multiple comparisons at $p < 0.05$ using false discovery rate (FDR).

III. RESULTS

Summary statistics (mean, standard deviation, minimum and maximum) for the IQ metrics are given in Table 1. The intrinsic connectivity brain networks (Fig. 2) are divided into groups based on their anatomical and functional properties and include the visual (VN), sensorimotor (SMN), cognitive/attention (CAN), auditory (AUD), subcortical (SCN), basal ganglia (BG), default-mode (DMN), and cerebellar (CN) networks. Figure 3 shows the results of the multivariate analysis. It displays the magnitude of the effects of the IQ metrics on networks' spatial maps (left), and power spectra (right). The univariate test results for the significant effects of (i) SNR, (ii) tSNR, (3) FD, and (iv) EFC on the intensities of several networks' spatial maps are shown in Fig. 4A. For each robust effect (FDR-corrected), the left panels in Fig. 4A are the composite contributions of significant effects over all networks in 3 most informative slices in $-\text{sign}(t)\log_{10}(p\text{-value})$ [14]. Right panels in Fig. 4A are bar plots of the average β -values and the color of the bars are proportional to the fraction of network spatial map voxels contributing to each effect. Univariate test results for the significant effects of (i) SNR, (ii) AOR, (iii) FD, (iv) DVARs, and (v) GCOR are illustrated in Fig. 4B. First row in Fig 4B shows the magnitude of the covariate terms as a function of frequency for each network as $-\text{sign}(t)\log_{10}(p\text{-value})$, and second row shows the bar plots of average β -values for covariate terms with the bar color being proportional to the fraction of contributing network's spectral power bins [5].

IV. DISCUSSION AND CONCLUSION

We applied a multivariate model selection strategy based on high model order ICA to determine the effects of different IQ metrics on intrinsic connectivity brain network spatial maps and power spectra while accounting for variances associated with age and gender. Two major metrics for fMRI image quality assurance include the static and temporal SNR of the acquired images. After FDR-correction for multiple comparisons, the univariate results from network spatial maps showed significant effects of both SNRs on the spatial map voxel intensity of IC 45 (BG). tSNR also impacted the spatial maps of IC 37 (DMN) and ICs 13 and 16 (CN). Voxel intensity of the ICA derived network spatial maps can be used as a proxy for intra-network connectivity. The effect sizes from spatial map univariate results indicate decrease in intra-network connectivity within DMN and CN with decrease in tSNR. Similarly, decrease in static SNR resulted in decrease in connectivity within BG. These findings on SNRs are consistent with previous studies indicating that decrease in either SNR means more noise. In the context of intrinsic connectivity brain network, we found lesser SNRs (less signal power) correspond to lower connectivity detection inside specific networks (DMN, CN, and BG).

Further, spectral power analysis results showed the effects of static SNR on the spectral power of IC 73, a central executive network, and IC 48, a dorsal attention network. The

central executive network comprises dorsolateral prefrontal and posterior parietal cortices [15]. The dorsal attention network includes bilateral frontal eye fields and intraparietal sulci [16], [17]. Thus, the effects of SNR are not localized to specific brain regions but can impact large-scale connectivity networks that include distinct, separate regions of brain. AOR, FD, and DVARs also showed effects on the spectral power of IC 17 (SMN). FD and DVARs additionally influenced IC 55 (salience network). We observe an increase in high frequency power with AOR and DVARs for SMN and salience network, and a decrease in the same high frequency power range of these networks with FD. Additionally, increase in FD (more instantaneous head movements), resulted in increase in spatial map intensities within two SMNs, which can be considered as increased false positive. The main effect of EFC was found on IC 45 (BG), a network which its close proximity to ventricles can make it susceptible to distortions and change in brightness metric measured by Shannon's entropy [11]. Finally, GCOR, a measure of differences between data due to various noises from motion and physiological noise to artifacts such as signal bleeding, displayed wide-spread modulation of the spectral power in most networks.

Considering that the multivariate approach that we used (i.e., ICA) is a denoising approach that separates artifacts resulting from motion, physiological, and scanner noises as artifactual components [18], as well as the small sample size of our subjects who had minimum noise in their images (as shown in Table 1), we did not find significant results for some IQ metrics. Further investigations of the effect of IQ metrics on brain network features using larger datasets such as the Human Connectomes Project can provide a valuable tool for more accurate interpretation of fMRI data.

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Fig. 1.
Schematic of the analysis pipeline

Fig. 2.
Spatial maps of intrinsic connectivity brain networks displayed at three most informative slices in neurological convention

Fig. 3. Multivariate statistics. Results from the MANCOVA models, demonstrating the significance of the three categories of IQ metrics on intrinsic connectivity brain networks' spatial maps (left) and power spectra (right), are displayed in $\log_{10}(p\text{-value})$ units.

Fig. 4.

A Univariate test results of network spatial map intensity alterations by (i) static signal to noise ratio (SNR), (ii) temporal signal to noise ratio (tSNR), (ii) framewise displacement (FD), and (iv) entropy focus criterion (EFC); **B** Univariate test results of network power spectra alterations by (i) static signal to noise ratio (SNR), (ii) AFNI outlier ratio (AOR), (iii) framewise displacement (FD), (iv) DVARS, and (v) global correlation (GCOR).

Table 1:

MEAN, STANDARD DEVIATION, MIN & MAX VALUES OF IQ METRICS

IQ Metrics	Mean	STD	Min	Max
AOR	0.004	0.004	0.001	0.016
AQI	0.012	0.004	0.006	0.021
FD	0.165	0.080	0.085	0.418
GSR _x	0.001	0.006	-0.007	0.015
GSR _y	0.039	0.012	0.018	0.060
DVARs	20.65	3.871	14.797	29.366
GCOR	0.031	0.016	0.010	0.070
tSNR	37.007	9.125	22.749	54.591
EFC	0.518	0.024	0.486	0.563
FBER	76.602	16.062	44.022	99.749
FWHM	10.514	0.389	10.044	11.398
SNR	2.476	0.111	2.237	2.665