Linear trend of resting-state fMRI time series (Post-print)

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Date: 2017-11-06T00:00:00+00:00

Abstract

Although linear trend removal has often been implemented as a routine preprocessing step in resting-state functional magnetic resonance imaging (RS-fMRI) data analysis, the spatial distribution of linear trend magnitude remains unclear. Furthermore, it is of interest whether any differences exist in linear trend magnitude between different resting states. For the first objective, we analyzed five RS-fMRI datasets from five different scanners (namely Beijing-Siemens-3T, Cambridge-Siemens-3T, CCBD-GE750-3T, Milwaukee-GE-3T, and Oulu-GE-1.5T). One-sample t-tests on the regression coefficient (i.e., the magnitude of linear trend) were performed for each dataset. For the second objective, we utilized two datasets, each comparing different states: one comprising eyes-open resting state (EO-RS) versus eyes-closed resting state (EC-RS), and the other comprising two steady-state tasks, namely real-time finger force feedback (RT-FFF) and sham finger force feedback (S-FFF) tasks. Paired t-tests were conducted between EO-RS and EC-RS, and between RT-FFF and S-FFF. One-sample t-tests revealed that the spatial patterns of linear trend in RS-fMRI time series differed considerably across different manufacturers. The 3T Siemens scanners exhibited positive linear trend in almost all regions of the brain, whereas GE scanners displayed primarily negative linear trend in most regions of the brain. Paired t-tests demonstrated certain differences between the paired conditions; differences between EO-RS and EC-RS were primarily observed in the cuneus and eyeballs, while differences between RT-FFF and S-FFF were identified in the thalamus, anterior cingulate gyrus, and right sensorimotor cortex. The present study indicated that, although the manufacturer-dependent linear trend in RS-fMRI time series was predominantly scanner-related noise, the linear trend may also constitute physiological noise (eyeballs) or even be physiologically meaningful, particularly during steady-state tasks.

Full Text

Preamble

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Abstract

Although linear trend removal has often been implemented as a routine preprocessing step in resting-state functional magnetic resonance imaging (RS-fMRI) data analysis, the spatial distribution of the magnitude of linear trend remains unclear. Further, it is unknown whether the magnitude of linear trend differs between different resting states. For the first aim, we analyzed five RS-fMRI datasets from five different scanners (namely Beijing-Siemens-3T, Cambridge-Siemens-3T, CCBD-GE750-3T, Milwaukee-GE-3T, and Oulu-GE-1.5T). One-sample t-tests on the regression coefficient (i.e., the magnitude of linear trend) were performed for each dataset. For the second aim, we used two datasets in which different states were compared: one containing eyes-open resting-state (EO-RS) vs. eyes-closed resting-state (EC-RS) and the other containing two steady-state tasks, i.e., real-time finger force feedback (RT-FFF) and sham finger force feedback (S-FFF) tasks. Paired t-tests were performed between EO-RS and EC-RS, and between RT-FFF and S-FFF.

One-sample t-tests showed that the spatial pattern of linear trend of RS-fMRI time series differed markedly between manufacturers. The 3T Siemens scanners showed positive linear trend in almost all parts of the brain, while GE scanners showed primarily negative linear trend in most parts of the brain. Paired t-tests revealed some differences between paired conditions; differences between EO-RS and EC-RS were mainly in the cuneus and eyeballs, and differences between RT-FFF and S-FFF were found in the thalamus, anterior cingulate gyrus, and right sensorimotor cortex. The current study indicated that, while the manufacturer-dependent linear trend of RS-fMRI time series was mostly scanner-related noise, the linear trend may also reflect physiological noise (eyeballs) or even be physiologically meaningful, especially during steady-state tasks.

Keywords: resting-state fMRI; linear trend of time series; manufacturer-specificity; eyes-closed and eyes-open; real-time feedback

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Introduction

Since the first study by Biswal and colleagues (Biswal et al., 1995), blood oxygen level dependent (BOLD) resting-state functional magnetic resonance imaging (RS-fMRI) has been widely utilized to explore spontaneous or intrinsic brain activity, as well as to investigate the pathological progression of brain disorders. Standard preprocessing procedures have been established, including slice timing correction, head motion correction, spatial normalization, spatial smoothing, linear trend removal, and temporal filtering.

Among these procedures, linear trend removal is a well-accepted practice (Bai et al., 2008; Zhang et al., 2008; Fox et al., 2009; Qiu et al., 2011). A common approach to remove linear trend is detrending (regression) with the general linear model (Bandetini et al., 1993; Cox, 1996; Zhang et al., 2008; Fox et al., 2009) during RS-fMRI preprocessing. Although it has been speculated that the linear trend of fMRI signal represents system noise arising from scanner instability (Huettel et al., 2004), few studies have systematically investigated the spatial distribution of the linear trend of RS-fMRI signal in the brain. Furthermore, no study has examined whether any portion of the linear trend of RS-fMRI signal differs between different resting states. Such differences might be of physiological importance.

The first aim of the current study was to systematically investigate the spatial distribution of the linear trend of RS-fMRI signal across the brain using data from various research sites with different scanners. The second aim was to investigate potential differences in linear trend between resting-state with eyes closed (EC-RS) and resting-state with eyes open (EO-RS). We also compared the linear trend between two states of continuous performance: real-time finger force feedback (RT-FFF) and sham finger force feedback (S-FFF) (Dong et al., 2012).

Materials and Methods

Participants and Imaging Protocols

We implemented our analyses on six imaging datasets (see Table 1 for details): (1) "Beijing EO/EC" dataset with two resting-state conditions (EC-RS and EO-RS without fixation) counterbalanced across participants; (2) "Beijing Feedback" dataset with two conditions (RT-FFF and S-FFF, counterbalanced) (Dong et al., 2012); (3) "Cambridge"dataset; (4) "CCBD"dataset; (5) "Milwaukee"dataset; and (6) "Oulu" dataset. Datasets 1, 3, 5, and 6 were from the "1000 Functional Connectomes Project" and the "International Neuroimaging Data-sharing Initiative" (INDI) (http://fcon_1000.projects.nitrc.org). Dataset 2 was scanned at Beijing Normal University Imaging Center. Dataset 4 was acquired from the Center for Cognition and Brain Disorders (CCBD) at Hangzhou Normal University. Data acquisition for each dataset was approved by the corresponding institutional review board. All participants gave written informed consent before scanning.

Experimental Design of "Beijing Feedback" Dataset

The data were from a study designed to investigate the brain mechanism of real-time feedback (Dong et al., 2012). During fMRI scanning, participants were asked to continuously maintain a pinch force at approximately 20 cm H O. In the RT-FFF condition, the pinch force was shown to the participant in real-time on a monitor. In the sham condition, a pinch force video of another participant was shown. These procedures were implemented using a multiple-channel MRI-compatible physiological monitor (model MP150, BIOPAC Systems, Inc., Goleta, CA). Detailed experimental procedures were described in the original paper (Dong et al., 2012).

Data Preprocessing

Unless otherwise stated, all preprocessing was performed using the Data Processing Assistant for Resting-State fMRI (DPARSF) (Yan and Zang, 2010) (http://www.restfmri.net), which is based on Statistical Parametric Mapping (SPM8) (http://www.fil.ion.ucl.ac.uk/spm) and the Resting-State fMRI Data Analysis Toolkit (REST) (Song et al., 2011) (http://www.restfmri.net). The first 10 image volumes were discarded for scanner calibration and to allow participants to acclimate to the scanning environment. Slice acquisition-dependent time shifts were then corrected per volume.

The time series of images for each participant were realigned using a six-parameter (rigid body) linear transformation with a two-pass procedure (registered to the first image and then to the mean of the images after the first realignment). Spatial smoothing was performed using a 4 mm Gaussian kernel. All volumes were then normalized to an EPI template to obtain transformations from individual native space to MNI space.

Linear Trend Estimation

Linear regression analysis was performed voxel-by-voxel to calculate the regression coefficient (beta) of the time series against time in individual native space. The beta maps were then registered into MNI space with resampled 3 mm^3 cubic voxels using transformations acquired from the spatial normalization procedure. One-sample t-tests were performed on the beta maps for each dataset. Paired t-tests were used to compare differences in beta between EO-RS and EC-RS, as well as between RT-FFF and S-FFF for the "Beijing EO/EC" and "Beijing Feedback" datasets, respectively. All statistical t-maps were corrected using Gaussian random field theory (GRF, voxel $p < 0.001$, cluster $p < 0.05$) within the whole bounding box (271,633 voxels total) to investigate linear trend both inside and outside the brain.

Results

Spatial Distribution of Linear Trend in fMRI Signal

The linear trend maps are shown in Figure 1 [Figure 1: see original paper]. The pattern of linear trend in fMRI signal exhibited a manufacturer-specific spatial distribution: Siemens scanners showed positive linear drift, while GE scanners showed negative linear drift in most parts of the brain. Additionally, linear trend in white matter was stronger than that in gray matter for all datasets. Specifically, the Cambridge Siemens scanner showed apparently higher drift than the Beijing Siemens scanner, partially due to its larger sample size. Among the three GE scanners, drift was highest for Oulu, lowest for CCBD, and moderate for Milwaukee. Although GE scanners showed primarily decreasing drift, the CCBD and Oulu scanners showed increasing drift in the orbitofrontal midline area.

Difference in Linear Trend Between Different States

In the EO-RS vs. EC-RS comparison, the visual area (V1) showed significantly smaller linear trend in the EO-RS state than in the EC-RS state, while the eyeball showed significantly larger linear trend in the EO-RS state than in the EC-RS state (Figure 2 [Figure 2: see original paper], Table 2). In the RT-FFF vs. S-FFF comparison, the bilateral thalamus, bilateral anterior cingulate gyrus (BA 32), and right sensorimotor cortex showed significantly smaller linear trend in the RT-FFF state than in the S-FFF state (Figure 2, Table 2).

Discussion and Conclusion

This study demonstrated a manufacturer-specific pattern of linear trend in RS-fMRI BOLD signal, suggesting thermal noise over time. However, it is difficult to interpret the opposite direction of linear drift between Siemens and GE scanners. Our results would be helpful for manufacturers to further analyze linear drift and improve signal stability.

Although these results strongly support that removing linear trend should be a routine preprocessing procedure for RS-fMRI, the significant differences in linear trend between EO-RS and EC-RS, as well as between RT-FFF and S-FFF, indicate that the linear trend of RS-fMRI BOLD signal is not entirely scanner noise. It would be informative to compare linear trend between groups or conditions before removing the linear trend.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (Grant Nos. 81020108022, 81271652, 31471084) and the National Institute of Mental Health (Grant No. 5R33MH086952). Dr. Zang is partly supported by the "Qian Jiang Distinguished Professor" program.

Conflict of Interest

None.

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Table 1. Detailed information of datasets

Dataset	Participants (M/F)	Handedness (R/L)	Scanner	Magnet (T)	TR (ms)	Flip Angle (°)	Slice Number	Age (mean/SD)	Conditions
Beijing EO/EC	21/21	22.3/1.6	SIEMENS	3	2000	90	33	22.3/1.6	Two counterbalanced sessions
Beijing Feedback	19/19	22.3/1.6	SIEMENS	3	2000	90	33	22.3/1.6	Two counterbalanced sessions
Cambridge	198	75/123	171/27	SIEMENS	3	3000	85	47	21.0/2.3
CCBD	21/20	23.9/1.6	GE 750	3	2000	90	50	23.9/1.6	Eyes closed
Milwaukee	15/30	53.4/5.6	31/64	GE	3	2000	90	40	21.6/0.6
Oulu	103	48/55	95/8	GE	1.5	1800	90	23	21.0/2.3

Notes:

a There were 48 participants in the "Beijing EO/EC" dataset and 43 in the "Beijing Feedback" dataset. After excluding four participants from "Beijing EO/EC" (due to poor spatial normalization or left-handedness) and five from "Beijing Feedback" (due to technical problems or excessive head motion) (Dong et al., 2012), 42 and 38 participants were selected with session order, sex, and age counterbalanced between EO-RS and EC-RS or between RT-FFF and S-FFF, respectively.

b Accordingly, the first 5 time points of each time series were discarded in preprocessing (for more details: http://www.nitrc.org/docman/view.php/296/716/fcon_1000_Preprocessing.pdf), 5 extra time points were removed in our study.

c There were 103 participants in the "Oulu" dataset; eight participants were removed because of poor spatial normalization or excessive head motion.

Table 2. Detailed information of differences between states in beta maps

Comparison	Region	Cluster Volume (mm^3)	t-score of Peak Voxel	Coordinates of Peak Voxel (x, y, z)
EO-RS vs. EC-RS	Right eyeball	-	-	42, 63, -39
	Left eyeball	-	-	-36, 51, -51
	Sub-Gyral (Cuneus)	-	-	27, 33, 15
	Sub-Gyral (Cuneus)	-	-	3, -81, 30
	Sub-Gyral	-	-	-27, -66, -9
	Sub-Gyral	-	-	30, -57, -3
	Sub-Gyral	-	-	48, -30, -12
	Sub-Gyral (Cuneus)	-	-	33, -66, 21

Comparison	Region	Cluster Volume (mm³)	t-score of Peak Voxel	Coordinates of Peak Voxel (x, y, z)
RT-FFF vs. S-FFF	Thalamus, Extra-Nuclear	-	-	-15, 12, 27
	Cingulate Gyrus	-	-	6, -6, -3
	Medial Frontal Gyrus, SMA	-	-	-6, 15, 36
	Extra-Nuclear	-	-	-30, 15, 0
	Extra-Nuclear	-	-	30, -36, 21
	Inferior Parietal Lobule	-	-	-24, -27, 18
	Precentral Gyrus	-	-	12, -3, 54
	Precentral Gyrus	-	-	36, -39, 54
	Precentral Gyrus	-	-	33, -24, 57

Figure Captions

Figure 1. Results of one-sample t-tests ($p < 0.001$, cluster $p < 0.05$, GRF corrected) on beta values acquired with Siemens (EC-RS, EO-RS, RT-FFF, S-FFF, and Cambridge) and GE (CCBD, Milwaukee, and Oulu) scanners. N indicates the number of subjects for each dataset.

Figure 2. Results of paired t-tests ($p < 0.001$, cluster $p < 0.05$, GRF corrected) between EO-RS and EC-RS (upper row), and between RT-FFF and S-FFF (lower row). N indicates the number of subjects.

Note: Figure translations are in progress. See original paper for figures.

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