A wavelet-based approach to improve the reproducibility of resting-state fMRI analysis

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Introduction

Resting-state fMRI studies [1] have shown great potential towards understanding the spontaneous brain activity in healthy subjects as well as patients with neurological disorders (Alzheimer's disease [2]). Although active brain regions have been identified qualitatively across subjects, such as the default mode network for resting-state brain, quantitative variability has been reported when repeated tests were conducted on the same subject [3]. A viable clinical tool requires a high level of reproducibility. In this work, we investigated quantitative effects of a wavelet-based analysis of resting-state fMRI signal to improve the reproducibility of detection of synchronous activity in brain regions.

Methods

A single healthy male subject (age 29 years) participated in this study. The subject was asked to relax and keep his eyes closed during the scan. Whole brain T_2* -weighted echo planar images were acquired on a GE 3T Signa® HDx MR scanner (GE Healthcare, Waukesha, WI) using an 8-channel head coil. The following imaging parameters were used: 36 contiguous 3-mm axial slices in an interleaved order, TE = 27.7 ms, TR = 2500 ms, flip angle = 80°, FOV = 22 cm, matrix size = 64 × 64, ramp sampling, 164 volumes (excluding the first four data volumes which were discarded), scan time = 7 min. This scan was repeated 5 times. A high-resolution T1-weighted whole-brain anatomical image was also acquired.

The fMRI time series is pre-processed in AFNI [4] in the following steps: slice time correction, volume co-registration, spatial blurring (FWHM = 4 mm), brain mask generation, deconvolution to remove potentially motion-introduced artifacts, removal of baseline, linear and quadratic system-induced signal trends and also removal of the global mean signal time courses in the brain, CSF and white matter (CSF and white matter regions identified from T1-weighted image using 'FAST' routine in FSL package [5]), Talairach transform using the T1-weighted anatomical volume. Based on the resting-state fMRI analysis literature [6], a 6 mm spherical region in the posterior cingulate/retrosplenial cortex (PC/Rsp) was selected as a seed region and medial frontal cortex (MeFC) and surrounding regions (anterior cingulate cortex and superior frontal cortex) were selected as a target region to inspect synchronous activity.

The preprocessed time courses were further analyzed using each of the following methods: (1) band-pass filtering based on fast Fourier transform (FFT) to the range of 0.009 Hz – 0.08 Hz (in AFNI [4]), (2) continuous wavelet transform (CWT) (Matlab, Natick, USA) using four types of wavelet families: (a) 2nd order symlet (sym2) in the 0.0089 Hz - 0.0889 Hz band (scales 3 to 30) , (b) Meyer wavelet (meyer) in the 0.0092 Hz - 0.0920 Hz band (scales 3 to 30), (c) 4th order Gaussian wavelet (gaus4)) in the 0.0091 Hz - 0.1000 Hz band (scales 2 to 22) and (d) biorthogonal spline wavelets (Nr=2, Nd=4) (bior2.4) in the 0.0089 Hz - 0.0889Hz band (scales 4 to 40). These wavelets were selected based on properties such as orthogonality, compact support, regularity or symmetry. Next, Pearson correlation coefficient between the processed mean time course or coefficients of CWT from PC/rsp (seed) and all voxels in the target region was computed and compared with the only pre-processed time courses. The active voxels in the target region were identified by thresholding the t-statistics of the correlation coefficients at $p \leq 10^{-5}$. To study the reproducibility of active regions in the target across 5 repeated scans, the following statistics were computed: mean active volume (in mm^3), standard deviation (SD) of active volumes (in mm^3) and overlap of active regions (in mm^3).

Table 1. Results from reproducibility analysis for active volume in the target region

Processing	*Mean (mm^3)*	*SD (mm^3)(%)*	*Overlap (mm^3)*
Pre-processed	27615.6	5063.9 (18.3)	13230.0
FFT	36335.2	2748.3 (7.6)	18303.0
Wavelet - sym2	40473.0	1708.8 (4.2)	19278.0
Wavelet - meyer	42352.2	1386.6 (3.3)	19143.0
Wavelet - gaus4	42357.6	1129.9 (2.7)	19548.0
Wavelet - bior2.4	42012.0	994.4 (2.4)	19548.0

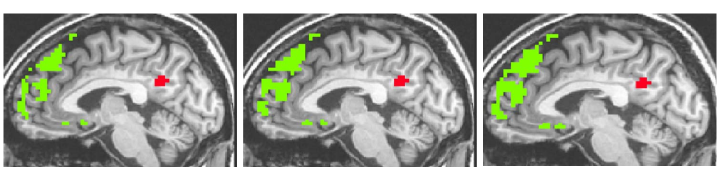

Fig. 1. Overlapped functionally active voxels in the target region (shown in green) for the seed region (PC/Rsp) (shown in red) in 5 repeated scans. (a) Only pre-processed, (b) FFT and (c) Wavelet (bior2.4) processed.

Results and discussion

Table 1 shows that the mean active volume in the target region increased and the standard deviation (percent is w.r.t. mean) decreased across 5 scans when using the wavelet-based analysis as compared to the only pre-processed and the FFT based filtering analysis cases. Also, the overlap in the active volumes across 5 scans increased when using the wavelet analysis. Amongst the wavelets, biorthogonal spline wavelets gave the smallest SD values while both the Meyer and the Gaussian wavelets gave higher mean active regions. In terms of the overlapped regions, both Gaussian and biothogonal spline wavelets performed better than other cases. Fig. 1 shows the overlapped active regions occurring in all the 5 repeated scans and the wavelet-based analysis case shows improvement over the only pre-processed and the FFT-based filtering cases.

Use of wavelets over the frequency domain filtering method allows us to explore the time-frequency dynamics which has been shown to exist in the brain activation pattern [7]. Recent resting-state fMRI studies [7, 8] have demonstrated the applicability of wavelet-based approach. In this work, we have demonstrated the use of the wavelet-based analysis approach to improve the reproducibility of the resting-state fMRI activity patterns (such as PC/Rsp to MeFC). This approach not only improved the reproducibility as indicated by a reduction in SD values across 5 scans, but also showed an increase in the detection of the active voxels in the target region. This shows that the wavelet-based approach could characterize the intrinsic brain activation better than the Fourier-domain filtering based approach which assumes stationary time signals.

Improvement in reproducibility of resting-state fMRI results with a reasonable scan time (7 min) indicates potential clinical use. Although reproducibility studies have shown improvement if imaging scan time is increased [3], but this could not be feasible with patients with neurological disorders (such as Alzheimer's disease) without causing patient discomfort. Further studies need to be conducted to optimize the wavelet parameters for specific applications, such as detecting the default mode network in Alzheimer's disease patients.

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