Effects of Rapid Head Motions on Group fMRI Functional Connectivity Evaluated with E-REMCOR

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Target audience: Researchers employing advanced multimodal fMRI and EEG techniques, researchers studying functional connectivity with fMRI, as well as everybody interested in head motion effects in fMRI and motion correction methods for fMRI.

Purpose: Studies of resting state functional connectivity for large groups of subjects by fMRI have shown that head motions cause systematic changes in functional connectivity patterns on the group level [1,2]. Recently, we introduced a method that uses EEG recorded simultaneously with fMRI to improve retrospective motion correction of fMRI data (E-REMCOR) [3]. Due to the high temporal resolution of EEG, E-REMCOR makes it possible to reduce the effects of rapid head motions (occurring on time scales shorter than *TR*) that cannot be adequately corrected by the traditional fMRI motion correction techniques. Here we report results showing the effects of E-REMCOR on group-level fMRI functional connectivity data. Our results demonstrate that rapid head motions affect functional connectivity of the medial prefrontal cortex (mPFC) seed region [4,5], a major hub of the default mode network (DMN), causing opposite-sign changes in its connectivity strength for anterior and posterior brain areas.

Methods: Twenty MDD patients (16 females) participated in the study. The experiments were performed on a GE Discovery MR750 3T MRI scanner with an 8-channel receive-only head coil array. A single-shot gradient- echo EPI sequence with FOV/slice=240/2.9mm, *TR/TE*=2000/30ms, flip=90°, SENSE *R*=2, image matrix 96x96, recon matrix 128x128, 34 axial slices, was employed for fMRI. Concurrent EEG recordings were performed using a 32-channel MR-compatible EEG system (Brain Products GmbH) in 0.016–250 Hz band with 0.1 µV resolution and 5 kS/s sampling rate. Each subject underwent a resting fMRI scan (eyes open, fixation cross) lasting 8 min 40 s (260 fMRI volumes). EEG data analysis was performed in BrainVision Analyzer 2. MRI and cardioballistic artifacts were removed using the average artifact subtraction method. Motion artifacts were then examined using ICA. For each subject, between two and six motion-related independent components (ICs) were identified in the EEG data as described in [3]. Each IC was high-pass filtered at 0.1 Hz (48 dB/octave) and integrated to yield two E-REMCOR regressors [3]. fMRI data analysis was performed in AFNI [6]. The E-REMCOR correction was implemented using AFNI's 3dTfitter program [3]. The baseline was modeled by 4th order polynomials, and the E-REMCOR regressors were polynomially detrended. Because of the high-pass filtering of the motion ICs, the E-REMCOR regressors approximated the effects of rapid head movements while leaving the effects of slow motions unchanged [3]. Both the original and the E-REMCOR corrected data were volume registered. The functional connectivity analysis was conducted in AFNI within the GLM framework. The fMRI time series were band-pass filtered between 0.01 and 0.1 Hz. A 12 mm diameter mPFC seed ROI was centered at (0 52 −6) MNI coordinates [5]. Its time course was used as a GLM regressor of interest. The nuisance covariates included six fMRI motion parameters, time courses of two ROIs within white matter and ventricle CSF, and the whole brain (global) signal [1,2,4,5]. Time derivatives of their time courses were also included in GLM. The baseline was modeled by 4th order polynomials. The correlation maps were transformed to Talairach space, resampled to 2 mm isotropic voxel size, smoothed (8 mm FWHM) and *r*-to-*z* transformed for group analysis.

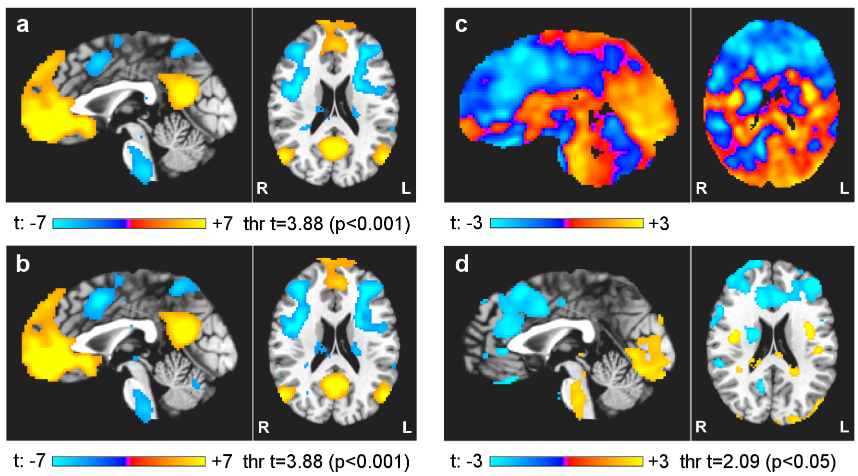

Fig. 1. a) Functional connectivity of mPFC based on the original fMRI data; b) connectivity of mPFC based on the E-REMCOR corrected data; c) difference (paired *t*-test) between the connectivity patterns in Fig.1b and Fig. 1a, no threshold; d) same as in Fig. 1c, with threshold for $p<0.05$.

Results: The subjects exhibited significant head motions during the scan. The maximum brain displacements ranged from 0.6 mm to 5.5 mm, with the average displacement of 1.9 mm. Fig. 1a shows the group functional connectivity map for the mPFC seed ROI based on the original fMRI data (without E-REMCOR). Fig. 1b exhibits a similar map based on the fMRI data pre-processed using E-REMCOR. Both maps correspond to $p<0.001$ (FDR $q<0.002$). The map for the E-REMCOR corrected data exhibits higher peak *t*-values for the clusters in DMN regions as follows. For PCC: t=8.88 at (1 −61 16) (1673 voxels) in Fig. 1a versus t=9.53 at (−1 −59 16) (1700 vox) in Fig. 1b. For mPFC: t=17.3 at (−1 43 −6) (9508 vox) in Fig. 1a versus t=17.4 at (−1 43 −6) (8601 vox) in Fig. 1b. For left lateral parietal cortex: t=7.55 at (−43 −73 32) (623 vox) in Fig. 1a versus t=8.09 at (−43 −73 32) (647 vox) in Fig. 1b. For right parietal lateral cortex: t=7.29 at (49 −65 20) (440 vox) in Fig. 1a versus t=7.74 at (49 −67 22) (432 vox) in Fig. 1b. The maps in Fig. 1c and Fig. 1d show the group difference (paired *t*-test) between the results in Fig. 1b and Fig. 1a.

Discussion: Our results suggest that rapid head motions increase the apparent functional connectivity strength between the mPFC seed region and the anterior brain areas, while reducing the connectivity with the posterior brain areas. These spurious effects are at least partially corrected by E-REMCOR (Fig. 1c), as evidenced by enhanced connectivity within DMN (cluster peak *t*-values in Fig. 1b vs Fig. 1a). The physical reason for such connectivity changes is the following. Rapid head rotations, taken into account by E-REMCOR, cause larger displacements in the anterior brain areas, leading to larger fMRI signal variations there [3]. Such spurious signal variations enhance correlations among the anterior areas and obscure possible correlations between the anterior and posterior areas. This explanation is consistent with the conclusion reached in [2] that an improved motion correction generally reduces short-range and enhances long-range correlations, especially along the anterior-posterior direction. Our results indicate that E-REMCOR is an efficient tool for an independent evaluation and correction of rapid head motion effects. Because E-REMCOR corrects fMRI data without discarding any volumes, it should be particularly useful in task fMRI with block or event-related designs.

References: [1] K.R.A. Van Dijk et al. *NeuroImage* 2012, 59:431. [2] J.D. Power et al. *NeuroImage* 2012, 59:2142. [3] V. Zotev et al. *NeuroImage* 2012, 63:698. [4] M.D. Fox et al. *PNAS* 2005, 102:9673. [5] K.R.A. Van Dijk et al. *J. Neurophysiol*. 2010, 103:297. [6] R.W. Cox. *Comput. Biomed. Res.* 1996, 29:162.