Functional connectivity of DMN is underestimated due to signal loss in parahippocampal regions and its remedy

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Target Audience: Researchers working on resting state fMRI

Purpose

The study of Grecius et al. indicated that default mode network (DMN) is closely involved with memory processing and resting-state activity in the posterior cingulate cortex (PCC) and hippocampus decreases in the Alzheimer's disease (AD) group[1]. However, in their study, the hippocampal coactivation in DMN was almost absent when the GE-EPI images were acquired using a 3.0 T MRI scanner. Grecius et al. suggested that the signal loss of hippocampus is most likely due to susceptibility artifacts at 3.0 T[1]. We assume that optimization of slice orientation reduces signal loss of the human hippocampus area and improves measurements of functional connectivity of DMN. In this study, we investigated the signal intensities of GE-EPI images and functional connectivity of DMN using three conventional slice orientations.

Material and Methods

We performed all imaging experiments using a 3.0 Tesla whole-body MR system (Siemens, Skyra, Germany) equipped with a 32-channel head coil in National ChengChi University (NCCU). Twenty normal right-handed volunteers (10 men and 10 women; aged 23.4 ± 1.5 years) participated in the experiments after providing institutionally approved consent. We first obtained scout localizers, and performed structure image using a 3D MP-RAGE sequence for co-registration. To investigate the impact of slice orientations on signal loss and functional connectivity, we designed a protocol with GE-EPI performed using three different slice orientations. The three slice orientations were the three orthogonal slice orientations, coronal (C), sagittal (S) and transversal (T) and with three phase encoding directions (C: right to left, S: anterior to posterior, T: anterior to posterior), respectively. The common GE-EPI parameters were: TR/TE of 2000/30 ms, 220 mm FOV, 5 mm slice thickness, 4 dummy scans, 204 measurements, and a matrix size of 64×64. Total scan time was approximately seven minutes. The voxel size was 3.4 × 3.4 × 5 mm^3. The EPI data set was termed D1. To study the differences between isotropic and anisotropic voxel sizes, we acquired another EPI data set, termed D2, using the same EPI protocol of D1 albeit with FOV of 240 mm, slice thickness of 3.8 mm, and 50 measurements. Ten subjects participated the experiment for D2 data set. The voxel size of D2 is close to isotropic, 3.75 × 3.75 × 3.8 mm^3. The three slice orientations were performed using a random order. To compensate the geometry distortion of GE-EPI images, we acquired field maps of the whole brain using a dual-echo gradient-echo sequence with parameters TR/TE_1/TE_2 of 529/4.92/7.38 ms, 220 mm FOV, 50 transversal slices, 5 mm slice thickness, a matrix size of 64×64. The GE-EPI images were first processed in FSL using FUGUE to correct geometric distortions of GE-EPI using the the field maps. The undistorted images were then processed by using SPM8 and MATLAB® (Mathworks, Natick, MA, USA). The procedures included normalization to MNI coordinates, slice timing, realignment, co-registration, segmentation and smoothing(FWHM=4mm). We parcellated the first 50 images of D1 and D2 into 90 cortical and subcortical ROIs in the cerebrum used the automated anatomical labeling template (AAL) and calculated average signal intensity of the ROIs. In addition to intensity analysis, we evaluated differences of the functional connectivity in the DMN network obtained using different slice orientations. The normalized EPI volume underwent regression analysis, (6 motion parameters, WM, CSF), band pass filtering (0.01 - 0.08Hz) and seed-based rsfMRI analysis using a sphere mask centered at the posterior cingulate cortex[2] (PCC, x = 0, y = -52, z = 27, radius=6mm). The obtained Pearson's correlation coefficient of each MNI coordinate was transformed to Fischer's z value. We then used t-test to evaluate the group differences of connectivity maps obtained using three slice orientations.

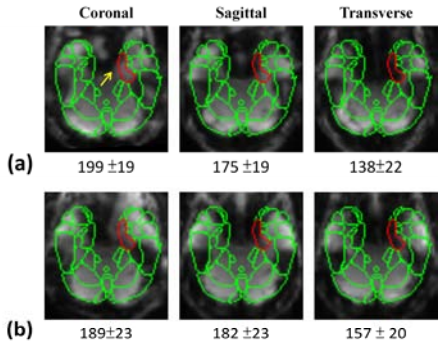

Figure 1 Normalized images (z = -25 mm) of (a) D1 and (b) D2. The green profiles are borders of AAL ROIs. The red profiles indicated by the yellow arrow are the border to AAL-40. The number beneath each image indicates the average signal intensity.

Results

Figure 1 displays normalized images (z = -25 mm) of D1 (Fig. 1a) and D2 (Fig. 1b). The green and red profiles outline the borders of AAL ROIs. The number beneath each image indicates the average signal intensity (D1: n = 20, D2: n = 10) of AAL-40 (ParaHippocampal_R, indicated by a yellow arrow). The signal intensities of AAL-40 obtained using coronal and sagittal orientations are significantly higher than those obtained using transverse orientation (P < 0.01). Table 1 lists the regions with signal intensities significantly different (P< 0.01) in three orientations. Of all the 90 AAL regions, we lists regions related to DMN network and with their average signal intensities lower that 40% of the Supp_Motor_Area_L region (AAL-19), a region which is assumed to be less affected by the susceptibility signal loss problem. Figure 2 displays the DMN connectivity maps obtained using the D1 dataset. Notice that network connectivity in parahippocampal region (indicated by a yellow arrow) can be observed in the maps obtained using coronal (green) and sagittal (blue) slice orientation. In the map obtained using the transverse orientation, the DMN connectivity in the parahippocampal region is relatively subtle. Group analysis (n = 20) reveals significant differences in the parahippocampal region (see Fig. 2b).

Regions	AAL	D1			D2		
Frontal_Sup_Orb_L	5	C > T	S > T		C > T	S > T	
Frontal_Sup_Orb_R	6	C > T		C > S	C > T		C > S
Rectus_L	27	C > T	S > T			S > T	
Rectus_R	28	C > T	S > T		C > T	S > T	
ParaHippocampal_L	39	C > T	S > T		C > T	S > T	
ParaHippocampal_R	40	C > T	S > T	C > S	C > T	S > T	
Temporal_Pole_Mid_L	87	C > T	S > T		C > T	S > T	
Temporal_Pole_Mid_R	88	C > T	S > T	C > S		S > T	
Temporal_Inf_L	89				C > T		C > S
Temporal_Inf_R	90					S > T	S > C

Table 1 AAL regions related to DMN and potentially affected by signal loss.

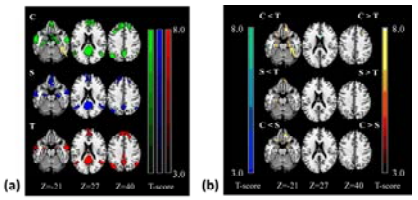

Figure 2 (a)The DMN connectivity maps and (b)group analysis reveals the differences of connectivity maps obtained using three different orientations.

Discussion and Conclusions

The previous study suggested that the signal loss of hippocampus is due to susceptibility artifacts. In previous studies, Chen et al. optimized slice orientation and voxel size for the human amygdala[2]. In this study, we proposed to optimize the slice orientation for the DMN study to reduce the signal loss in the regions related the DMN network. From the AAL-based evaluations of D1 (3.4 × 3.4 × 5 mm^3) and D2 (3.75 × 3.75 × 3.8 mm^3, close to isotropic voxel size), the results indicated signal intensities of the DMN network obtained using the coronal and sagittal slice orientations are mostly higher than those obtained using the transverse slice orientation. From resting state fMRI experiments, our results show that the DMN connectivity near the hippocampus region can be clearly identified when we acquire the EPI images using the coronal and sagittal slice orientations. It has been reported that field gradients along slice and phase encoding direction prominently introduce signal loss is GE-EPI images. Changing the slice orientations or tilt angle could reduce the signal loss for specific regions. In conclusion, our results suggested that the hippocampal coactivation in DMN can be recovered using the coronal and sagittal slice orientations.

Reference

1. Greicius, M.D., et al., Proc Natl Acad Sci U S A, 2004. 101(13): p. 4637-42.
2. Chen, N.-K., et al., NeuroImage, 2003. 19(3): p. 817-825