Effects of Transverse Relaxation on Functional Connectivity of Default Mode Network

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INTRODUCTION

Low-frequency (<0.1Hz) spontaneous fluctuations in resting-state fMRI have been used to study functional connectivity in brain networks (1, 2). However, the underlying mechanism and contrast-to-noise ratio (CNR) of the connectivity remain inconclusive (3). While the CNR of stimulation-induced brain activation has been well studied, much less is known about the optimization of functional connectivity (4). In the current work, we used a multiple gradient-echo sequence to investigate the transverse relaxation (T_2^*) effects on the spatial pattern, connectivity strength and spectral power of functional connectivity in the default mode (DM) network at 3T.

MATERIAL & METHODS

Ten healthy subjects participated in the experiments on a 3T Allegra system with a head volume coil. A four-echo (TE=7.7/22/37/52 ms) gradient-echo EPI sequence was used to collect resting scan (200 measurements, TR=3s). Subjects were instructed to close their eyes and not to think of anything in particular during the scan. Images were acquired on the whole brain (35 slices) along the AC-PC line, with FOV of 220 mm, MTX of 64×64, slice thickness of 4mm, and bandwidth of 4112 Hz/voxel. Data were pre-processed with motion correction, detrending, and low-pass filtered (<0.1 Hz) using MATLAB, and then underwent spatial normalization (resampled to an isotropic resolution 3×3×3 mm^3), smoothing (Gausian kernel = 6 mm) and statistical analyses by AFNI. To correct for potential influences of physiological noise, cardiac and respiratory estimations were calculated using a post-processing method with temporal independent component analysis (ICA) (5). A spherical seed with 6 mm diameter was chosen from the posterior cingulated cortex (PCC) [4, -54, 24] in the normalized space. Four reference time courses were extracted from the seed region of the resting data acquired at four different TEs, respectively. Each of the references was used to compute voxel-wise cross-correlation coefficient (CC) in the entire brain, for data with corresponding TE. Six motion parameters, respiratory/cardiac estimators and the averaged time-series retrieved from the segmented white matter mask were regressed out as nuisance covariates in the process. The CC maps of different TEs were converted to normal-distributed z-score maps, and then group-level analysis were performed to reveal significant connectivity maps ($p < 0.05$, corrected) at each TE. An overall connectivity map was generated from averaged contrast of all TEs above the statistical threshold ($p<0.005$, cluster = 243 mm^3).

RESULTS

Fig.1 shows the functional connectivity maps of the DM network across different TEs. The spatial extent of the functional connectivity in the shortest TE (7.7 ms) spread more widely around the seed than those of other TEs, and the distant connections to the prefrontal lobe were nearly not observable. Fig.2 shows the average CC values (Mean ± intersubject standard deviation) between the seed and the voxels in the overall connectivity map (Fig.1), as a function of echo time. The connectivity strength increased rapidly from TE of 7.7 to 22 ms, held flat between 22 to 37 ms, and decreased slowly from 37 to 52 ms. The optimal TE for the DM network would be around 30 ms at 3T. Fig.3 shows the average power spectrum (normalized to the DC value of each time course) of the significantly connected brain areas, obtained from the data with different TEs. In the frequency domain, the low-frequency (0.01-0.05 Hz) power, which contributes the most to functional connectivity (6), was enhanced at longer echo times.

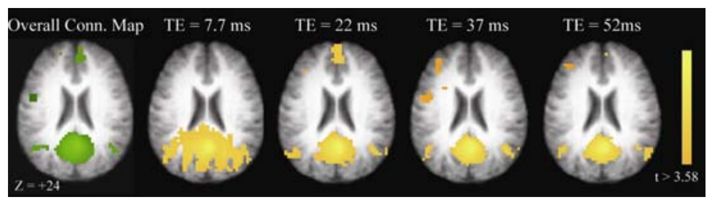

Fig.1 Spatial maps of functional connectivity across different TEs. The most-left one demonstrates ROI areas for following ROI-based calculations such as cross correlation (fig. 2) and spectrum (fig.3).

DISCUSSION & CONCLUSION

In the current study, the influence of echo time on functional connectivity was evaluated in the DM network. It was found that an optimal TE exists between 22 and 37 ms at 3T, for maximal connectivity strength. In functional MRI with external stimulations, it is well known that the optimal CNR is achieved when TE is around effective transverse relaxation time (T_2^*). The similar characteristic observed in ongoing brain activity suggests that the functional connectivity may share the same origin as stimulation-evoked brain activation.

The connectivity map at the shortest TE (7.7 ms) showed wide-spread local connections, while lacking long-distance connections to the prefrontal lobe. This spatial pattern is probably caused by low CNR (due to little T_2^* weighting) but high signal-to-noise ratio (SNR) (due to small signal attenuation). The low CNR results in less sensitivity to detect brain connectivity, particularly in distant regions (6, 7). On the other hand, the high SNR may make it more sensitive to synchronized fluctuations that are not weighted by T_2^*. Another conjecture is that the wide connections at the shortest TE is predominantly contributed from the fluctuations of intravascular components rather than that of extravascular components, which would be enhanced in the gradient-echo sequences with the increase of echo time (8). Power spectrum of the shortest TE showed considerable deviations from those of longer TEs mainly in the frequency range (0.01-0.05 Hz) that contributes the most to the functional connectivity in the DM network (6), consistent with the correlation analysis. The spectral power elevated further as TE increased from 22-52 ms. However, connectivity strength kept stable in this TE range, probably due to lower SNR at longer TEs. Both temporal and frequency analyses indicate that appropriate TE weighting is necessary to achieve sensitivity to the signal fluctuations contributed to functional connectivity.

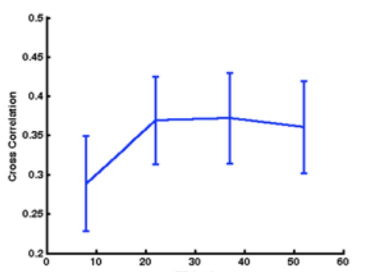

Fig.2 Average connectivity strength as a function of TE. Similar to the stimulation-evoked BOLD response, the optimal TE for the highest contrast is between 22 and 37 ms.

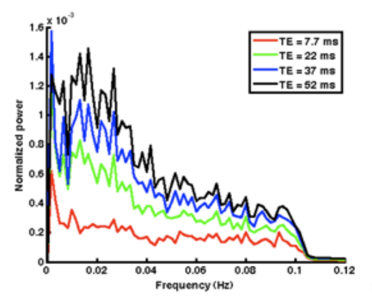

Fig.3 Normalized power spectrum from functionally connected brain regions, at different TEs. The spectrum from the shortest TE (7.7 ms) deviates the most from others between 0.01 to 0.05 Hz.

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