Flip Angle Effects on Resting State fMRI Studies

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Introduction:

Resting state functional MRI (rs-fMRI) reflects the BOLD signal induced by spontaneous neuronal activities when the brain is at rest. Compared with the 1~5% of functional contrast in task/event related fMRI, the amplitude of such spontaneous signal variation is buried at the noise level. Therefore, rs-fMRI is especially sensitive to physiological noise, which often is the dominant source of noise. Physiological noise may originate from motion, respiration, cardiac pulsation as well as CSF flows, which are usually being accounted for via regression methods. Recently it has been demonstrated that using a flip angle (FA) as low as 9° can reduce the relative weighting of physiological noise in BOLD signal while still sustaining sufficient BOLD contrast [1]. In this study, we will study how different flip angles affect rs-fMRI signal characteristics and the calculation of functional connectivity, and analyze the underlying mechanism of the origin of resting state signals.

Methods:

Seven healthy volunteers (4 males, age 25±4 years) participated in the study with written consents. RS-fMRI time series were acquired on a Siemens 3T Verio system using GE-EPI with following parameters: TE/TR = 30/2000ms, voxel size = 2.3×2.3×3.5mm^3, 31 slices and 200 volumes. Four sets of resting data were collected using FA = 80°, 30°, 10° and 6°, respectively. For post processing, all functional images were first coregistered and normalized to MNI space, and then regressed out the 6 movement parameters generated during coregistration, detrended to remove baseline drifting, low pass filtered with a 0.01~0.08Hz filter, and finally spatially smoothed using a Gaussian filter with 6mm FWHM. Temporal SNR (tSNR), amplitude of low frequency fluctuation (ALFF), fractional ALFF (fALFF) and coherent regional homogeneity (cReHo) were calculated and averaged among subjects. Connectivity maps of default mode network (DMN, [4, -53, 26]) and visual network ([4, 81, 8]) were calculated using seeding ROI methods.

Results:

The subject averaged maps of ALFF, fALFF, cReHo and tSNR, as well as the one sample t-test results of DMN and visual network are shown in Fig. 1. And the original and normalized histological plots of voxel number vs. correlation coefficient (cc) of these two networks are shown in Fig.2. It can be seen that most significant changes in all 4 parametric maps take place when FA decreases from 30° to 10°. Slight changes can be seen when from 80° to 30° and from 10° to 6° respectively, with the exceptions of largely unchanged fALFF from 80° to 30°, and of the significant changes in cReHo from 10° to 6°. For both functional networks, the patterns can be clearly distinguished even for FA of 10°, and are still discernable at 6°.

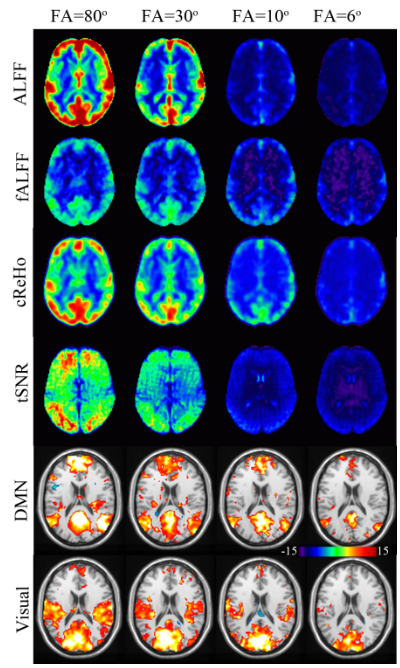

Fig.1 ALFF, fALFF, cReHo, tSNR maps and one sample t-test results of DMN and visual networks with FA of 80°, 30°, 10° and 6°. All images are shown at the same slice position, and are displayed with the same window settings for each row.

Discussion:

Physiological noise is a major concern in rs-fMRI because it not only will obscure the intrinsic resting state signals and reduce the resultant connectivity strength, but also may introduce false positive connectivity since its effects can be global. Currently the major measure for removing the physiological effects is regression using recorded (cardiac/respiratory) or extracted (CSF/motion) regressor [2]. However, modeling these effects as regressor may not account for all unwanted effects. For instance, to regress out the CSF effects, it is usually done by extracting the time course from an ROI in the ventricle as the regressor, but the CSF effects in the subdural space may not be accurately accounted for by this regressor due to the different flowing dynamics. Using a flip angle much lower than Ernst angle, on the other hand, may have the potential to globally reduce the physiological noise in the signal time series [1]. Since it was demonstrated that using a flip angle of as low as 9° could still sustain high BOLD contrast [1], we thus preliminarily chose 4 flip angles, i.e. 80° as the Ernst angle, 10° as this minimal flip angle for sustaining BOLD effects, and 30° and 6° as above and below this critical angle.

Although lower FA is expected to lead to reduced values in all the parametric maps, the reductions are however not uniform for different FA or tissues (Fig.1). The fact that the most significant reduction takes place between 30° and 10° confirms that there exists a critical FA at which physiological effects becomes non-dominant. In all parametric maps shown, the greatest reduction takes place mainly in GM, where contains hemodynamics related physiological effects [3]. However, the reduction in GM of ALFF (reflects the amount of low frequency signal), cReHo (reflects the temporal homogeneity of the region) and tSNR did not affect the network connectivity to the same extent. Both DMN and visual networks (as well as other networks not shown here) can be reliably extracted with 10° FA, and the major clusters are still well shown at 6° (Fig.1). Specifically, with reduced FA, long range connectivity slightly reduces while short range connectivity remains almost unchanged. This suggests that low FA indeed can sustain a robust calculation of the functional connectivity. We also extracted all the voxels with cc > 0.5 from both networks, and the distribution histogram can be seen to be network specific (Fig.2). For DMN, the total voxels numbers decrease rather linearly according to FA values, and the normalized histograms look almost identical for all FAs. As a result, all the essential regions of DMN, long and short range, are 'connected' even with 6° FA. The visual network, on the other hand, have very similar voxel number and distribution histogram between 80° and 30°, and between 10° and 6°, but differ significantly between these two FA groups. The normalized distribution show relatively fewer high-cc voxels but more medium-cc voxels at low FA. According to the connectivity maps in Fig.1, this is mainly due to reduction in long range connectivity. It is interesting to note that fALFF reduces more in WM than in GM. As fALFF reflects the relative level of the low frequency components for connectivity calculation, reduced fALFF value will potentially lead to reduced correlation to the seed region. Therefore, lower fALFF in WM than in GM will be beneficial for having higher cc values for GM voxels, and our results (networks shown in Fig.1) are in accordance to this prediction.

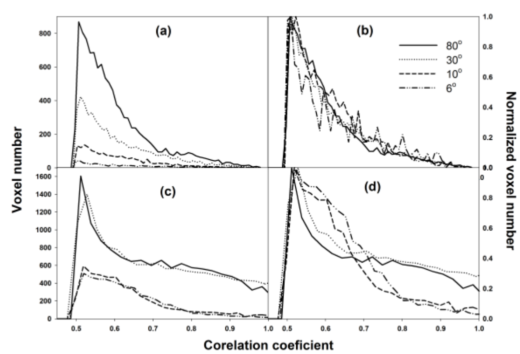

Fig.2 Voxel number histograms of functional correlation coefficient of DMN (a, b) and visual network (c, d). Threshold was selected as cc>0.5.

In conclusion, the low FA may be a better way to reduce physiological effects for rs-fMRI in a global, tissue specific manner, while sustaining high functional connectivity correlation that's more specific to GM. Further work will focus on more quantitative analysis of the physiological effect reduction as a function of FA, as well as determining the optimal FA at which minimal false positive (due to relatively reduced physiological noise) but good true positive (due to sufficient SNR) connectivity results can be obtained. From the current results, such FA is estimated to be in the range of 10°~30°.

Reference:

[1] Gonzalez-Castillo. Neuroimage, 2011; [2] Birn. Neuroimage. 2012; [3] Zang, Neuroimage, 2004;