

An improved 3D GRASE pCASL method for whole-brain resting-state functional connectivity

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Introduction: Resting-state functional-connectivity (RSFC) has received increasing interest in clinical neuroscience, due to its potential to help translation of fMRI into clinical care [1]. While blood oxygenation level-dependent (BOLD) functional connectivity has been increasing popular, arterial spin labeling (ASL) based functional connectivity has received little attention [2,3]. 3D GRASE (Gradient- and spin-echo) background suppressed (BS) pseudo-CASL [4], which is a hybrid sequence with a combination of gradient and spin echoes, has been shown to have some advantages over EPI (high SNR, 3D acquisition, improved coverage in high susceptibility regions, such as medial orbitofrontal cortex (MOFC)) [5]. However, its role in RSFC has not been investigated. In this work, we modified a 3D GRASE sequence to increase the brain coverage, and assessed its role for whole-brain RSFC. Given two potential disadvantages of the proposed method (temporal blurring and vascular artifacts [6]), its validity for RSFC needs to be investigated. Thus, the aim of this work is to perform ASL functional connectivity, and to compare the results with those from BOLD. In particular, our hypothesis is that our method can detect MOFC as part of default mode network (DMN), which has been shown previously by PET [1], while BOLD does not perform well in this area.

Methods: Separate ASL and BOLD runs were acquired (7.5 min each) within the same session in 6 healthy volunteers on a Siemens 3T Trio scanner. **ASL data:** A 3D-GRASE pCASL was used (TR=3750ms, effective TE=56.5ms, 5/8 partial Fourier, resolution: 4x4x6mm³, 20 partitions with 30% oversampling, matrix size=64x51x20, total readout time=300ms, refocusing flip angle=162°, 600ms post-labeling delay). The pCASL pulse consisted of a series of RF pulses played for 1284ms. For the control pulse, the phase of the RF pulses alternated between 0 and 180°. 3D TOF images were acquired to determine the labeling offset for each subject [7]. To increase SNR, background-suppression was applied with two hyperbolic secant inversion pulses (T11/T12=1913/523ms before the 90° pulse, respectively). To increase brain-coverage, k-space was undersampled by sharing outer k-space areas between adjacent label (or control) acquisitions (i.e., with even labelling images acquiring even PE lines; and odd labelling images acquiring odd lines); the central k-space (15 PE lines) was fully sampled to minimise temporal-blurring. **Data Processing:** Data were preprocessed with the following steps: motion correction, smoothing (FWHM=6mm), high-pass filtering (>0.08Hz), followed by label-control subtraction. Then, all subjects' 4D data were concatenated temporally and analyzed using independent component analysis (MELODIC in FSL) to estimate group-level functional connectivity networks. **BOLD data:** 150 whole-brain T2*-weighted EPI (resolution: 3mm isotropic, matrix =72x72x44, TE/TR=30/3000ms). Data processing: motion correction, smoothing (FWHM=6mm), high-pass filtering (1/150Hz). Then ICA was performed in the same way as for the ASL data.

Results: Ten independent components were obtained from the ASL data using ICA, 6 of which were considered as resting-state networks, with 2 of the other components isolating the vascular contributions; 22 components were obtained from the BOLD data, 8 of which were selected as resting-state networks. The 6 selected ASL networks (including visual, attention, temporal, sensorimotor and DMN), were similar to those from our BOLD data (Fig. 1) and also consistent with previous BOLD results [8]. However, two differences were detected between the two methods. The executive control network was detected in the BOLD data, but not in the ASL data. Secondly, the visual network was detected as a single component (including medial and lateral parts) in the ASL data, but as two separate components in the BOLD data.

The DMN estimated from the ASL data showed greater inclusion of the MOFC in comparison to the BOLD estimate (Fig. 1, top row). Masking the DMN with an MOFC mask highlighted that a greater number of voxels in this region were detected as part of DMN with the ASL data in comparison to the BOLD data (Fig. 2).

Discussion: While our modified 3D-GRASE sequence shares similarities with segmented 3D-GRASE, the use of fully-sampled central k-space makes our sequence less affected by temporal blurring. The similarity between the RSFC from our method to that from BOLD data suggests that 3D-GRASE pCASL is capable of investigating RSFC. The failure to detect the executive control network in the ASL data is possibly due to a lower sensitivity resulting from the fewer sampling points (60 pairs) compared to the larger sampling in BOLD data (150 images). The inclusion of the medial and lateral visual networks into a single component in ASL data may be a result of the lower temporal sampling rate of ASL (2x3.75s vs. 3s for BOLD), which might make separating these closely related networks more difficult. A key benefit of our 3D GRASE method is that high susceptibility regions can be acquired successfully (cf. signal dropout in gradient-echo BOLD EPI data), as demonstrated by the better detection of the MOFC region in the DMN. This method may therefore provide a viable means for studies that especially focus on the MOFC region, such as decision making tasks.

In conclusion, our method provides true whole-brain 3D coverage (without slice-gap) for RSFC study using ASL data, which is known to provide a more direct measure and better localization of activation [9]. Improved coverage in high susceptibility regions, such as MOFC, makes those studies that particularly focus on these regions viable.

References: [1] Raichle et al., PNAS 2001; 98:676-82; [2] Zou et al., NeuroImage 2009; 48: 515-24; [3] Chuang et al., NeuroImage 2008; 40: 1595-605; [4] Fernandez-Seara et al., HBM 2007; 28: 1391-400; [5] Fernandez-Seara et al., MRM 2005; 54: 1241-47; [6] Chappell et al., MRM 2010; 63:1357-65; [7] Aslan et al., MRM 2010; 63:765-71; [8] Damoiseaux et al., PNAS 2006; 103: 13848-53; [9] Duong et al., PNAS 2001; 98: 10904-9.

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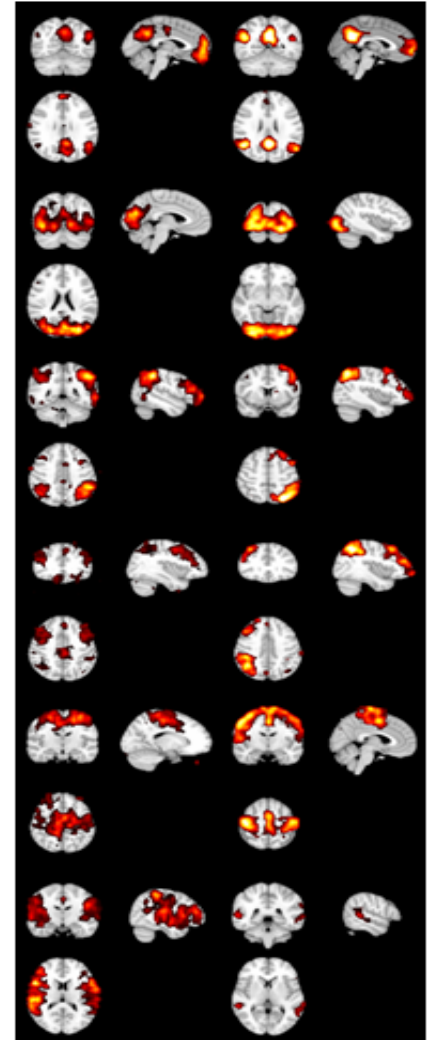


Figure 1: Six group-level resting-state networks estimated from ASL data (Left) and BOLD data (Right). (Note: the additional medial visual and executive control networks detected in the BOLD data are not shown.)

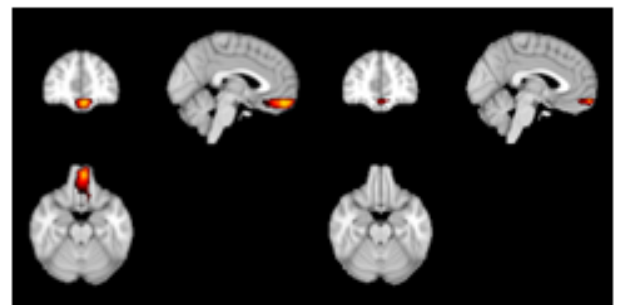


Figure 2: Activations detected in MOFC as part of DMN of ASL data (Left) and BOLD data (right).