

# Evaluation of Dual-Echo Pseudo-Continuous ASL for Resting-State BOLD Functional Connectivity Measurement

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## Target Audience

This work is of interest to researchers in the areas of fMRI image analysis, functional connectivity and brain physiology.

## Purpose

The BOLD signal results from the interplay between hemodynamic and metabolic aspects of neuronal activity, and is widely used in functional connectivity studies. An important complement to BOLD in studying brain function is cerebral blood flow (CBF), measurable using arterial spin labelling (ASL). Very recently, it has become possible to obtain high-quality dynamic BOLD and CBF measurements simultaneously using a dual-echo pseudo-continuous ASL (pCASL) approach<sup>[1]</sup>. While pCASL can reliably measure CBF, its potential to reliably measure resting-state BOLD connectivity would greatly augment its utility. This ability is still unestablished, particularly due to potential ASL contamination in pCASL-based BOLD, and to its intrinsically longer repetition time. In this study, we used an analysis approach that minimizes ASL contamination in pCASL-based BOLD for resting-state connectivity measurement. We show, for the first time, that pCASL BOLD provides connectivity maps highly comparable to conventional BOLD, and more importantly, a similar level of intra-subject reproducibility across the default-mode network (DMN), a resting-state network of great interest in several neurological diseases.

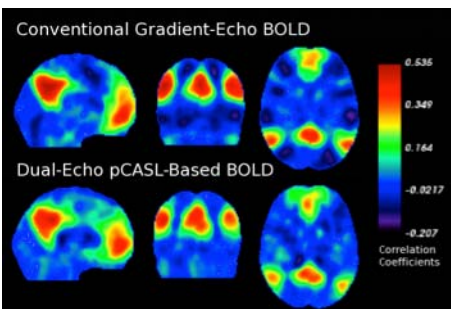
## Method

Sixteen healthy participants (7 males, 9 females, age = 41.2±17.9 yrs) were imaged with a Siemens Trio 3 T system (Erlangen, Germany). All participants received two conventional gradient-echo BOLD scans: TR = 2 s, voxel size = 3.4×3.4×4.6 mm<sup>3</sup> over 120 frames. Eight of the subjects were also scanned over 2 sequences using dual-echo pCASL: TR = 3.5 s, same voxel size, 100 frames. A 3D anatomical scan (1×1×1 mm<sup>3</sup>) was acquired using MPRAGE from all participants. All scans were completed within the same scanning session for each participant. For dual-echo pCASL, the BOLD frames were extracted from in between each ASL tag and control frames. Every pair of adjoining pCASL BOLD frames was then averaged to generate 119 new frames (a.k.a. the running-average method) to minimize ASL contamination in BOLD. Preprocessing, performed using the CONN toolbox (MIT), consisting of motion correction, sliced timing correction, registration to anatomical, conversion to MNI152 atlas, and smoothing to 8×8×8 mm<sup>3</sup>. Signals from cerebral spinal fluid

and white matter was then regressed from preprocessed images, followed by band pass filtering (0.01 Hz to 0.1 Hz). Voxel-wise correlations based on BOLD signals were calculated and averaged over the DMN for each scan of each subject. Reproducibility was measured using intra-class correlation coefficient (ICC) defined as  $ICC = \frac{MSb - MSw}{MSb + (k-1)MSw}$ ,  $ICC \in [0, 1]$ , where  $MSb$  and  $MSw$  are the within-subject and between-subject mean differences, and  $k$  is within-subject degrees of freedom<sup>[2]</sup>. Similarity between the functional connectivity produced by conventional and pCASL BOLD was assessed using cosine similarity (SI), the inner product of the two connectivity maps, and  $SI \in [-1, 1]$ .

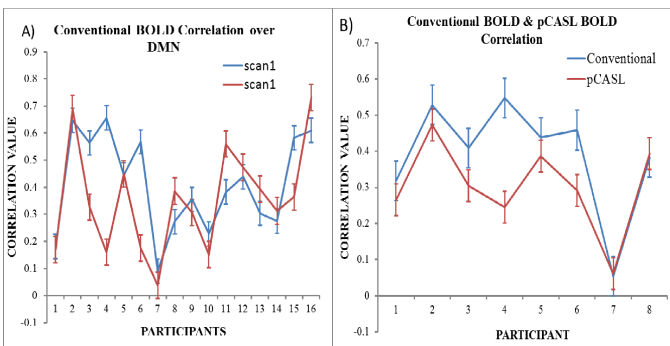
## Results

Figure 1 demonstrates the highly similar networks that closely resemble the DMN, in the conventional and pCASL BOLD correlation maps. The ICC for conventional BOLD was 0.8006, suggesting strong within-subject reproducibility. As shown in Figure 2A), within subject conventional BOLD correlation values matched well for most participants, consistent with ICC results. Furthermore, t-test on scan1 and scan2 correlation values did not show significant differences ( $p = 0.73$ ). Extending from these results, the



**Figure 1:** Voxel-wise group-averaged connectivity maps of the default-mode network across all participants. Red indicates high connectivity.

same reproducibility analysis was performed on pCASL BOLD. ICC of pCASL BOLD was 0.75. And T-test agreed with this result ( $p=0.46$ ). As conventional and pCASL BOLD have demonstrated the same level of strong intra-subject reproducibility, the correlations from the two scans for the same subject were averaged. Figure 2B shows matching seed-correlations between conventional and pCASL BOLD for most participants. Additionally a  $SI=0.91$  indicates nearly complete agreement, supported by  $t$ -test results ( $p=0.68$ ).



**Figure 2:** Average seed-based correlation value across the DMN for all participants: A) Across the 2 scans obtained from conventional BOLD acquisition; B) Mean conventional BOLD correlation plotted with mean dual-echo pCASL BOLD correlation.

and CBF with adequate SNR and minimal cross-talk is uniquely beneficial for investigating functional networks and their physiological interpretation.

**References:** [1] Wong, E. C., et al. NMR in Biomedicine 1997 10(4-5), 237–249; [2] Bosnell R et al. NeuroImage 2008 42:603–610.