Identification of Resting State Networks Using Whole-Brain CASL

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Introduction: There is increasing interest in task-absent functional MRI for the identification of "resting-state networks" [1,2]. Previous studies using ASL techniques [3] to show resting state networks (RSNs) have been confined to a restricted field-of-view [4,5]. However, to our knowledge, ASL has not yet been used to study RSNs across the whole brain with single timeseries acquisitions. This is mainly due to the fact that existing ASL techniques are unable to provide satisfactory imaging coverage due to T1 decay, which limits the time available for multi-slice acquisition before the label decays [6]. In this study, we implemented a novel true whole-brain CASL technique with EPI readout to study dynamic characteristics of cerebral blood flow during the resting state. We extracted the major co-varying networks in the resting brain, as imaged in 8 subjects at rest. The major brain networks seen are highly similar to recent published results obtained using BOLD fMRI [7]. We also characterised very low-frequency RSN temporal behaviour for the first time.

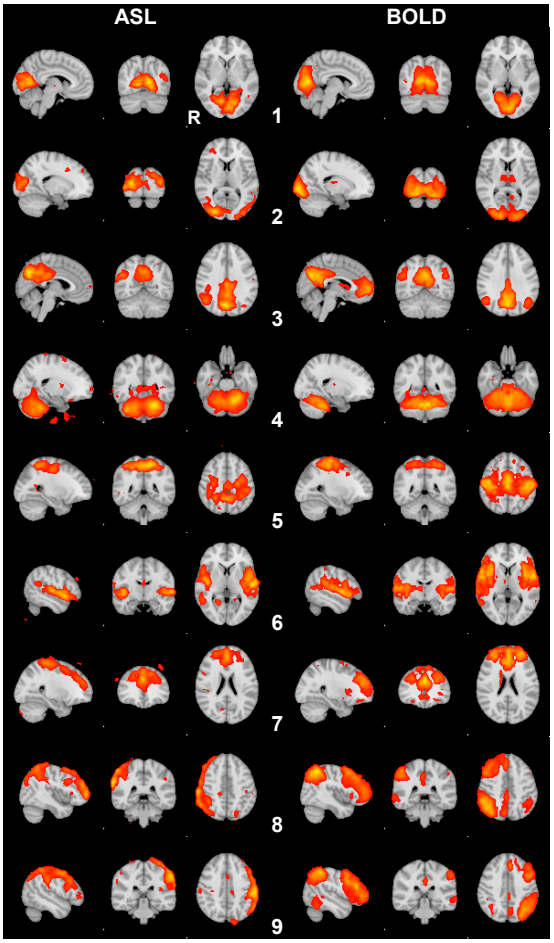

Figure1: Activation maps of nine pairs of networks extracted from 8 subjects' ASL data at rest (Left) and from 36 subjects' BOLD fMRI data at rest (Right).

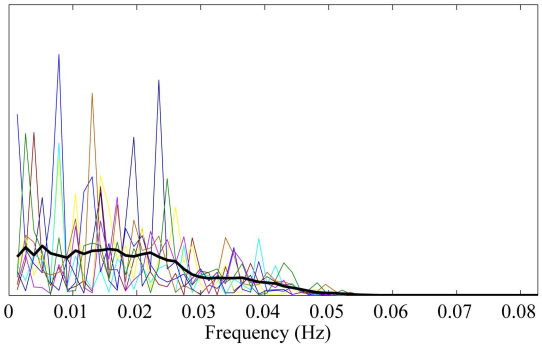

Figure 2: Power spectra of the low frequency ASL signals within the primary visual network. Each colour represents subject. The mean of all 8 subjects is shown in black.

Methods: Whole Brain ASL: A CASL sequence using gradient-echo EPI readout (TE=11ms, 6/8 k-space). 20 axial slices (4×4×6mm voxels, 1.2mm inter-slice gap) was prescribed for each subject, providing a true whole-brain coverage. Signals within the inferior and the superior halves of the slice stack (each with 10 axial slices) were acquired separately, in an alternating manner. For tag acquisitions, 1.6s of continuous tagging was used followed by a post labelling delay of 0.5s and the acquisition of Slice Stack One. A further 1.6s of tagging was then applied followed by a post labelling delay of 1s before the acquisition of Slice Stack Two. The different post labelling delays account for differences in arterial arrival time between Slice Stack One and Slice Stack Two. Control labels used a cosine-modulated MTC-matched pulse train [8]. The labelling offset was located 10cm inferior to the centre of the 20 slices. Acquisition was in ascending order and required ~5.7s for a whole brain volume. 8 healthy volunteers (2 female, 6 male, age 20-37) were scanned using a Siemens 3T TIM Trio system fitted with a single-channel T/R head coil. **Resting State:** Each subject was scanned for 20 mins of rest with eyes closed. **Data Processing:** Data were analyzed using MELODIC, the independent component analysis (ICA) tool in the FMRIB Software Library (FSL) [9]. Data were motion corrected followed by spatial smoothing (FWHM 8mm), tag-control subtracted, and then registered to MNI152 standard space (using FLIRT linear registration to the subjects' structurals, and FNIRT nonlinear registration of the structurals to standard space). No highpass temporal filtering was applied. The data was processed group-wise following temporal concatenation of all subjects' 4D datasets. ICA defined 40 components representing group-averaged networks of brain regions with ASL perfusion signals that were temporally correlated. We extracted single-subject timecourses corresponding to each of the group RSNs, in order to investigate their temporal power spectra.

Results and Discussion: Fig. 1 shows nine RSNs extracted from the 40 ICA components from the 8-subject ASL dataset (Left), paired for reference against 9 RSNs from a 36-subject BOLD fMRI dataset (Right) [7]. Of the "ten major" resting state networks found in BOLD resting-FMRI data and in the BrainMap meta-activations database [7], we identified 9 in our ASL data showing clear correspondence, including visual, default mode, cerebellar, sensorimotor, auditory, executive control and frontoparietal networks. Fig. 2 shows the power spectra of the low frequency ASL signals within the primary visual network (individual subjects in colour, group-mean spectrum in black). The other RSNs showed very similar spectral characteristics. Because BOLD data suffers from drift (e.g., due to hardware instabilities), the lowest frequencies (<0.01Hz) cannot be estimated from BOLD (and are generally removed by a high-pass filter). We have previously shown [10], using haemodynamic deconvolution of low-TR BOLD data, that the 'neural' power spectrum of RSNs above 0.01Hz is flat (i.e., the dropoff above 0.02Hz apparent in Fig 2 is due to the lowpass effect of the haemodynamic response to neural signal). It is apparent from our ASL data that below 0.02Hz, the power spectrum is also relatively flat. This supports the notion that RSNs are neurally broadband processes, spanning a wide range of frequencies as low as 0.001Hz.

Conclusion: We have implemented a novel true whole brain CASL technique with EPI readout, and thereby been able to extract different networks in the resting brain based on dynamic characteristics of cerebral blood flow.

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