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Editorial

Arterial Spin Labeling Fmri: Is It Ready For Functional Connectivity?

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Abstract

Arterial spin labeling (ASL) measures cerebral blood flow (CBF) noninvasively and it therefore directly correlates neural activity. As an alternative to BOLD fMRI, ASL fMRI has attracted increasingly interest in neuroimaging, of which functional connectivity is the main focus. While it was struggling to conduct functional connectivity using ASL before, this situation has been changed upon the recent development of advanced techniques. Studies have shown that pCASL combined with 3D GRASE sequence is capable of detecting functional brain networks. This suggests that up-to-date ASL technique is ready for investigating functional connectivity.

Keywords: Arterial Spin Labeling; Cerebral Blood Flow; Magnetic Resonance Imaging; Functional Connectivity

Arterial spin labeling (ASL) provides a completely noninvasive tracer for cerebral blood flow (CBF) measurement, which utilizes magnetically labeled blood water as an endogenous tracer for quantification of brain perfusion [1]. Therefore, ASL MRI does not require injection of radioactive tracers or contrast agent, so it is feasible to repeat scanning in subjects over time. This is particularly attractive for repeated CBF measurements in patient follow-up, longitudinal and pharmacological studies.

As a popular noninvasive neuroimaging technique, functional magnetic resonance imaging (fMRI) employs MRI technique to measure brain activity by detecting associated changes in CBF. So far, BOLD fMRI is the most commonly used fMRI technique. However, BOLD fMRI signal is measured in arbitrary MR units, whereas ASL fMRI signal is an absolute measurement of CBF. Moreover, BOLD signal is a complex interaction of CBF, cerebral blood volume (CBV) and cerebral metabolic rate of oxygen (CMRO2) [2]. In this regard, ASL provides an alternative and complementary approach to BOLD for fMRI studies.

Surprisingly, while ASL technique has been developed for more than 2 decades, its applications in brain functional connectivity have only been thoroughly explored recently. Presumably, the lag of ASL fMRI in functional connectivity is due mainly to intrinsically low SNR and/or readout sequence, which has not been greatly improved until recently. Chronologically, ASL techniques can be categorized into the following types: pulsed ASL (PASL), continuous ASL (CASL), pseudo-continuous ASL (pCASL). The technique of pCASL has been recommended as the optimal technique for ASL studies in a consensus statement [3], which combines the advantages of PASL and CASL, offering higher SNR. By virtue of 3D imaging, favorably higher SNR can be achieved [4]. These recently developed techniques potentially enable the functional connectivity studies using ASL fMRI.

The earliest functional connectivity study using FAIR PASL is conducted by Biswal et al. [5]. More recently, Zou et al. employed the similar sequence to investigate static and dynamic characteristics of CBF [6]. On the other hand, CASL has also been employed for investigating functional connectivity [7]. Overall, these studies have successfully detected functional connectivity, but have a common limitation, i.e. only partial brain coverage, which is only suitable for investigating certain brain networks. Recently, based on the recent development of pCASL and its combination with 3D GRASE [4], a study utilizing k-space sharing technique has been conducted to investigate whole-brain resting-state functional connectivity [8]. This study has shown that similar networks have been extracted by employing independent component analysis (ICA) from both ASL and BOLD fMRI data. This demonstrates that ASL has the capability not only to extract brain networks, but also to calculate mean CBF within each network. Furthermore, by applying graph theoretical approaches to resting-state brain networks, nonlinear relationships among network metrics and CBF measurements has been further unraveled [9]. More recently, a test-retest study employing pCASL combined with 3D GRASE has been conducted to quantitatively compare networks extracted from both ASL and BOLD data. It has been shown that while ASL provides lower but sufficient reliability compared to BOLD, ASL provides highly reproducible CBF in networks [10]. Furthermore, it has been shown that functional connectivity can be conducted at voxel-level using ASL fMRI [11], of which the low SNR of voxel-wise ASL signal can be enhanced by denoising. Not surprisingly, functional connectivity studies using ASL fMRI have been gradually increased. However, we can only name a few above given the limited space.

As we have already seen from the history of ASL technique development, it is expected that more advanced techniques, such as higher magnetic field strength, novel MRI pulse sequence and advanced post-processing methods, will be hopefully developed to enhance the intrinsically low SNR of ASL data in near future, which will even further facilitate the functional connectivity studies using ASL fMRI.

Given those published results and our experiences in investigating functional connectivity studies, the authors suggest that ASL fMRI be ready for functional connectivity studies when the up-to-date techniques are employed. As an emerging filed, there are certain open questions remain to be tackled. Regardless, this should provide an alternative ASL fMRI to BOLD fMRI, which has already been shown to complement BOLD fMRI.

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