



Short communication

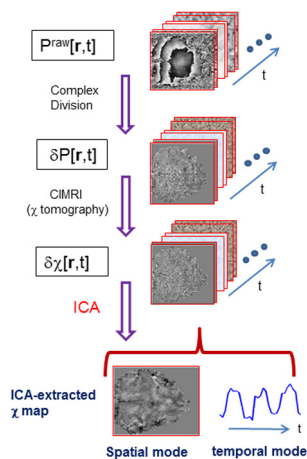
# Task-evoked brain functional magnetic susceptibility mapping by independent component analysis ( $\chi$ ICA)

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## HIGHLIGHTS

- Complex division extracts temporal phase changes.
- Brain functional  $\chi$  dataspace is reconstructed by CIMRI.
- Both ICA and SPM could extract a task-evoked functional map from a 4D fMRI dataset.
- $\chi$ ICA-extracted functional map reveals bidirectional  $\chi$  responses.
- High-resolution fMRI data enables function-structure colocalization.

## GRAPHICAL ABSTRACT



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## ABSTRACT

**Background:** Conventionally, independent component analysis (ICA) is performed on an fMRI magnitude dataset to analyze brain functional mapping (AICA). By solving the inverse problem of fMRI, we can reconstruct the brain magnetic susceptibility ( $\chi$ ) functional states. Upon the reconstructed  $\chi$  dataspace, we propose an ICA-based brain functional  $\chi$  mapping method ( $\chi$ ICA) to extract task-evoked brain functional map.

**New methods:** A complex division algorithm is applied to a timeseries of fMRI phase images to extract temporal phase changes (relative to an OFF-state snapshot). A computed inverse MRI (CIMRI) model is used to reconstruct a 4D brain  $\chi$  response dataset.  $\chi$ ICA is implemented by applying a spatial InfoMax ICA algorithm to the reconstructed 4D  $\chi$  dataspace.

**Results:** With finger-tapping experiments on a 7T system, the  $\chi$ ICA-extracted  $\chi$ -depicted functional map is similar to the SPM-inferred functional  $\chi$  map by a spatial correlation of  $0.67 \pm 0.05$ . In comparison, the AICA-extracted magnitude-depicted map is correlated with the SPM magnitude map by  $0.81 \pm 0.05$ . The understanding of the inferiority of  $\chi$ ICA to AICA for task-evoked functional map is an ongoing research topic.

**Comparison with existing methods:** For task-evoked brain functional mapping, we compare the data-driven ICA method with the task-correlated SPM method. In particular, we compare  $\chi$ ICA with AICA for extracting task-correlated timecourses and functional maps.

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**Conclusion:**  $\chi$ ICA can extract a  $\chi$ -depicted task-evoked brain functional map from a reconstructed  $\chi$  dataspace without the knowledge about brain hemodynamic responses. The  $\chi$ ICA-extracted brain functional  $\chi$  map reveals a bidirectional BOLD response pattern that is unavailable (or different) from AICA.

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## 1. Introduction

Independent component analysis (ICA) is a data-driven means to decompose a mixed signal into independent components (IC). This signal decomposition technique has been widely accepted for brain functional magnetic resonance imaging (fMRI) data analysis (Calhoun et al., 2001b, 2002; McKeown et al., 1998; McKeown and Sejnowski, 1998). Recent research shows that conventional fMRI data, a magnitude component of complex-valued MRI data, is a distorted representation of brain activity due to the magnitude's non-negativity (Chen and Calhoun, 2011) and complex modulo nonlinearity (Chen and Calhoun, 2013, 2015b). Moreover, the MRI signal is formed by MRI transformations (e.g., tissue magnetization in  $B_0$  field), bearing a dependence on the MRI parameters (Chen and Calhoun, 2015b). In principle, by solving an inverse problem associated with an fMRI data acquisition, we can reconstruct the brain tissue magnetic susceptibility property (denoted by  $\chi$ ) that is the underlying magnetic source of the blood oxygenation level dependent (BOLD) fMRI effect. The reconstructed brain  $\chi$  map provides a more direct representation of the intrinsic brain state. With brain  $\chi$  reconstruction, we can examine intrinsic functional  $\chi$  mapping of the brain (Balla et al., 2014; Chen and Calhoun, 2015a; Chen et al., 2013). We are motivated by this innovation to decode a reconstructed brain  $\chi$  dataset by ICA (denoted by  $\chi$ ICA), as reported in detail herein.

Through the use of a GRE-EPI (gradient-recalled echo planar imaging) sequence, an fMRI experiment produces a timeseries of complex  $T_2^*$  images representing snapshot of brain activity. The complex-valued  $T_2^*$  image formation is subject to a cascade of MRI transformations, including the tissue magnetization in  $B_0$  field and an intravoxel spin dephasing average in signal detection. The MRI transformations impose a dependence on parameters such as  $B_0$ , flip angle, echo time, and voxel size. Measurement of brain activity such as a finger tapping should ideally be free from such MRI transformations. This tenet has prompted further examination of intrinsic functional  $\chi$  mapping (Balla et al., 2014; Chen and Calhoun, 2012a, 2014a, 2015a). In past decades, the BOLD contrast mechanism (Boxerman et al., 1995a, 1995b; Menon et al., 1992; Ogawa et al., 1992, 1993) has been widely accepted. The BOLD fMRI dataset acquired by a GRE-EPI sequence consists of complex-valued  $T_2^*$  images. However, typically only the magnitude image of BOLD fMRI data has been used to estimate a brain functional state (Haacke et al., 1999; Huettel et al., 2009). Recent research has enabled the brain  $\chi$  reconstruction by computationally solving an inverse MRI problem (CIMRI, Chen and Calhoun, 2012a, 2014b). It is expected that the reconstructed brain  $\chi$  data are free from the MRI technological dependence, thereby providing a more direct representation of a brain state.

For a task-evoked BOLD fMRI study, the task paradigm serves as the external stimuli, and the signal timeseries at a voxel (extracted from a voxel in 4D  $T_2^*$  dataset) represents its response to the task stimuli. Given a 4D dataset, the task-correlated functional map can be generated by the spatial parametric mapping (SPM) software (<http://www.fil.ion.ucl.ac.uk/spm/>). The SPM-based functional mapping is based on a model timeseries of the task paradigm, which is modeled by a convolution of the task waveform with a canonical hemodynamic response function (hrf). In practice, variability in both intra- and inter-subject hemodynamics (Arichi et al., 2012; Buxton et al., 2004; Hu et al., 2010; Li et al., 2000;

Zheng et al., 2002) complicates the modeling of the hrf. In addition, the task model has also been shown to vary both within and among individuals.

On the other hand, a data-driven ICA method can be used for fMRI data analysis (Calhoun et al., 2001a, 2001b; McKeown et al., 1998; Moritz et al., 2000). Given a 4D dataset acquired from a BOLD fMRI experiment, we can perform spatial ICA to decompose the timeseries into a collection of pairs of independent spatial modes (IC modes) and temporal modes (IC timeseries). Of the ICA-decomposed modes, we are concerned with the spatial mode whose timeseries is maximally correlated with the task timeseries. In comparison with the SPM functional map that involves a model timeseries, ICA requires no knowledge about the hrf and signal formation mechanism. Conventionally, ICA is applied to the magnitude (amplitude) part of a complex-valued BOLD fMRI dataset (denoted by AICA), decomposing a spatiotemporal data matrix into a number of spatial independent modes (Calhoun et al., 2001b; Formisano et al., 2004; Hu et al., 2005; Kansaku et al., 2005; McKeown et al., 1998; McKeown and Sejnowski, 1998; Xu et al., 2013a). In this paper, we seek to decode the brain fMRI data by performing ICA in the reconstructed 4D  $\chi$  dataspace ( $\chi$ ICA), much in the same way as has been done for conventional AICA (Calhoun et al., 2001b). Since the reconstructed 4D  $\chi$  dataset is morphologically different from the 4D  $T_2^*$  magnitude dataset, we expect to see the pattern discrepancy between the  $\chi$ ICA- and AICA-extracted functional maps. It is also of interest to observe the conformance of brain functional  $\chi$  maps obtained from two different approaches: the model-dependent SPM and the data-driven  $\chi$ ICA.

## 2. Theory and methods

We show the  $\chi$ -based brain functional ICA decomposition method in Fig. 1, which consists of task-evoked BOLD fMRI data acquisition, brain  $\chi$  reconstruction, and  $\chi$ ICA (decomposition of the  $\chi$  dataset by ICA). The conventional AICA method is also included for the sake of comparison. In what follows we address the dataflow in Fig. 1 in details.

### 2.1. BOLD fMRI data acquisition

Assume a task-evoked brain activity that causes a blood magnetic susceptibility perturbation,  $\delta\chi(\mathbf{r}, t)$ , which imposes on a static brain parenchymal tissue state,  $\chi_0(\mathbf{r})$ . The full  $\chi$ -expressed brain state is given by

$$\chi(\mathbf{r}, t) = \chi_0(\mathbf{r}) + \delta\chi(\mathbf{r}, t), \quad (1)$$

which represents an original continuous spatiotemporal  $\chi$  process that is free from MRI parameter dependence (such as  $B_0$  dependence and spatiotemporal discreteness; see below).

Lying inside a scanner ( $B_0$ ), the brain tissue is subject to a magnetization process (magnetic polarization along  $B_0$ ) that causes an intracranial magnetic field disturbance (Chen and Calhoun, 2012b; Marques and Bowtell, 2005, 2008). This is represented by

$$b(\mathbf{r}, t) = B_0\chi(\mathbf{r}, t) * h_{\text{dipole}}(\mathbf{r}) \quad (2)$$

where  $b(\mathbf{r}, t)$  represents the  $z$ -component of the  $\chi$ -induced fieldmap,  $h_{\text{dipole}}(\mathbf{r})$  denotes the magnetic field ( $z$ -component) of a point magnetic dipole, and  $*$  denotes the 3D spatial convolution.

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