Mapping of midbrain nuclei connectivity networks using Time-domain Phase-REgularized Parallel (T-PREP) reconstruction of high-resolution fMRI

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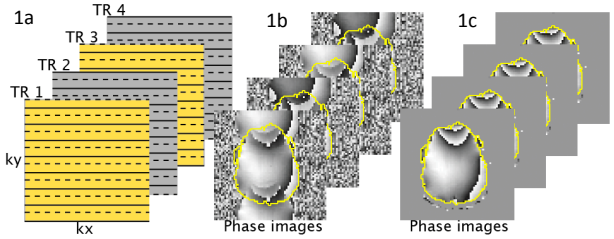
INTRODUCTION

Mapping of intrinsic connectivity networks (ICNs) does not require subjects' active engagement in cognitive or neuropsychological tests, and thus can be widely applied to imaging different patient populations, even anesthetized individuals. However, conventional fMRI protocols used in ICN mapping only provide data at a relatively low spatial-resolution (e.g., 4 mm^3 isotropic). Although low-resolution ICN mapping may be sufficient to detect disruptions of major large-scale networks, it cannot measure the networks comprising nodes that are smaller in size or located in some critical brain regions, such as the midbrain nuclei. To address this limitation, here we report a novel time-domain phase-regularized parallel (T-PREP) reconstruction algorithm, retaining the fidelity of BOLD time-course profiles derived from under-sampled fMRI data, so that midbrain connectivity ICNs can be reliably measured from high-resolution resting-state fMRI.

THEORY AND METHODS

The T-PREP algorithm is developed to stabilize and improve the SENSE reconstruction of fMRI data, reducing the noise amplification due to non-ideal coil sensitivity profiles (i.e., the g-factor).

In SENSE parallel reconstruction, the proton density values of N overlapping voxels in reduced-FOV data, acquired from M coils, can be obtained by solving $C\rho = s$, where *C* is an $N \times M$ coil sensitivity matrix; ρ is an N-element column vector representing the complex signal values in non-aliased images (unknown); and *s* is an M-element column vector representing the image-domain complex signals detected by different coils in aliased images. The original SENSE implementation (with M complex equations; and N complex unknowns) can be further decomposed into real and imaginary parts (with 2M real equations; and 2N unknowns). If the image-domain phase accumulation can be measured or estimated prior to SENSE reconstruction, then the condition number can be significantly improved (2M equations; and only N unknowns). This is termed phase-constrained SENSE reconstruction (Lew et al. MRM 2007: 58(5) p.910). Since an iterative approach is needed to estimate the background phase, the original phase-constrained reconstruction implementation is time-consuming and may not always be robust.



In our developed T-PREP method, high-quality phase maps are firstly generated through time-domain analysis of undersampled fMRI data. As schematically illustrated in Fig 1a (for 2 x acceleration), the k-space under-sampling scheme alternates between odd and even time points (as used in UNFOLD, k-t-BLAST and TSENSE). The images reconstructed directly with 2D FFT (Fig 1b) have more consistent phase values in parent or non-aliased voxels across multiple time points. On the other hand, the phase values of aliased voxels alternate between two consecutive time points. Phase maps without aliasing artifacts can be generated (Fig 1c) using k-t-BLAST or its variations (Pedersen et al. MRM 2009: 62(3) p.706). The generated high-quality phase map can then be used to regularize the SENSE reconstruction for each fMRI time point (through constraining the phase values), generating high-fidelity and high-SNR maps.

We have acquired high-resolution fMRI data (1.5mm isotropic) from healthy volunteers at 3 Tesla, using T-PREP technique, with the following scan parameters: TR 2.5 sec; TE 36 msec; in-plane matrix size 160 x 160; FOV 24 cm x 24 cm; and axial-plane slice thickness 1.5 mm. FSL software package was used to process fMRI data obtained with the figner-tapping motor task. The matlab programs developed in-house and the FSL ICA toolbox were used to generate ICN maps from the acquired resting-state fMRI data.

RESULTS AND DISCUSSION

Figure 2 shows the activation z-maps from 3 slices with a finger-tapping motor task. Bilateral activation sites in putamen and thalamus, specifically the ventral posterior lateral nuclei (green arrows), are observed.

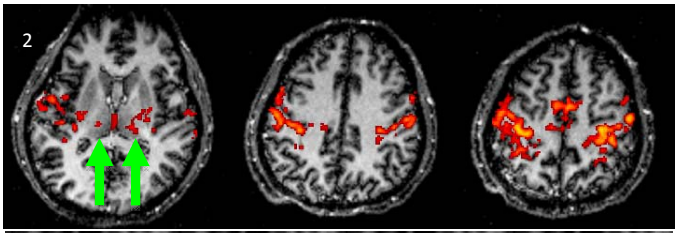
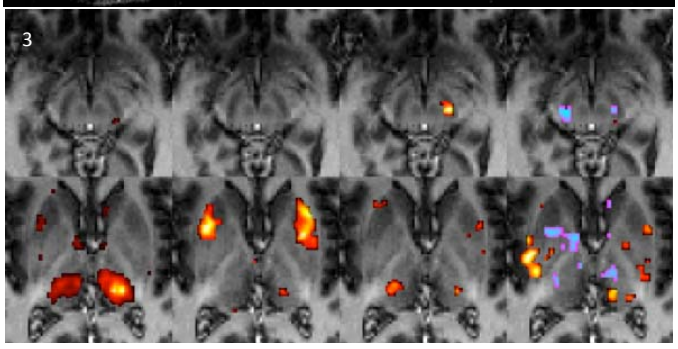


Figure 3 shows four of the ICA components (in 4 columns) produced by FSL-Melodic ($p<0.05$) from two axial slices (in 2 rows: only 1/3 of the FOV is shown here) of resting-state fMRI data. The slice shown in the upper row includes the substantia nigra, subthamalic nuclei and red nuclei. The slice in the lower row includes caudate nuclei, putamen, globus pallidus, and thalamus. The nuclei in these midbrain regions are among the most important nodes in motor and emotion networks.



The first two ICA components in Figure 3 demonstrate the bilateral connectivity networks mainly within the thalamus and striatum. It can be seen that the third ICA component illustrates the connectivity among substantia nigra, putamen, and ventral posterior lateral nuclei (which is also observed in motor-task fMRI: Figrue 3a). Based on the known physiological model, the third ICA component very likely corresponds to the dopaminergic (excitatory) network. The fourth ICA component shows the negative correlation between substantia nigra (shown in blue/purple) and other regions of the putamen (shown in red/yellow). Based on the known physiological model, the fourth ICA components with negative correlation very likely corresponds to the GABAergic (inhibitory) networks.

To our knowledge, this is the first high-resolution midbrain connectivity network map measured from resting-state fMRI in human. We expect the developed T-PREP high-resolution fMRI techniques will be extremely valuable for studies of various neurological diseases.