Feasibility and limitations of independent component analysis in the investigation of blood-brain-barrier permeability

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Introduction

First-pass dynamic susceptibility-weighted contrast-enhanced MRI is a well-established method to determine hemodynamic parameters in normal and pathologic brain tissue (1). However, the observed dynamic signal usually conveys combination of image noise, lesion-related signal enhancement, and signal contributions from parenchyma and vasculature. The signal detection can therefore be viewed as the extraction of signal characteristics with unknown nature from dynamic image set. In contrast to model-based methods that are subject to specific assumptions, independent component analysis (ICA) uses high-order signal statistics to separate sources blindly. ICA has been applied in the analysis of brain functional MRI and event-related potential (ERP) signals to extract task-related MR signals (2,3). In a recent study, ICA was reported useful to remove confounding effects of large vessels (4). Nevertheless, interpretation and validation of the extracted components are not always easy. In this abstract, we applied ICA to explore dynamic MR signals and attempted to depict areas where blood-brain-barrier (BBB) breaks down. Brian glioma and ischemic stroke subjects were analyzed. Discrepancies were found and potential limitations were addressed by computer simulation.

Materials and Methods

Two cohorts of patients were included. One consisted of subjects with histopathologically proven glioma and the other comprised ischemic stroke patients in subacute or later stages. Echo-Planar T2*-weighted perfusion imaging was performed (TE=44ms, FOV=230mm, Matrix size=102×128, slice thickness=5mm, 6 slices in each measurement). Time interval was one second with 75 consecutive measurements following bolus injection of 0.2 mmol/Kg Gd-DTPA (Magnevist, Schering, Germany). The set of concentration-time curve was analyzed using the Fast ICA algorithm (5). Prior to ICA, principle component analysis was applied to reduce raw data dimension from 75 to 20, with over 98% eigenvalues retained. Independent component maps and the corresponding signal-time curves were inspected by the operator referring to both spatial and temporal features.

Simulation

Five sets of concentration-time curves were generated following the gamma-variate function, $f(t)=k*t^{\alpha}\exp(-t/\beta)$. For control set, experimental values were chosen for k,αandβ, allowing 2% variation respectively (Fig. 1a). By manipulating these parameters and time-shift in reasonable range, four sets were generated to simulate conditions of abnormal maximal signal rise (MSR), mean transit time (MTT)+MSR, delay, delay+MTT+MSR (Fig. 1b~1e). White noise was superimposed to make signal to noise ratio 10. All signal sources were rearranged to form dynamic image set followed by ICA procedures described above.

Results

ICA extracted components simulating delay and delay+MTT+MSR (Fig. 2b,2c) but failed in MSR or MTT detection (Fig. 2d). Fig 3 shows the independent component map that possibly corresponds to the contribution of BBB breakdown in a stroke subject. Note that the signal ascends after t = 25 sec which is about the average peak time (observable blood flow: t = 18~28 sec on the lesion territory) when the first-pass of contrast agents begin to wash out. On the other hand, no such component was found in glioma subjects.

Discussion

Indeed, ICA extracts information from data pools without a priori knowledge of the sources. Cautions should be taken in the application and interpretation though. Multiple components that either have the same anatomic correlation or not are possible identified. Simulation demonstrates that ICA is more sensitive to delay effect than MSR or MTT variation, which partially explains the failure in detecting BBB breakdown in glioma subjects. The concentration-time curve at tumor region is usually characterized by elevated MSR without marked transit delay or elongation. By contrast, ischemia is accompanied by delayed blood flow in combination with variant flow volume and increased MTT. With prudent explication, ICA can be an efficient method to screen pixels of BBB breakdown in stroke followed by further evaluation.

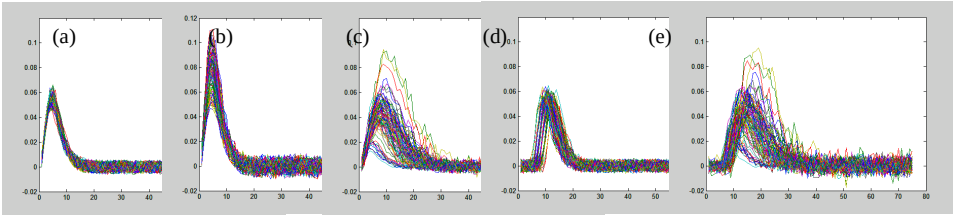

Fig 1. Computer generated concentration-time curves were used to simulate situations in normal and alterations of MSR, MTT+MSR, delay, delay+MTT+ MSR, from (a) to (e).

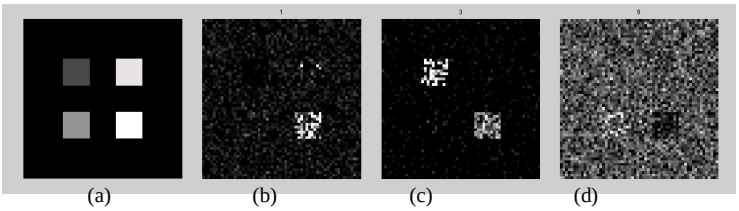

Fig 2. (a) Curve sets were rearranged to form an image set. Black background, top left, top right, bottom left and bottom right are control, delay, MTT+MSR, MSR and delay+MTT+MSR, respectively. Twenty ICA component maps were obtained and inspected. (b) Delay+MTT+MSR was explicitly extracted. (c) A component was found to detect delay and delay+MTT+MSR. (d) No component got MSR or MTT+MSR separately.

References

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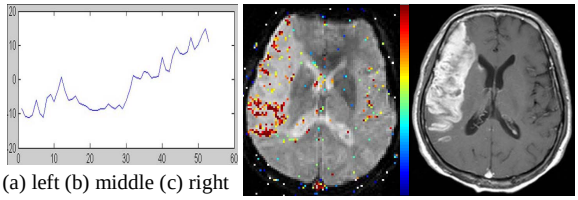

(a) left (b) middle (c) right

Fig 3. (a) Time course of the component possibly relating to BBB permeability. (b) Component map. (c) Post-contrast T1-weighted image.