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Mapping Brain Neurochemical and Functional Coupling Using Dynamic SPICE

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Synopsis

Neuronal metabolite (e.g., glutamate, GABA) concentrations in the brain are known to be correlated with neural activity. Currently, fMRS is the primary tool for measuring neurochemical changes in response to brain activity. However, fMRS has several major practical limitations, including low spatial resolution, low SNR, and very limited brain coverage. In this work, a new dynamic ^{1}H-MRSI technique is used to address these difficulties. This technique can map dynamic metabolic changes from the whole brain at high spatial and temporal resolutions. In addition, it can simultaneously acquire fMRI images to track brain functional activity during the scan. With this unique capability, we have carried out functional MRSI experiments with motor tasks to investigate the coupling between neural metabolism and neural activity. The experimental results clearly show an increase in Glx in the motor cortex during the motor activation.

Introduction

The characterization of neurovascular and metabolic couplings is essential for understanding the complex interactions between neuronal activity and neurochemical changes. Investigating the dynamic changes of neurochemicals in response to brain functional activation could contribute to further understanding brain energy metabolism and metabolic pathways. Currently, fMRS is the primary tool for measuring metabolic changes associated with brain activities[1]. Using fMRS, a number of studies have been done, which have detected the dynamic changes of neurochemicals, like glutamate, lactate and GABA related to human psychological functions[1-4]. However, fMRS has low spatial resolution (around centimeters), low SNR, and poor brain coverage (single voxel measurements), which have significantly limited its practical utility. In this work, we investigate neurochemical changes of the brain using a novel dynamic ^{1}H-MRSI acquisition and processing scheme based on SPICE[5]. This technique can acquire time-resolved MRSI spatiospectral functions with 2.0×2.8×3.0 mm^3 nominal spatial resolution and 3.7-min frame rate and a series of fMRI images simultaneously. With this capability, we are able to investigate neurochemical and functional coupling of the whole brain at high spatial resolution. Our technology and experimental study may open up a new opportunity for investigating brain function and metabolism.

Methods

The in vivo motor task experiments were performed on a 3T scanner (Siemens Prisma). The dynamic ^{1}H-MRSI scan included 2 fixation blocks and 2 task blocks, lasting for 15 minutes (shown in Fig. 1). In the task block, the subject was instructed to perform repeated cycles of finger tapping for 40 seconds and resting for 16 seconds. The finger tapping task was performed using both hands and the tapping frequency was around 1 Hz. The entire study includes 3 scans and 12 event blocks on healthy subjects.

The dynamic ^{1}H-MRSI sequence is based on a recently proposed imaging technique that extends SPICE (SPectroscopic Imaging by exploiting spatiospectral CorrElation[5]) for simultaneous MRSI and fMRI acquisition. The technique can acquire high-resolution non-water-suppressed ^{1}H-MRSI data (TR/TE: 160/1.6 ms, FOV: 230×230×48 mm^3, Matrix size: 116×80×16, Repetition: 4, Frame rate: 224 s) simultaneously with a time series of fMRI images (Matrix size: 76×76×40, Repetition: 300, Frame rate: 3 seconds).

Our processing pipeline provides several functions to effectively analyze the dynamic MRSI and fMRI data, which include: 1) normalization using the unsuppressed water signals to remove any field drift and T2* modulation in different frames induced by BOLD and physiological effect; 2) identification of the activation region based on the functional networks extracted from the fMRI signals using an ICA-based method[6]. In this study, the motor cortex is manually identified based on the functional network structure and the temporal changes of the associated fMRI signals; 3) spectral quantification for the whole brain using a subspace approach[7]; and 4) statistical analysis of the metabolite signals in the motor cortex and compare the difference between task and resting frames.

Results

Figure 2 shows the metabolite maps and representative spectra of the first resting frame. Figure 3 shows the somato-motor network (SMN) extracted from the fMRI data and its corresponding task time course. The functional time course matches the block design very well, which implies that the subject followed the designed task well during the ^{1}H-MRSI scan. Figure 3 also shows the dynamic Glx (Glutamate+Glutamine) maps of 4 frames obtained in one of the experiments. These dynamic Glx maps cover the whole brain which make it possible to investigate the dynamic changes of different brain regions. In this study, we were focusing on the neurochemical changes in response to functional activation in the motor cortex. Therefore, the spectra in the motor cortex from three scans (a total of 2132 spectra in the task frames and 2132 spectra in the resting frames) were used to analyze the Glx changes. Figure 4 presents the spectral quantification results on the averaged spectra from both the task frame and resting frame, which show a noticeable difference in the Glx level between the task state and the resting state. This experimental result is consistent with the previous findings[8,9].

Conclusion

We have successfully carried out a functional MRSI study on neurochemical coupling of brain function. To the best of our knowledge, this is the first functional MRSI study that maps the metabolic changes of a large portion of the brain (FOV: 230×230×48 mm^3) at high resolution (2.0×2.8×3.0 mm^3) instead of the single-voxel measurements obtained in conventional fMRS studies. Our technology and experimental results may open up a new opportunity for investigating brain function and metabolism.

Acknowledgements

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Figures

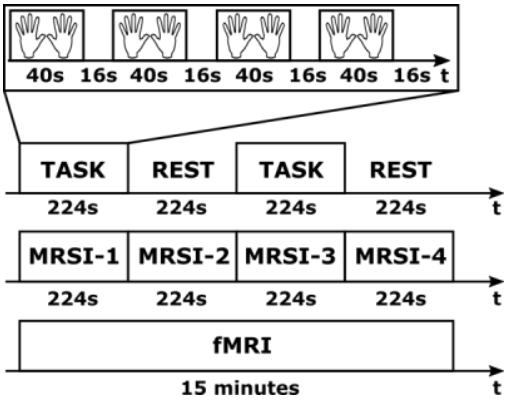


Figure 1. Timing diagram for our in vivo motor-task experiments. The experiment includes 2 task blocks and 2 resting blocks. Each block lasts 224 seconds and the whole scan lasts 15 minutes. The ^{1}H-MRSI scan contains 4 frames matching the 4 task/resting blocks; fMRI images are simultaneously acquired at a temporal resolution of 3 seconds.

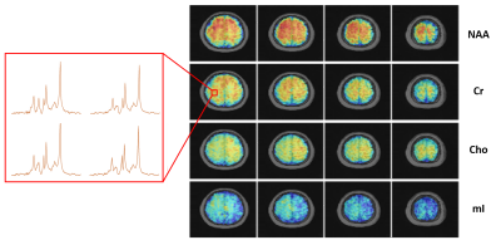


Figure 2. High-resolution metabolite maps and representative spectra from the first resting frame. The nominal resolution of the metabolite map is 2.0x2.8x3.0 mm^3 and the FOV covers 230x230x48 mm^3.

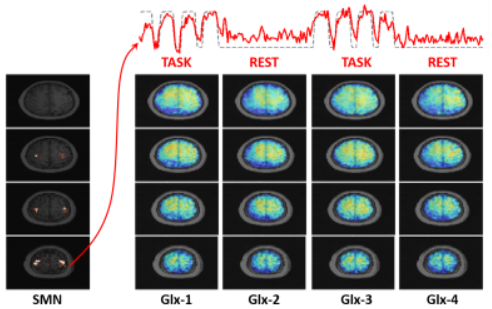
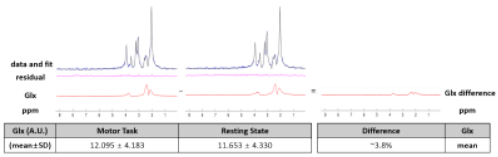


Figure 3. High-resolution glutamate + glutamine (Glx) maps at different times. The temporal resolution is 224 seconds per frame. The somato-motor network (SMN) and its fMRI signal changes are also shown.



Glx (A.U.)	Motor Task	Resting State	Difference	Glx
(mean±SD)	12.095 ± 4.183	11.653 ± 4.330	~3.8%	mean

Figure 4. Spectral quantification results from the averaged spectra in the motor cortex from both the motor task frames and the resting frames. The results show an increase in the Glx level from the resting frame to the task frame, which is consistent with previous findings[8,9].