# Functional MRI study of brain function under resting and activated states

# Wei Chen, Xiao Liu, Xiao-Hong Zhu, Nanyin Zhang

Abstract: Numerous magnetic resonance techniques imaging (MRI) have been developed with various imaging contrasts, which can be tightly linked to brain functions, electrophysiology and diseases. Recent MRI technology developments have resulted in several important functional MRI (fMRI) methods based on the blood oxygenation dependent (BOLD) level contrast. These fMRI methods have been applied to mapping brain activation in laminar level as well functional connectivity network in a resting brain. We have found a strong correlation between the spontaneous BOLD brain activity and fluctuation indicating a tight neurovascular relation.

# INTRODUCTION

Functional magnetic resonance imaging (fMRI) technique based on the blood oxygenation level (BOLD) contrast dependent [1-4] can noninvasively detect neural activity change by measuring the secondary hemodynamic/metabolic responses, and has advantages on its compromised spatial coverage and spatial resolution. These fMRI methods are becoming prominent neuroimaging modalities for mapping brain activation and studying brain cognitive functions. The ability of fMRI for

Manuscript received June 18, 2009. This work was supported in part by NIH grants of NS41262, P41 RR08079 and P30NS057091; the Keck foundation.

W. Chen is with Center for Magnetic Resonance Research, Department of Radiology, University of Minnesota, 2021 6<sup>th</sup> Street SE, Minneapolis, MN 55455, USA (Tel: 612-625-8814; Fax: 612-626-2004; wei@cmrr.umn.edu ).

X. Liu is with University of Minnesota; xiaoliu@cmrr.umn.edu

X.-H. Zhu is with University of Minnesota; zhu@cmrr.umn.edu

N.Y. Zhang is with Center for Comparative Neuroimaging (CCNI), Department of Psychiatry, University of Massachusetts Medical School, 55 Lake Avenue North, Worcester MA 01655 (Tel: 508-8565482; Fax: 508-8568090; Nanyin.Zhang@umassmed.edu mapping functional structures can be further improved by using high/ultrahigh field scanners. We have tested such ability for mapping the functional subunits in the laminar layer level in the lateral geniculate nucleus and resting brain connectivity at high field.

#### <u>High-resolution fMRI for mapping brain activation</u> <u>in deep brain nucleus and cortico-thalamic</u> <u>network</u>

Although neuroimaging methods have been used successfully to map large-scale cognitive networks distributed across the human cortices. mapping and differentiation functional of localized brain organization within fine brain structures has been limited due to inadequate imaging sensitivity for achieving high spatial resolution. The BOLD-based fMRI technique has become one of the most useful neuroimaging techniques. The high sensitivity available at high fields makes fMRI capable for mapping brain activation in small brain structures, such as the lateral geniculate nucleus (LGN) in the thalamus [5] to the ocular dominance columns in the human primary visual cortex [6, 7], on the millimeter and sub-millimeter spatial scale.

LGN is a primary target of retinal afferents that cross at the optic chiasm and project bilaterally to LGN via the optic tract. LGN in turn projects to the primary visual cortex (V1) through optic radiation. It should be crucial to map the activation from both LGN and V1 simultaneously in order to providing a better understanding of visual activation and network. We had examined the feasibility of high-resolution fMRI for detecting brain activation in LGN during visual stimulation [5]. Our study reveals that fMRI can be used to robustly detect the LGN activation from single subjects. Figure 1 illustrates one example of fMRI maps showing detected activation in LGN and V1 during a (A) full-field and (B) half-field visual stimulation [5]. The fMRI maps clearly illustrate a well-defined retinotopic relationship in the human brain, i.e., visual stimulation only actives the contralateral visual systems in the early vision stages such as LGN and V1. One important and relevant application

of high-resolution fMRI at high fields was to detect the brain activity in V1 and LGN during visual imagery [8]. This study indicates that the early vision stages could involve more complex processing related to cognitive task (i.e., visual imagery).



**Fig. 1** High-field fMRI mapping of brain activation in the human LGN and V1 areas during visual stimulation. (A) Full-field visual stimulation showing bilateral activation in both LGN and V1. (B) Left- and right-field visual stimulations showing activation only in contralateral LGN and V1.

Recently, we have further investigated the superior capability of high-resolution fMRI for non-invasively mapping the functional laminar structures of LGN in the cat. The LGN laminae associated with contralateral- and ipsilateral-eye inputs were successfully differentiated and identified with remarkable consistence with histology and morphology in terms of laminar orientation, thickness shape, and evedominance [9]. The capability of fMRI for noninvasively mapping the LGN laminar structures overcomes the limitation of neuron recording, and it opens a new opportunity for studying the critical roles that LGN plays in various brain functions.

To date there is still no proper neuroimaging methods suitable for noninvasively providing both detailed spatial and temporal information of neural interaction across large-scale brain networks. This limitation has impeded the advance of neuroscience research. In an attempt to overcome this challenge, Ogawa et al applied a paired-stimulus paradigm, which is composed of a pair of stimuli separated by a variable interstimulus interval (ISI), to decode temporal information of neural interaction from amplitude modulation of BOLD responses elicited by the neural interaction pursued [10]. Considering the vital roles that cortico-thalamic networks play in brain communication and function, extending the applicability of this method to studying corticothalamic neural interaction should be significant. We have applied the paired-visual-stimulus paradigm to simultaneously measure the BOLD amplitude modulations as a function of ISI in LGN and V1 in the cat brain. The results reveal that the dynamic fMRI approach is sensitive to neuronal inhibitory and facilitatory interactions and it should be useful for noninvasively investigating large-scale cortico-thalamic neural networks.

# <u>Studying brain connectivity and network using</u> <u>fMRI</u>

Recent studies have also found that the spontaneous BOLD signals acquired under the resting state without tasks and stimulations are characterized with slow (< 0.1 Hz) and coherent fluctuation within specific brain networks. like the motor systems [11]. It was hypothesized that the spatiotemporal correlations of spontaneous BOLD signals reflect the underlying functional connectivity. These findings suggest that the resting brain is not silent but very active in a very organized manner. Therefore, the BOLD-based fMRI may provide a powerful tool for imaging functional resting-state brain connectivity in the of brain stimulation absence and task performance. Recently, we have tested the neurovascular coupling relation between the spontaneous EEG signal and the BOLD fluctuation in a rat brain. The results indicate that the mapped connectivity network could reflect the coherent neuronal activity in a resting brain [12]. We have also applied the functional connectivity MRI (fcMRI) technique for studying the functional network in the human visual system under the resting and activated states. We have observed a network modulation during a sustained visual stimulation.

# CONCLUSION

In summary, the fMRI methods can play essential roles for investigating and understanding neural network, brain function and dysfunction. New progresses have provided new insights regarding human brain functional and connectivity network under resting and activated states.

#### REFERENCES

- [1] S. Ogawa, T.-M. Lee, A. R. Kay, and D. W. Tank, "Brain magnetic resonance imaging with contrast dependent on blood oxygenation," *Proc. Natl. Acad. Sci. USA*, vol. 87, pp. 9868-9872, 1990.
- [2] S. Ogawa, D. W. Tank, R. Menon, J. M. Ellermann, S.-G. Kim, H. Merkle, and K. Ugurbil, "Intrinsic signal changes accompanying sensory stimulation: functional brain mapping with magnetic resonance imaging," *Proc. Natl. Acad. Sci. USA*, vol. **89**, pp. 5951-5955, 1992.
- [3] K. K. Kwong, J. W. Belliveau, D. A. Chesler, I. E. Goldberg, R. M. Weisskoff, B. P. Poncelet, D. N. Kennedy, B. E. Hoppel, M. S. Cohen, R. Turner, H. M. Cheng, T. J. Brady, and B. R. Rosen, "Dynamic magnetic resonance imaging of human brain activity during primary sensory stimulation," *Proc. Natl. Acad. Sci.* USA, vol. 89, pp. 5675-5679, 1992.
- [4] P. A. Bandettini, E. C. Wong, R. S. Hinks, R. S. Tikofsky, and J. S. Hyde, "Time course EPI of human brain function during task activation," *Magn. Reson. Med.*, vol. 25, pp. 390-397, 1992.
- [5] W. Chen, X.-H. Zhu, K. R. Thulborn, and K. Ugurbil, "Retinotopic mapping of lateral geniculate nucleus in humans using functional magnetic resonance imaging," *Proc Natl Acad Sci USA*, vol. 96, pp. 2430-2434, 1999.
- [6] K. Cheng, R. A. Waggoner, and K. Tanaka, "Human ocular dominance columns as revealed by high-field functional magnetic resonance imaging," *Neuron*, vol. 32, pp. 359-74, 2001.
- [7] E. Yacoub, A. Shmuel, N. Logothetis, and K. Ugurbil, "Robust detection of ocular dominance columns in humans using Hahn Spin Echo BOLD functional MRI at 7 Tesla," *Neuroimage*, vol. 37, pp. 1161-77, 2007.
- [8] W. Chen, T. Kato, X. H. Zhu, S. Ogawa, D. W. Tank, and K. Ugurbil, "Human primary visual cortex and lateral geniculate nucleus activation during visual imagery," *NeuroReport*, vol. 9, pp. 3669-3674, 1998.
- [9] N. Zhang, X. H. Zhu, J. K. Park, Y. Zhang, Y. Li, and W. Chen, "Functional MRI

Mapping of Laminar Structures in Cat Lateral Geniculate Nucleus," presented at Proc. Intl. Soc. Mag. Reson. Med., Toronto, Canada, 2008.

- [10] S. Ogawa, T.-M. Lee, R. Stepnoski, W. Chen, X. H. Zhu, and K. Ugurbil, "An approach to probe neural systems interaction by functional MRI at neural time scale down to milliseconds," *Proc Natl Acad Sci U S A*, vol. 97, pp. 11026-11031, 2000.
- [11] M. D. Fox and M. E. Raichle, "Spontaneous fluctuations in brain activity observed with functional magnetic resonance imaging," *Nat Rev Neurosci*, vol. 8, pp. 700-11, 2007.
- [12] X. Liu, X. H. Zhu, Y. Zhang, and W. Chen, "Studying Coherent BOLD Fluctuation and Functional Connectivity of Cortico-thalamic Visual Network in Anesthetized Cat Brain and their Dependence on Anesthesia Depth," presented at Proc. Intl. Soc. Mag. Reson. Med., Toronto, Canada, 2008.