MRI Technologies in Recent Human Brain Mapping

Yuka SASAKI[1,2,3)]

[1)]*Athinoula A. Martinos Center for Biomedical Imaging, Department of Radiology, Massachusetts General Hospital, 149 13th Charlestown, MA 02129, USA*

[2)]*Department of Radiology, Harvard Medical School, Boston, MA 02115, USA*

[3)]*ERATO Shimojo Implicit Brain Function Project, California Institute of Technology, Pasadena, CA 91125, USA*

(Received 2 December 2006 / Accepted 16 February 2007)

The recent magnetic resonance imaging (MRI) technology and techniques used in human brain mapping are remarkable. They are getting, faster, stronger and better. The advanced MRI technologies and techniques include, but not to limited to, the magnetic resonance imaging at higher magnetic field strengths, diffusion tensor imaging, multimodal neuroimaging, and monkey functional MRI. In this article, these advanced MRI techniques are briefly overviewed.

Keywords: functional magnetic resonance imaging (fMRI), diffusion tensor imaging (DTI), magnetoencephalography (MEG), electroencephalography (EEG), monke fMRI

DOI: 10.1585/pfr.2.S1004

1. Introduction

Functional magnetic resonance imaging (fMRI) is indispensable in recent human brain mapping. FMRI technique usually measures blood oxygen level dependent (BOLD) signals for estimation neural activity in the brain [1, 2]. The precise relationship between neural signals and BOLD signals is under investigation. However, BOLD activity, in general, rely on oxygenation, blood flow, and volume. BOLD signals seem to reflect the input and intracortical processing of a given area rather than its spiking output [3].

Recent MRI techniques are remarkable, thanks to the improvements of MR technologies. The Martinos Center, which I belong to is a world leading biomedical imaging center, located at the department of radiology, Massachusetts General Hospital, in Boston, Massachusetts, USA. There are more than 70 faculty members as of December, 2006, with more than 100 post-docs and students. The faculty members from various backgrounds such as medical physics, bioengineering, psychology, psychiatry, or computational scientists etc get together and challenge basic biosciences and medical investigation while developing the cutting-edge imaging tools.

In this article, I will introduce some of the advanced MR technologies and techniques mostly developed in our center. In the following, the MRI at higher magnetic fields, diffusion tensor imaging, multimodal neuroimaging, and monkey fMRI will be briefly described.

2. Higher Magnetic Fields

In the beginning of fMRI era, 1.5 Tesla was the most popular machine. However, it is a 3T MR machine, which has been most popularly used all over the world. Recently, MR physicists and MR commercial makers has been collaborating to develop much higher magnetic field strengths MR machines for human brain mapping, such as 7T MRI in our center. The higher the magnetic field gets, the MR images would be theoretically much better because of the higher signal to noise ratio [4, 5].

Utilizing this higher signal to noise ratio of 7T MRI, anatomical and functional imaging has been started [6]. My colleagues in the center has successfully imaged the enthorhinal layer II [7], a microstructure in the hippocampas. Clinically, the cells in enthorhinal layer II are affected with neurofibrillary tangles, one of the two pathological hallmarks of Alzheimer's disease. They detected the entorhinal layer II islands, scanning human autopsied temporal lobe blocks in a 7T human scanner with a solenoid coil. In the spatial resolution reached to 70 to 100 micron isotropic data, the entorhinal islands were clearly visible throughout the anterior-posterior part of entorhinal cortex. Sensitivity and spectral resolution of proton echo-planar spectroscopic imaging has been greatly improved with 7T [8].

3. Diffusion Tensor Imaging

Diffusion tensor imaging (DTI) is a method that could quantify alterations in tissue structure due to pathological processes, and potentially differentiate among pathologies and specify affected fiber pathways [9]. DTI measures water diffusive properties in the brain, which are likely influenced by a number of factors such as degree of myelination, as well as the density, diameter distribution, and orientational coherence of axons [10]. DTI has recently gained significant popularity due to new acquisition and analysis techniques, along with advances in MR technolo-

author's e-mail: yuka@nmr.mgh.harvard.edu

gies [11]. DTI measures have been used for understanding degeneration in presymtomatic and early Huntington's disease [12], and age-related changes in prefrontal white matter [9]. Furthermore, DTI has shown that choice reaction time performance correlated with diffusion anisotropy in white matter pathways supporting visuospatial attention [13], suggesting that interindividual variability in behavioral reaction time performance may depend on the white matter properties within the relevant neural circuit. Thus, DTI offers a good tool to examine relationship between white matter properties, or connectivity [14] and brain function, as well as degeneration changes with disease.

4. Multimodal Neuroimaging

Functional magnetic resonance imaging (fMRI) is a representative technique for non-invasive neuroimaging used mostly in humans. FMRI measures blood oxygen level-dependent (BOLD) signal using hemodynamics [1, 2]. fMRI allows us to measure brain activity on the order of millimeters and is regarded as an excellent tool for spatial localization. We have used this technique to spatially localize cortical areas related to visual illusions [15–17], some important visual functions [15, 18–22] and motor functions [23–25]. Although fMRI yields high spatial resolution, its temporal resolution is only on the order of seconds, impeding the acquisition of sufficient temporal resolution measurements of brain activity. Magnetoencephalography (MEG) and electroencephalography (EEG) record the magnetic and electrical fields, respectively, that are generated in association with synchronous nerve cell activity. In contrast to fMRI, MEG and EEG give millisecond order temporal resolution, but much lower spatial resolution than fMRI [26]. Thus, MEG and EEG are suitable for investigating the temporal microstructure of brain activity [27]. The MEG facility in our Center allows us to measure both MEG and EEG simultaneously. The magnetic and electrical field potential changes that are time-locked with sensory, motor, or cognitive events are called event-related potentials (ERPs) and consist of a series of voltage oscillations that reflect the time course of neuronal activity with resolution on the order of milliseconds [27, 28].

Researchers have attempted to combine data from MEG and MRI for integration of fine temporal and spatial information [26, 29–34]. Anatomically constrained MEG spatiotemporal analysis [26, 29, 31, 34] is one such technique. This technique relies on the reasonable assumption that the synaptic potentials giving rise to the summated MEG and EEG observed on the scalp are confined to the cortical ribbon [29, 35] to solve the inverse problem (a mathematically ill-posed problem that cannot be solved uniquely unless certain assumptions are applied [28]) which is specific to the estimation of current generators using MEG/EEG data. Members of the Martinos Center have developed continuous, weighted estimates of activation over the entire cortical surface using a continuous estimation approach [12, 26, 29]. With this approach, a cortical surface is partitioned into a large number of small patches, with each patch represented by a current dipole in the middle of the patch, thus approximating arbitrary spatial distribution of synaptic currents within the cortex. This is called dynamic statistical parametric mapping (dSPM), with which continuous spatiotemporal maps (or "movies") of brain activity can be obtained. The dSPM maps are displayed on the inflated cortical surface [33, 36], thereby combining the fine temporal information obtained by MEG/EEG with fine spatial information obtained with MRI. Using dSPM, the clinical MEG group at the Martinos Center has successfully identified fine spatiotemporal brain activity in epileptic discharges [34]. The clinical MEG group is now routinely using this method to localize interictal spikes, identifying spikes in MEG/EEG recordings, and make movies to illustrate localized brain activity during spikes in a few milliseconds.

In dSPM analysis, EEG data are analyzed similarly to MEG data except that the model of the head used includes surfaces of the inner skull, outer skull, and scalp. Appropriate conductivity values for different tissue types are used in the calculations of signal propagation to measure points on the scalp [37, 38]. MEG and EEG techniques measure a magnetic aspect (MEG) and an electrical aspect (EEG) of the signal generated by the same neural events; they yield complementary information, as they are sensitive to different biophysical properties [39, 40]. MEG is sensitive only to the activity arising from current generators (dipoles) oriented tangentially to the skull, whereas EEG reflects summated activity across the tangential and radial dipoles. Previous studies have shown that spatial localization with the combination of the two methods is superior to either technique alone [37, 41].

5. Monkey fMRI

Macaque brain is often used as a model for the human brain, but homologies between macaque and human brains are yet to be clarified [42]. While neurophysiological findings in vision owe a lot to macaque brain, comparisons between results from single-unit recordings in macaque brains and results from fMRI in human brain is not easy because they are different in both methods and species. To fill such a gap, monkey fMRI is a promising technique. My group has developed [15] and investigated intriguing visual function such as symmetry perception [43] and novel radial orientation bias [17] using fMRI to test human perception, and then tested whether macaques have such perceptions. Our investigation revealed that symmetry perception does exist in monkeys and that a novel radial orientation bias also does exist in monkeys, even though previous single-unit recordings did not fully reveal such perception in monkeys.

Monkey fMRI can be used to study neural origin of BOLD signals. Monkey fMRI offers valuable opportunities for simultaneous intracortical recordings of neural signals and fMRI responses [3]. In addition, monkey fMRI can be used as guidance for subsequence single-unit recording [44], where Tsao *et al.* conducted monkey fMRI first, then identified a cortical region which generated a specific MR responses to faces. Later, she measured spiking activity in this fMRI-identified region, finding 97% of the cells were strongly face selective.

Monkey fMRI can be utilized to solve pharmacological questions [45]. The coupling between neurotransmitter-induced changes in neuronal activity and the resultant hemodynamic response is central to the interpretation of neuroimaging techniques. Choi *et al.* have used monkey fMRI to investigate brain hemodynamic changes mediated by dopamine receptors [45].

6. Conclusion

In this article, some of the advanced MR techniques were briefly overviewed. When MR technologies and techniques are advanced to that extent, then expertise in nuclear physics, medical physics, biomedical engineering are required for development and maintenance of them. For data analysis, which is becoming more and more complex and humongous in size, expertise in statistics, and computer sciences are also required. To solve medical or cognitive problems, expertise in medics, psychiatry, and psychology will be required. In short, advanced human brain mapping will need interdisciplinary work, perhaps consisting a large research center. Furthermore, a director who understands researches that would span basic sciences to applied sciences will be needed for supervision of all research activity. The establishment of such research center is the key to the success to unveil mystery of brain functions.

Acknowledgements

This work is partially supported by Exploratory Research for Advanced Technology, Shimojo Implicit Brain Function Project, and Massachusetts General Hospital. The authors' imaging work was supported by National Center for Research Resources P41RR14075, the Mental Illness and Neruoscience Discovery Institute, the Athinoula A. Martinos Center for Biomedical Imaging.

[1] S. Ogawa *et al.*, Proc. Natl. Acad. Sci. USA **13**, 5951 (1992).
[2] K.K. Kwong *et al.*, Proc. Natl. Acad. Sci. USA **12**, 5675 (1992).
[3] N.K. Logothetis, J. Pauls, M. Augath, T. Trinath and A. Oeltermann, Nature **6843**, 150 (2001).
[4] C. Triantafyllou, R.D. Hoge and L.L. Wald, Neuroimage **2**, 551 (2006).
[5] C. Triantafyllou *et al.*, Neuroimage **1**, 243 (2005).
[6] J. Pfeuffer, H. Merkle, M. Beyerlein, T. Steudel and N.K. Logothetis, Magn Reson Imaging **10**, 1343 (2004).
[7] J.C. Augustinack *et al.*, Ann. Neurol. **4**, 489 (2005).
[8] R. Otazo, B. Mueller, K. Ugurbil, L. Wald and S. Posse, Magn. Reson. Med. **6**, 1200 (2006).
[9] D.H. Salat *et al.*, Ann. NY Acad. Sci. 37 (2005).
[10] C. Beaulieu, NMR Biomed. **7-8**, 435 (2002).
[11] T. Benner, A.J. van der Kouwe, J.E. Kirsch and A.G. Sorensen, Magn. Reson. Med. **1**, 204 (2006).
[12] H.D. Rosas *et al.*, Mov. Disord. **9**, 1317 (2006).
[13] D.S. Tuch *et al.*, Proc. Natl. Acad. Sci. USA **34**, 12212 (2005).
[14] G.K. Deutsch *et al.*, Cortex **3**, 354 (2005).
[15] F.P. Leite *et al.*, Neuroimage **2**, 283 (2002).
[16] Y. Sasaki and T. Watanabe, Proc. Natl. Acad. Sci. USA **52**, 18251 (2004).
[17] Y. Sasaki *et al.*, Neuron **5**, 661 (2006).
[18] Y. Sasaki *et al.*, Proc. Natl. Acad. Sci. USA **4**, 2077 (2001).
[19] S. Koyama *et al.*, Curr. Biol. **22**, 2027 (2005).
[20] S. Nishida, Y. Sasaki, I. Murakami, T. Watanabe and R.B. Tootell, J Neurophysiol. **5**, 3242 (2003).
[21] D.Y. Tsao *et al.*, Neuron **3**, 555 (2003).
[22] Y. Tsushima, Y. Sasaki and T. Watanabe, Science (2006).
[23] K. Sakai *et al.*, J Neurosci. **5**, 1827 (1998).
[24] H. Imamizu *et al.*, Nature **6766**, 192 (2000).
[25] O. Hikosaka *et al.*, J Neurophysiol. **1**, 617 (1996).
[26] A.M. Dale and E. Halgren, Curr. Opin. Neurobiol. **2**, 202 (2001).
[27] S.A. Hillyard and L. Anllo-Vento, Proc. Natl. Acad. Sci. USA **3**, 781 (1998).
[28] M. Hamalainen, R. Hari, R. Ilmoniemi, J. Knuutila and O. Lounasmaa, Rev. Mod. Phys. **413-497**, (1993).
[29] A.M. Dale *et al.*, Neuron **1**, 55 (2000).
[30] N. Fujimaki, T. Hayakawa, M. Nielsen, T.R. Knosche and S. Miyauchi, Neuroimage **1**, 324 (2002).
[31] F.H. Lin, J.W. Belliveau, A.M. Dale and M.S. Hamalainen, Hum. Brain Mapp. **1**, 1 (2006).
[32] M. Scherg, Brain Topogr. **2**, 103 (1992).
[33] S.P. Ahlfors *et al.*, J Neurophysiol. **5**, 2545 (1999).
[34] H. Shiraishi *et al.*, Epilepsia **8**, 1264 (2005).
[35] A.M. Dale and M.I. Sereno, J. Cogn. Neurosci. 162 (1993).
[36] A.M. Dale, B. Fischl and M.I. Sereno, Neuroimage **2**, 179 (1999).
[37] A.K. Liu, J.W. Belliveau and A.M. Dale, Proc. Natl. Acad. Sci. USA **15**, 8945 (1998).
[38] A.K. Liu, A.M. Dale and J.W. Belliveau, Hum. Brain Mapp. **1**, 47 (2002).
[39] D. Cohen and B.N. Cuffin, Electroencephalogr. Clin. Neurophysiol. **1**, 38 (1983).
[40] D. Cohen and B.N. Cuffin, Brain Topogr. **2**, 95 (1991).
[41] C. Baumgartner *et al.*, Neurosci. Lett. **1**, 103 (1991).
[42] R.B. Tootell, D. Tsao and W. Vanduffel, J. Neurosci. **10**, 3981 (2003).
[43] Y. Sasaki, W. Vanduffel, T. Knutsen, C. Tyler and R. Tootell, Proc. Natl. Acad. Sci. USA **8**, 3159 (2005).
[44] D.Y. Tsao, W.A. Freiwald, R.B. Tootell and M.S. Livingstone, Science **5761**, 670 (2006).
[45] J.K. Choi, Y.I. Chen, E. Hamel and B.G. Jenkins, Neuroimage **3**, 700 (2006).