Brain Imaging Studies and Design of Platform in Japan

Ryoji Suzuki

Human Information System Laboratory at Kanazawa Institute of Technology

&

Brain Information Group at National Institute of Information and Communications Technology

rsuzuki@m2.spacelan.ne.jp

1. Introduction

Brain imaging has become one of key technologies for the study of human brain mechanisms, in spite of arguments against brain imaging as neo-phrenology. In the following sections, I will introduce some interesting examples among activities concerning brain imaging studies in Japan, which can elucidate dynamical aspects of brain functions. They will show the possibilities of brain imaging technology as not only the tools to get the anatomical information, but those to get insight into the brain mechanisms. Thus it might be useful for brain scientists to have a network through which they can access any database and/or analytical methods of brain imaging. I will address the possibility of establishing a platform of Neuroinformatics in brain imaging field in Japan.

2. Non Exhaustive Review of Activities for Brain Imaging Technology in Japan

More than 40 institutes are using noninvasive brain imaging technologies such as functional Magnetic Resonance Imaging (fMRI), Magnetoencephalography (MEG), Positron Emission Tomography (PET), Near Infrared Spectroscopy (NIRS) for researches in brain science. Following I will review the activities concerning fMRI, MEG, NIRS and PET studies in Japan, not in exhaustive way, but by some examples within my view.

Concerning fMRI, more than 10 institutes have installed high-field (more than 3T) MRI. Probably one of the earliest installations was 4T MRI at Brain Science Institute of RIKEN (BSI, RIKEN) in 1996 and the highest field machine is 7T MRI at Center for Integrated Human Brain Science of University of Niigata (CIHBS) installed in 2002. Most of these machines have been imported from western countries, although the principle of BOLD method was found by Japanese scientist, Dr. Seiji Ogawa at Bell Lab. After retired from Bell Lab, he has established Ogawa Laboratories for Brain Function Research founded by Hamano Life Science Research Foundation in

Tokyo in 2001, where he installed 3T MRI and is devoting himself in developing new methods of MRI for brain research.

On the other hand, more than 30 MEG machines have been imported and installed at research institutes and universities with the supports from the government. Among them, National Institute for Physiological Science (NIPS) at Okazaki is one of the earliest users since 1991 and contributed to supporting researchers from other institutes and popularizing how to use MEG. In 1990, Ministry of International Trade and Industry (MITI) established Superconducting Sensor Laboratory for developing MEG and other application systems of SQUID, getting together with several companies such as Yokogawa Electric Corporation (YOKOGAWA), Shimadzu, Hitachi and so on. Dr. Hisashi Kado from Electrotechnical Laboratory directed this national project and succeeded in developing a 256-channel MEG system in 1994. After having finished this national project, Dr. Kado and some of his colleagues joined us at KIT and organized a new lab; Applied Electronics Lab (AEL). Having cooperated with YOKOGAWA, they could succeed again in developing a new 320-channel MEG system in 2003. This system can be used to get signals from the deep part of brain such as hippocampus, because the sensors are not the gradiometers, but magnetometers. The conventional gradiometer type MEG for practical use has also been developed at AEL. Its commercial product, which is now available from YOKOGAWA, is approved for clinical use by Ministry of Health, Labor and Welfare. Even with this type of MEG, we could get signals from hippocampus with good quality. (Hamada et al., 2004)

Concerning NIRS, status is rather different. Japanese companies, Shimadzu, Hitachi and Hamamatsu Photonics have produced commercial products and many research groups in brain science have utilized these products. In comparison with the large machine such as fMRI, MEG, and PET, NIRS is very convenient to be used, because the subject is not necessary to be restricted in a small cabin like MRI, MEG, and PET. However, the basic researches on the relation between the NIRS signals and the brain activity are still required and continued at National Institute of Information and Communications Technology (NICT) and other institutes. Dr. Hideo Eda at NICT summarizes NIRS status in Japan as follows: the terminology on NIRS in Japanese language is not consistent in the Japanese community and the data from different machines cannot be compared to each other. Working group for standardization has started by the initiative of Hitachi Medical Corporation as a subcommittee in the Japan Electronics and Information Technology Industries Association (JEITA). They are discussing the terminology in Japanese language, the unit of hemoglobin parameters measured by NIRS and the calibration protocol of instruments.

Concerning PET, National Institute of Radiological Sciences is one of the most active institutes for PET study in Japan. The institute organizes the Brain Imaging Project and carries out imaging studies of mental disorders and brain functions using PET, MRI and fMRI. Another activity on PET technology I would like to mention is carried out by Medical and Pharmacological Research Center

(MPRC) in Ishikawa Prefecture, where conventional PET tracers such as FDG are synthesized for diagnosis of cancer, dementia and so on. Besides this activity, researches on new tracers for diagnosis of the abnormality in the neuronal information transmission system are being carried out. This center has also the project of establishing the database to get the standard PET image of the brain of Japanese people by using 3-dimensional stereo-tactic surface projection. This activity might be useful to NI project in brain imaging.

3. Brain Imaging can Elucidate the Dynamical Aspects of Brain Functions

Here I will introduce some examples of brain imaging studies within my view, which will elucidate the dynamical aspects of brain functions by using new analytical method or by combining two imaging technologies such as fMRI + MEG (or EEG).

1) fMRI study of ‘Aha!’ reaction (or “Insight” of problem solving) by Dr. Kazuhisa Niki et al. at Neuroscience Research Institute, National Institute of Advanced Industrial Science and Technology (NSRI, AIST)

   Dr.Niki describes in his paper that “The ‘Aha!’ reaction is a brief moment of exceptional thinking where an unexpected change in one’s mental perspective reveals the solution to an otherwise intractable problem.” The event-related fMRI study demonstrated that the right hippocampus was critically highlighted and that a wide cerebral cortex was also involved in the “insight” event. This is the first neuroimaging study to have investigated the neural correlates of “insight” in problem solving. Combining the results from their parallel EEG experiment, Dr. Niki and his colleagues could identify the brain area related to ‘Aha’ response in more detail. Although most analyses were made by SPM99, they developed a new method for analyzing fMRI data; Multivariate Information Analysis based on the quantity of mutual information and is promising in brain imaging analysis. (Luo and Niki, 2003; Luo et al., 2004)

2) MEG study on neural coding of color by Prof .Yoshi Tamori et al. at Human Information System Laboratory (HISL), KIT

   A YOKOGAWA 160-channel MEG system at HISL, KIT was used to measure the responses to a set of color stimuli. By using their original non-parametric geometric Independent Component Analysis (gICA) algorithm based on the isotropy condition of connections among adjacent tangential spaces in the neural activities, they could obtain the localized response to the corresponding color stimuli with the fine spatiotemporal resolution. The response is moving inside area V4α, showing a characteristic orbital path. Their results suggest that the neural coding of chromaticity topologically corresponds to well known geometrical coding of chromaticity in terms of a continual deformation between neighboring representations. (Yokoyama et al., 2004) This study shows us that if the protocol of psychological experiment is carefully prepared and data is analyzed with a powerful mathematical tool such as gICA, our MEG system can provide us a fine spatial and temporal resolution in the order of 1 [mm] and 1 [ms] respectively.

3) Brain imaging study of human language processes and sleep state by Dr. Norio Fujimaki, Dr. Satoru Miyauchi and their colleagues at Brain Information Group, NICT

Dr. Fujimaki and his colleagues invented a new method of fMRI-constrained MEG source analysis with which not only the temporal resolution, but the spatial resolution is improved. They applied it to data of lexical decision, inner speech, and visual search experiments and analyzed brain activations for visual-form, phonological and semantic processes of characters and words. An interesting result they obtained by fMRI study is the dependence of brain activations on reading speeds when rapid readers read sentences. In the case of rapid reader, the activity of Wernicke's area decreased which suggests the rapid reader can read sentences with fewer phonological processes.

Dr. Miyauchi invented a new method called Be-fMRI (Brain event-related fMRI) in which EEG and fMRI are measured simultaneously and time series data of EEG power spectrum and fMRI data are analyzed by the multiple regression analysis. Applying this method to sleep wave, he could identify the local areas related to the events during sleep such as NREM and REM sleep. (Fujimaki et al., 2002; Fujimaki et al., 2004)

4) An fMRI study on the mechanisms for switching multiple internal models by Dr. Hiroshi Imamizu at ATR Computational Neuroscience Laboratory directed by Dr. Mitsuo Kawato.

This study is a good example that the brain imaging is very powerful to clarify the mechanisms of brain functions, if the moderate computational model is considered. Dr. Imamizu and his colleagues studied on the mechanisms for switching multiple internal models by analyzing fMRI activities. Two representative computational models are proposed. One is called mixture-of-experts architecture, in which switching is commanded by a single "gating network". The other one is called MOdular Selection And Identification for Control (MOSAIC), in which the internal models themselves play crucial roles in switching. Consequently, the former model predicts that neural activities related to switching and internal models can be temporally and spatially segregated, while the latter model predicts that they are closely intermingled. fMRI activities were observed during switching performance and the results suggest that switching mechanisms in the frontal cortex can be explained by the mixture-of-experts architecture, while those in the cerebellum are explained by the MOSAIC model. (Imamizu et al., 2004)

4. Possibility of Establishing Platform of Neuroinformatics in Brain Imaging in Japan

Above mentioned studies are small examples. Many more studies including technological developments are actively performed in Japan. Among them, the integrated researches of the brain imaging have started.

As the first example, Hokkaido University has established Research and Education Center for Brain Science (RECBS) in Sept.2003, which has 3 groups concerning brain imaging; MEG group, Optical measurement group and fMRI group and aims to make the progress in the integrated brain science and education.

Second example is the activity of Center for Integrated Human Brain Science (CIHBS), University of Niigata. Director, Prof. Tsutomu Nakata says that a final objective of human neuroscience is the elucidation of brain functional organization of human-specific brain functions, for example, language and abstract thinking, then CIHBS has installed 3T and 7T high field MRI and organized the Integrated Neuroscience Department which focuses on the research and education of physiological human brain function based on integrated applications of state-of-the art, non-invasive technologies such as functional MRI, diffusion tensor analysis and high density electrical mapping.

Third example appears at Tohoku University. The New Industry Creation Hatchery Center (NICHe) takes "Functional Brain Imaging" as one of Industry Creation Sections where preeminent researchers are released from the burden of education so as to apply themselves to R&D and Prof. Ryuta Kawashima has been assigned. The purpose of his research is to elucidate the principles of brain functions and to transfer the principles to information engineering.

In Tokyo Metropolitan area, there are many active sites in brain imaging. Among them, BSI at RIKEN is one of the leading institutes in brain imaging, where MEG and Optical Imaging are also actively utilized as well as the above mentioned 4T MR I is. The activities of Neuroscience Research Institute at AIST, Tsukuba, National Institute of Radiological Science in Chiba and Ogawa Laboratories for Brain Function Research were already introduced. University of Tokyo, Tokyo Denki University and others also actively proceed in brain imaging. MEG with the largest number of channels has been installed at Graduate School of Frontier Science, University of Tokyo (Takeda Lab.) by YOKOGAWA in 2003.

Early stage activity of NIPS in Okazaki is already introduced. In 2002, they installed a new 306-channel whole-head type MEG and the active researches are in progress by Prof. Ryusuke Kakigi and his colleagues.

Kansai area has another cluster of the institutes for brain imaging. Kyoto University, Osaka University, Kobe University, ATR, NICT (Kansai Advanced Research Center), AIST (Ikeda) and others constitute this cluster.

Here, I will introduce "open lab" activities by ATR and NICT.

The ATR Brain Activity Imaging Center (BAIC) was established to allow researchers to more readily conduct fMRI experiments. BAIC is an open institution, so anybody can use BAIC facilities at some reasonable cost, if their studies are ethical. Experienced MRI technician and experimental psychologists support their experiment. Therefore they can run their fMRI experiments easily even if it is their first time. BAIC is very popular for researchers in Kansai area and the machine time is almost occupied.

KARC of NICT in Kobe installed 1.5T-MRI and MEG almost 10 years ago. NIRS was also developed by Dr. Eda and his colleagues and used for brain imaging. Recently, KARC installed 3T MRI. These machines will be opened to the researchers outside KARC.

Besides these examples, there are many sites where the brain imaging studies are actively conducted by a few but excellent researchers. Particularly, researches on the analytical methods should be introduced here. They are Dr. A. Chicocki (BSI. RIKEN), Prof. A. Matani (Univ of Tokyo), Prof. K. Sekihara (Tokyo Metropolitan Institute of Technology), Dr. M. Sato (ATR), Prof. T. Suzuki (Osaka Univ), Dr. T. Kochiyama (Kagawa Univ), Dr. Y. Tamori (KIT) and others. They have cooperated with experimental researchers respectively. (I am sorry I cannot review exhaustively here, but will complete the list of sites and researchers very soon.)

Now, we understand that we have many resources in Japan to organize NI platform in brain imaging and we have just started towards it.

Here, I should emphasize that the brain imaging technology has a great potential as a tool for studying human brain functions, if and only if the brain imaging experiments are conducted based on the computational model and the powerful analytical method. Furthermore, working together with cellular and genetic methods the brain imaging technology is expected to give a unified view of the role of the human brain in supporting the mind. (Posner, 2003)

Our platform must be organized with this point of view.

Following is the list of home pages of institutes related to brain imaging studies. (Not completed) For more information, please visit them.

- Hokkaido University, Research and Education Center for Brain Science:
  http://www.hokudai.ac.jp/recbs/(Japanese)
- Tohoku University, New Industry Creation Hatchery Center, Functional Brain Imaging Section
  http://www.niche.tohoku.ac.jp/ics.php(Japanese)
  http://www.niche.tohoku.ac.jp/en/(English)
- University of Niigata, Center for Integrated Human Brain Science
  http://coe.bri.niigata-u.ac.jp/(English)

- Neuroscience Research Institute, AIST
  http://unit.aist.go.jp/neurosci/(Japanese)
  http://unit.aist.go.jp/neurosci/english/index.html(English)
- Brain Science Institute
  http://www.brain.riken.go.jp/(English)
- Ogawa Research Institute for Brain Functions :
  http://www.hlsrf.or.jp/(Japanese)
  http://www.hlsrf.or.jp/eng/(English)
- National Institute of Radiological Science:
  http://www.nirs.go.jp/(Japanese)
  http://www.nirs.go.jp/ENG/nirs.htm(English)
- Graduate School of Frontier Science, University of Tokyo
  http://www.k.u-tokyo.ac.jp/index.html.en(English)
- Tokyo Denki University, Research Center for Advanced Technology
  http://www.rcat.dendai.ac.jp/(Japanese)
- ATR Computational Neuroscience Laboratory:
  http://www.cns.atr.jp/(English)
- ATR Brain Activity Imaging Center
  http://www.baic.jp/(Japanese)
  http://www.baic.jp/english.html(English)
- Brain Information Group at NICT :
  http://www-karc.nict.go.jp/d333/(Japanese)
  http://www-karc.nict.go.jp/d333/english/(English)
- Medical and Pharmacological Research Center (Ishikawa Prefecture):
  http://www.mprcf.or.jp/(Japanese)
- Applied Electronics Laboratory, KIT
  http://wwwr.kanazawa-it.ac.jp/~aelkit/(Japanese)
  http://wwwr.kanazawa-it.ac.jp/ael/(English)
- Human Information System Laboratory, KIT
  http://his.kanazawa-it.ac.jp/(Japanese)

Acknowledgements

To write up this report, I was supported by Dr. K. Niki of NSRI, AIST, and Dr. N. Fujimaki, Dr. H. Eda and Dr. Y. Terazono of Brain Information Group, NICT. I appreciate their excellent contributions.

References

1. Hamada Y, Sugino K, Kado H, Suzuki R: Magnetic fields in the human hippocampal area evoked by a somatosensory oddball task, Hippocampus, 14(4), 426-433 , 2004
2. Luo J, Niki K.: Function of hippocampus in "insight" of problem solving, Hippocampus, 13(3), 316-323, 2003
3. Luo J, Niki K, Phillips S: Neural correlates of the 'Aha! reaction', Neuroreport, 15(13), 2013-2017, 2004
4. Yokoyama N, Shoda K, Tamori Y: Neural Coding of Color, Forma, 19(1), 13-23, 2004
5. Fujimaki N, Hayakawa T, Nielsen M, Knosche TR, Miyauchi S: An fMRI-constrained MEG source analysis with procedures for dividing and grouping activation, Neuroimage, 17(1), 324-343 2002
6. Fujimaki N, Hayakawa T, Munetsuna S, Sasaki T: Neural activation dependent on reading speed during covert reading of novels, Neuroreport, 15(2), 239-343, 2004
7. Imamizu H, Kuroda T, Yoshioka T, Kawato M: Functional magnetic resonance imaging examination of two modular architectures for switching multiple internal models, J Neurosci, 24(5), 1173-1181, 2004
8. Posner MI: Imaging a science of mind, Trends Cogn Sci, 7(10), 450-453, 2003