Measuring Brain Function —Front Line of Aging Society

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OVERVIEW: Hitachi has contributed to the invention and technical innovation of non-invasive devices for imaging brain function that work by ultra-sensitive measurement of light, magnetic fields, and other properties. As the world is at the forefront of the trend toward aging societies, the maintenance of brain health is an important social issue for it, and techniques such as optical topography and simplified magneto-encephalography that support the diagnosis of brain function are being developed. These products and services also need to provide benefits in the area of preventive medicine, and brain function measurement and other human science techniques are likely to be incorporated into research and development of products and services. These human-oriented technologies promise to create a society that is safe, secure, and convenient.

INTRODUCTION

TO date, there have been 28 Nobel Prizes awarded for brain science research. These include three prizes awarded for techniques for imaging living organisms: the inaugural Nobel Prize for physics awarded to Wilhelm Conrad Röntgen in 1901 for the discovery of X rays, the 1979 prize awarded to A. M. Cormack and G. N. Hounsfield for the invention of X ray CT (computed tomography), and the 2003 prize awarded to P. C. Lauterbur and P. Mansfield for discovering the principles of MRI (magnetic resonance imaging). These discoveries and inventions make it possible to reveal the internal "morphology" of living organisms and are used in hospitals and clinics around the world.

On the other hand, obtaining and understanding of life and organisms also requires the ability to measure "function." The brain in particular is a special organ when it comes to "morphology" and "function." In terms of regenerative medicine and similar, for example, normal organs such as the lungs or liver achieve their function by growing "morphology." With the brain, however, simply growing "morphology" does not automatically produce "function" and instead "function" can only be instilled by establishing algorithms in the brain through training. Measurement of brain function is essential for understanding and diagnosing the brain.

That functions are localized in particular regions of the brain is known from clues such as the location of brain damage and from electrical stimulation during brain surgery[(1), (2)]. This has created a need for techniques for obtaining brain function images that show localized brain activity. Non-invasive techniques for brain function measurement can be broadly divided into methods that measure the changes in neuroelectric potential caused by brain activity and methods that measure the associated changes in blood flow. Historically, the first technique for non-invasive imaging of human brain function was EEG (electro-encephalography)[(3)], followed by the invention of MEG (magneto-encephalography)[(4)], fMRI (functional magnetic resonance imaging)[(5), (6)], and OT (optical topography)[(7), (8)]. Table 1 shows a technical comparison of these different non-invasive imaging techniques for brain function.

Table 1. Technical Comparison of Non-invasive Imaging Techniques for Brain Function
The measurement methods can broadly be divided into those that measure changes in neural potential and those that measure changes in blood flow.

	Measurement signal	Time resolution (s)	Spatial resolution (mm)	Equipment size	Measuring environment	Deep measurement	Subject openness
EEG	Neural population activity	0.001-	-	Small	○	△	◎
MEG	Nerve group activity	0.001-	-	Large	△	△	△
fMRI	Hemodynamic change (deoxygenated Hb)	20-	0.5-	Large	×	◎	×
OT	Hemodynamic change (oxygenated/deoxygenated Hb/blood volume)	0.1-	25-	Small	○	×	◎

EEG: electro-encephalography MEG: magneto-encephalography
fMRI: functional magnetic resonance imaging OT: optical topography Hb: hemoglobin

Use of non-invasive imaging equipment has progressed our analytical understanding of brain, nerve, and other functions. Use of the equipment in clinical situations is also becoming steadily more widespread.

Japan is one of the first countries to face the prospect of an aging society with the elderly (defined as those 65 years and older) expected to exceed 25% of the population by 2015. Ensuring safety and security are important issues in a super-aging society. Brain disease has high social costs in such a society[9], and measurement of brain function will become an essential diagnostic tool in medicine. Beyond medicine, it also seems likely that consideration of the brain will need to have a central role in deciding which policies, technologies, and other measures to adopt in order to realize genuine human-oriented safety and security in our living environments and in how we arrange the broader society in which we live[10]. Given this background, the measurement of brain function is likely to be an important technology for providing an objective indicator when assessing the issues faced by society in the future and for finding solutions to these issues.

This article describes these non-invasive imaging techniques for brain function and brain function measurement techniques that provide miniaturization along with safety and security in those countries that are among the first to face an aging population.

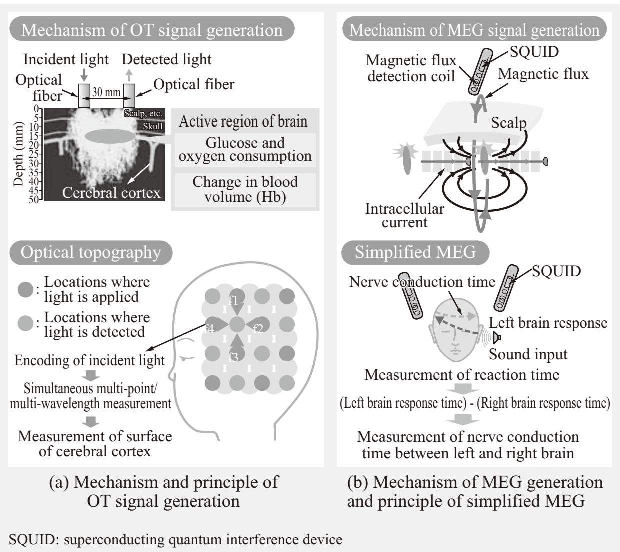


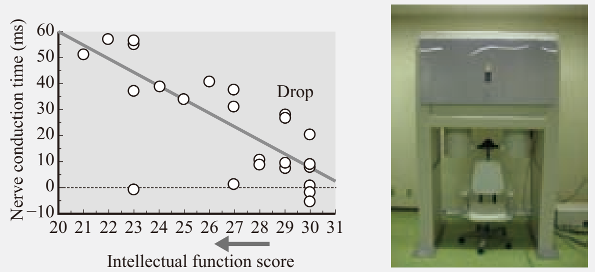
Fig. 1—Principles of OT and MEG.
The mechanism of brain activity signal generation and the near infrared spectroscopy principle behind OT[11], the principle of OT, the mechanism of MEG signal generation, and the principle of simplified MEG respectively are shown.

BRAIN FUNCTION MEASUREMENT TECHNIQUES

Along with the invention of OT, Hitachi's past work on non-invasive imaging techniques for brain function has included the development of technology for clinical applications that uses MEG and the miniaturization of simplified MEG. The principles behind OT and MEG are explained below.

OT measures changes in the density of oxygenated and deoxygenated hemoglobin produced by changes in blood flow resulting from activity in the brain. When activity occurs inside the brain, glucose and oxygen are consumed to produce the energy for that activity. To make up for this consumption, the blood flow to active regions increases. As a result, light shone in through the scalp is absorbed by the hemoglobin in the blood causing a change in the measured signal. The light shone in through the scalp is absorbed and scattered inside the brain so that the light detected at the scalp is attenuated to a level of less than one in one million of the incident light. High-sensitivity measurements can be performed by modulating the incident light in the kHz range and locking in detection of the received light. By encoding the incident light using different modulation frequencies, simultaneous multi-point/multi-wavelength measurement can be performed [see Fig. 1 (a)]. This simultaneous multi-point/multi-wavelength measurement technique allows measurement of surfaces to be performed from point measurements and this has resulted in the world's first light-based non-invasive imaging technique for brain function[7, 8].

MEG is a way of making measurements, from outside the head, of the very weak magnetic fields generated by nerve cell activity (intracellular current) in the brain. Although the magnitude of a magneto-encephalogram (100×10^{-15} T) is approximately one hundred million times smaller than the earth's magnetic field, it can be measured using superconductors by using a highly sensitive SQUID (superconducting quantum interference device) magnetic sensor. Because MEG can measure the magnetic fields generated by intracellular currents directly, it is not easily affected by non-conductors such as the skull and has a high spatial and temporal resolution relative to EEG [see Fig. 1 (b)]. By utilizing these features that are not available in techniques like EEG, MEG has been adopted for use in clinical diagnosis and in researching higher brain functions such as perception, recognition, memory,



(a) Quantification of dementia (data supplied by the National Cardiovascular Center)

(b) Special-purpose machine for measuring nerve conduction time (simplified MEG)

Fig. 2—Quantitative Measurement of Dementia by MEG.
The correlation between intellectual function score and interhemispheric neural conduction time (a) and a simplified MEG system developed for the quantitative evaluation of dementia (b) are shown.

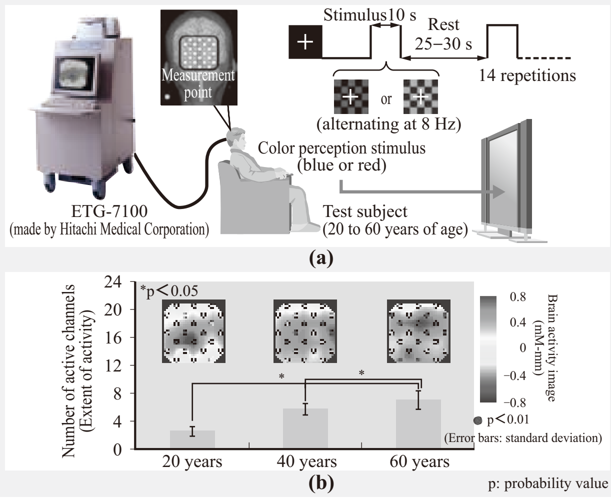


Fig. 3—Use of OT to Determine Age-dependence of Sensory Reaction to Display.
Figure (a) shows how the test was set up and the sensory stimulus produced. Figure (b) shows the age-dependence of brain activity in response to a visual stimulus.

awareness, and language.

Hitachi has applied a method for imaging the distribution of electric current in the brain using multi-channel MEGs in clinical applications where it is able to measure chronic dizziness, and has also succeeded in quantifying the degrees of dementia by measuring interhemispheric neural conduction times[12] [see Fig. 2 (a)]. Hitachi has also developed a simplified MEG technique that features small equipment size and is mainly used to measure interhemispheric neural conduction time [see Fig. 2 (b)].

SAFETY AND SECURITY IN COUNTRIES WITH RAPIDLY AGING POPULATIONS

Environment and Brain Function

The brain is an organ designed to integrate information about the internal and external environment collected by the senses and use this to determine its own physical and mental state. It is believed that more than 90% of the information processing in the brain takes place at a sub-conscious level, and brain function measurement techniques provide a way of objectively observing these mechanisms of which we are not consciously aware.

For example, although our environments are full of man-made audiovisual information, we do not usually feel the effect that this information is having on us. However, it is known that if someone who has lost an arm in an accident, for example, is shown a visual image of their missing arm using virtual reality, a powerful stimulus is applied to the brain and dramatic bodily reactions are produced[13]. In the future, rather than just audiovisual information, a systematic evaluation of our surrounding environment based on the workings of the brain will be an vital part of creating a safe and secure way of life. It is likely that our future living environments will be designed based on systematic knowledge.

Simple brain function measurement techniques such as OT are easy to apply to the evaluation of our day-to-day environment. One research topic involved conducting measurements aimed at analyzing the fundamental characteristics of the age-relationship between visual information from television and brain activity (see Fig. 3).

An experiment was conducted on 36 male and female subjects aged between 20 and 60 years. The experiment measured the activity of the experimental subject's visual cortex as they viewed a checkerboard pattern displayed on a television screen that alternated in color with a frequency of 8 Hz between a red and black pattern and a blue and black pattern. The results showed that the active area of the brain became enlarged with greater age. This indicates that, when viewing the same visual stimulus, older people use a larger region of their brain than younger people.

Advances in brain function measurement techniques such as this have made it possible to evaluate human beings scientifically. This means that we are entering an era in which people themselves can be used as a way of scientifically evaluating the usefulness and safety of products and services that enhance quality of life. The usefulness and safety of products and services in the past relied on the beliefs of manufacturers and the ethic values of users [see Fig. 4 (a)]. However, use of human science techniques such as brain function measurement provides a means of evaluating the value of goods and information objectively and this will see human measurement become part of the cycle of processes by which these products and services are produced. This is analogous to the way in which scientific methods have become part of the process of developing technology [see Fig. 4 (b)]. As societies become matured, the emphasis in determining the value of goods and services will shift from efficiency to safety and security, and there will be growing demand to make these goods and services more human-oriented. For example, there is strong demand at a personal level for healthcare-related values such as maintaining bodily functions and mental health. It is believed that products and services that possess these human-oriented values will themselves help reduce social costs such as healthcare, thereby making possible improvements in productivity and creating an aging society that is also active.

Brain Health and Aging

As explained above, the process of creating human-oriented products and services is very similar to the clinical trials used in the medical world. Accordingly, it is worthwhile to extrapolate from research into the field of clinical medicine, and Hitachi has therefore been working with the National Cardiovascular Center to conduct clinical research on elderly patients using multi-channel MEG. It was through this research that a correlation between the level of dementia and the neural conduction time measured by MEG was uncovered. The research involved using a newly developed multi-channel MEG system to measure the neural conduction time between the two hemispheres of the brain in response to an audible stimulus, as shown in Fig. 1 (b). The results showed that the time taken for neural conduction between the left and right hemispheres had a strong correlation with the severity of dementia [see Fig. 2 (a)]. It was also found that the neural conduction time started to slow approximately one to two years prior to the onset of dementia[15], indicating that conduction time can be used as a prognosis tool. Work is now underway toward developing a simplified MEG system that is able to measure neural conduction time easily without requiring a magnetically shielded room through the use of an improved detection coil shape[16][see Fig. 2 (b)].

As described above, MEG is a non-contact and non-invasive measurement that is applicable for a wide range of neurological conditions and are useful tools for elucidating higher brain functions. Because the technique is non-invasive, it has the potential to be used as an objective measure of the changes in function that occur with aging, and similar research methods should be applicable to the development of technology for sustaining mental and physical functions.

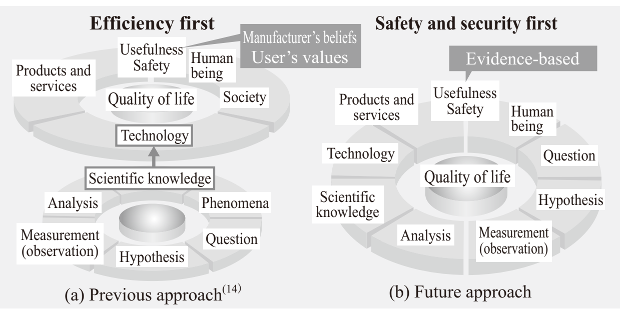


Fig. 4—Human Science Processes Embedded in Human-oriented Products and Services.
In past products and services (a), scientific knowledge was transformed into technology to develop products and services with an emphasis on efficiency. For future products and services (b), however, a growing emphasis will be placed on safety and security in terms of what value they add to our quality of life. Accordingly, human science will become a part of the cycle of technical progress as the level of usefulness and safety that products and services provide to people come to be evaluated scientifically from the perspectives of both mind and body.

COMPACT BRAIN FUNCTION MEASUREMENT TECHNIQUES

A new trend in the understanding of brain mechanisms is emerging whereby different brain function measurement techniques are combined. Whereas the emphasis in the past has been on gaining an understanding of brain function through progress in brain measurement, the focus is now shifting toward more active utilization of brain signals, including the development of electrodes and magnetic and optical devices that operate directly on the brain, and toward research and development in areas such as biocompatible materials and making brain function measurement equipment smaller. Use of brain signals to control an external device is no longer the topic limited in science fictions[17], and work on the information theoretical elucidation of internal brain processes is progressing from animals to humans. Work has also started on inserting electrodes inside the brains of patients with neurological disorders such as nervous seizures and using the data thus obtained to observe processes inside the brain. Looking at the broad trends in current research, progress is being made on modeling the process of information processing in the brain from patients with brain damage by using invasive devices in the hope that in the future this will lead to techniques for supporting rehabilitation that use ultra-miniaturized non-invasive brain function measurement technologies.

Because electronics and semiconductor technology has provided the basis for the OT techniques developed to date, there is no reason in principle why ultra-miniaturized OT systems cannot be produced, and this opens up great potential for applying this technology in support of rehabilitation. An experimental wearable OT system has already been developed that weighs only 1 kg (400 g for the measurement unit)[18] (see Fig. 5).

Miniaturization also opens up the possibility of combining different brain function measurement techniques. Table 1 shows how each different brain function measurement technique collects different aspects of a single biological system. Accordingly, an even deeper understanding of the situation inside the brain can be obtained by complimenting each measurement signal with information acquired by other techniques. For example, qualitatively different types of information can be obtained by combining different measurement techniques for functions such as sleep where methods from fields like psychology and cognitive science are not applicable[19].

Fig. 5—Wearable OT.
Experimentally developed wearable OT system weighs only 1 kg (400 g for the measurement unit).

CONCLUSIONS

This article has described non-invasive imaging and measurement techniques for brain functions, safety and security in countries with rapidly aging populations, and compact brain function measurement techniques.

Hitachi has developed the OT and simplified MEG techniques for non-invasive imaging and measurement of brain function. Currently, the company is actively working on research and development of clinical applications for these measurement techniques. Also, the creation of a safe and secure society has become an urgent issue for a modern world that is progressively aging. Hitachi believes that products and services based on human-oriented technologies that help maintain mental and bodily functions will have a valuable role in resolving these issues.

The OT display experiments were conducted by Akiko Obata and Takeshi Hoshino and the wearable OT system was developed in cooperation with Masashi Kiguchi and various departments at Hitachi Kokusai Denki Engineering Co., Ltd.

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