C297-E089C

SHIMADZU
Excellence in Science

Solutions for

Functional Brain Analysis with Near-Infrared Spectroscopy

Shimadzu Provides Powerful Support for Brain Function Research in a Wide Variety of Fields

The 21st century is said to be the century of the brain, where neuroscience is an advanced interdisciplinary field of study, with significant progress in research being made in a broad range of areas, from basic research to clinical applications in medical and biological fields to even industrial applications.

There are many aspects of how the brain relates to the “mind,” such as how we think, memorize, recognize, and feel emotions, that are still not well understood. Researching such brain science is truly at the frontier of life-science research, all over the world, work is being conducted on a wide variety of research projects in integrated areas that involve multiple fields.

Brain function research is not limited to traditional research areas, such as psychiatry, neurology, human development, and psychology. There is now increasing interest from various rehabilitation or applied engineering fields and the social and human sciences as well, and economics. This range of research is expanding at an increasing rate.

Furthermore, a variety of measurement technologies and instruments have been developed as methods to research brain function. Some of the methods include EEG (electroencephalography), fMRI (functional magnetic resonance imaging), PET (positron emission tomography), and MEG (magnetoencephalography) (*see* Table 1). One new method which was developed and has been raising expectations in recent years, is fNIRS (functional near-infrared spectroscopy). This method is capable of measuring brain function noninvasively by using infrared light, which offers superior penetration of the body. fNIRS has several advantages over other measurement methods, such as fewer constraints on the subject. Consequently, as a measurement method that allows a high degree of freedom, applications of the technology are increasing at a rapid rate. One of the main benefits of fNIRS is its high compatibility with other measurement methods, which means it is capable of simultaneous measurements.

Table 1 Typical Instruments Used to Measure Brain Function

	MEG Magnetoencephalography	PET Positron Emission Tomography	fMRI Functional Magnetic Resonance Imaging	EEG Electroencephalography	fNIRS Functional Near-Infrared Spectroscopy
Measurement Subject	Magnetism Neuro-electrical current	Gamma rays Cerebral blood flow and blood volume Changes in metabolites	Electromagnetic Waves Changes in cerebral blood flow (Deoxy-Hb)	Electric Potential Neuro-electrical current	Near Infrared Light Changes in cerebral blood flow (Deoxy-Hb Oxy-Hb)
Time Resolution	Milliseconds	Minutes	Seconds	Milliseconds	One hundred milliseconds
Features	Quickly captures first-order reactions of neurons	Quantifiable	Provides information about form	Quickly captures first-order reactions of neurons	Allows measurement of nearly routine activity

For Research Use Only. Not for use in diagnostic procedures.

Shimadzu is a pioneer in NIRS measurement to observe the brain by light

In the late 1980s, Shimadzu started researching using near infrared light to measure the oxygen kinetics in biological tissue, which led to releasing the OM-100A in 1991, Japan's first clinical noninvasive oxygen monitor. At the time, it was mainly used to evaluate the oxygen kinetics in vascular diseases and muscles. Based on the technology cultivated for those applications, we successively developed and released multi-channel type optical brain-function imaging systems designed specifically for the brain (LABNIRS).

Brain function varies depending on the part (area) of the brain. Such as language area, which is used to understand and manipulate words, the motor cortex, which is used to move various parts of the body, and the prefrontal cortex, which thought to be responsible for higher cognitive functions, e.g. recognition and decision making.

If there was an easy and noninvasive method of measuring the brain that allows evaluating the functions of specific areas of the brain, then that method could be used for a wide range of applications, such as research of early detection of dementia or determining the effectiveness of rehabilitation or the loss of brain function in mental disorders.

In engineering fields, active progress is being made in researching technology to operate machinery using brain activity, referred to as brain-machine interface (BMI) technology.

As a pioneer of NIRS measurement technology, Shimadzu has been working with researchers in a variety of fields to promote research in the observation of the brain using light and has contributed to the development of brain function research in many different areas.

Contents

Principle of Using Near Infrared Light to Measure Brain Function

Near infrared light refers to wavelengths longer than visible light, in the wavelength range from 700 nm to 1400 nm, where many compounds in living organisms exhibit high absorption intensity. These longer wavelengths exhibit a high absorption by water.

In contrast, shorter wavelengths, in the visible range (400 to 700 nm), are absorbed more readily by many constituent components of biological organisms. Consequently, these wavelength ranges cannot be used to penetrate biological organisms. Since the infrared wavelength range is able to penetrate biological organisms relatively well, it is sometimes referred to as a biological window (Fig. 1).

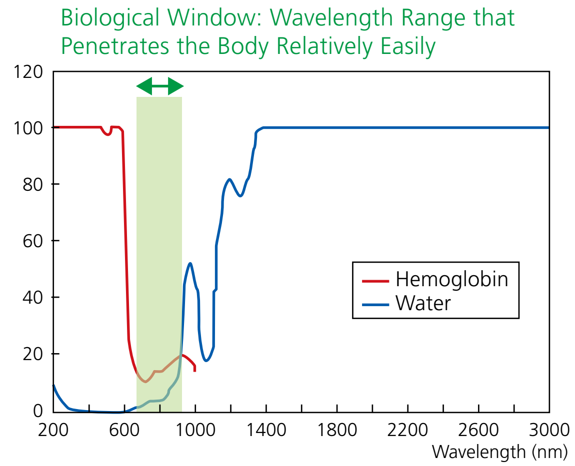


Fig. 1 Absorbance of Water and Hemoglobin in the Infrared Wavelength Range

Hemoglobin (Hb), a protein that functions as a carrier of oxygen in the blood, is a biological substance known to exhibit high absorption of near infrared wavelengths in the 700 to 900 nm range. The hemoglobin molecule has the characteristic of exhibiting a different absorption spectrum for oxygenated hemoglobin (Oxy-Hb), which has oxygen bonded to the molecule, and deoxygenated hemoglobin (Deoxy-Hb), where oxygen is separated from the molecule. Their absorption is equivalent (molecular absorption coefficients are equal) near 805 nm, where the molecular absorption coefficient for Deoxy-Hb is greater toward shorter wavelengths and the molecular absorption coefficient for Oxy-Hb is greater toward longer wavelengths (Fig. 2). Since the molecular absorption coefficients for hemoglobin at each wavelength are already known, measuring the change in absorption at two or more wavelengths allows calculating the change in Oxy-Hb and Deoxy-Hb. Shimadzu near-infrared optical brain-function imaging systems use three wavelengths — 780, 805, and 830 nm.

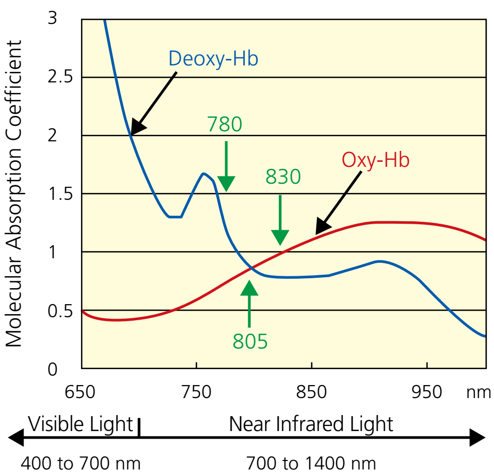


Fig. 2 Absorption Spectrum of Hemoglobin

Although near infrared wavelengths penetrate organisms well, organisms also readily scatter light. Therefore, it is difficult to detect straight transmission of light when measuring something the size and thickness of a human head. Consequently, to measure brain function using near infrared light, reflected light by scattering is measured (Fig. 3).

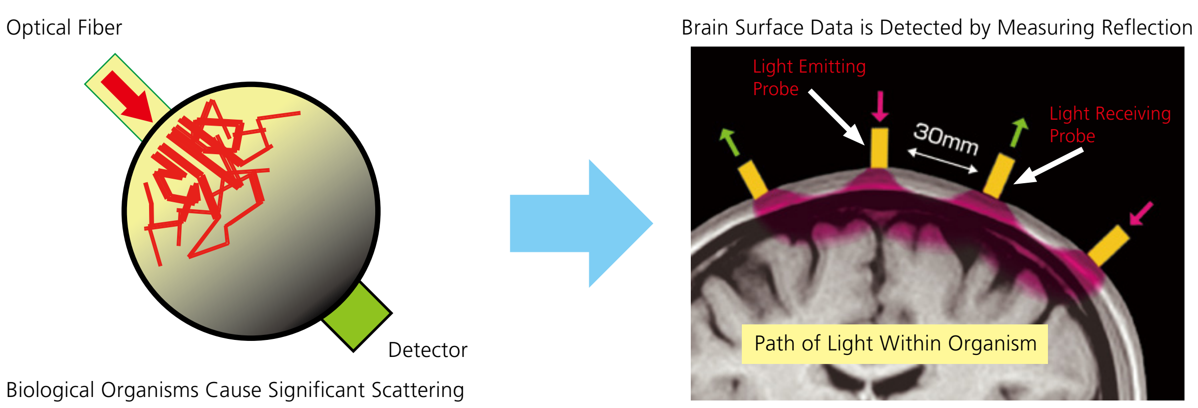


Fig. 3 Illustration of Reflection Measurement Method from Head Surface and Light Propagation

Infrared light is transmitted to the head surface by optical fibers distributed at fixed intervals. Normally, in the case of adults, a lattice of optical fiber probes for emitting and receiving are spaced 30 mm apart (Fig. 4). The light irradiated on the head surface passes through the scalp and skull before reaching the cerebral cortex, the surface of the brain, where it is absorbed or scattered. After traveling via a complicated path, only a small portion of the attenuated light reaches the optical fibers for receiving the light. This slight amount of light is amplified by a photomultiplier tube and detected with high sensitivity over a broad dynamic range, thereby accurately capturing the slight changes in Hb concentration in the brain due to brain activity.

Fig. 4 Distribution of Transmitter Fibers (red) and Receiver Fibers (blue) (4 × 4 array of 24 channels)

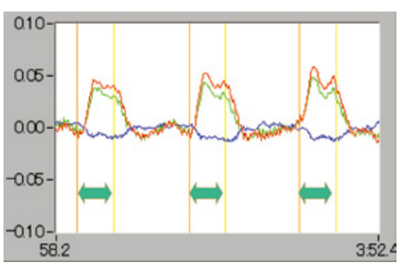


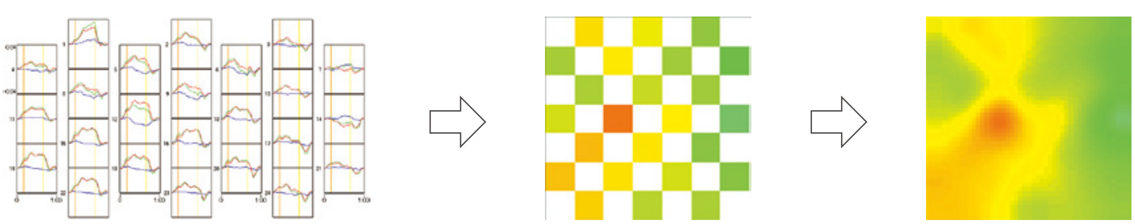
Fig. 5 Time-Series Changes in Hb due to Task

Since the exact path traversed by the light through the body (optical path length) cannot be determined, it is not possible to calculate the Hb concentration as an absolute value. Therefore, the change in Hb (change in Hb concentration multiplied by the path length) is determined instead.

Fig. 4 shows an example of using a 4 × 4 matrix of fibers, consisting of 8 pairs of transmitter and receiver fibers. Each pair of transmitter and receiver fibers is referred to as a channel; in this case, there are 24 channel measurement points.

Fig. 5 shows a graph of the change in hemoglobin over time as a finger-tapping task is repeated. Since the task involves tapping a finger, measurements were performed with the fibers arranged on the head so that the measurement channels cover the motor cortex. The figure shows data for channels that indicated a change corresponding to the task.

It shows how the motor cortex is activated by performing the task and how Oxy-Hb and Total-Hb levels increase during activity. When the task is finished and the subject returns to rest, Hb returns to a given level and remains stable. Changes in Hb can be mapped 2-dimensionally, as shown in Fig. 6, by color coding time-series data for each channel based on signal intensity and performing spatial data interpolation. In this case, areas shown in red indicate activity. By using optional MRI fusion software, brain activity can be understood more clearly by overlaying activity data on brain surface data (Fig. 7).



Time-Series Data for Each Measurement Channel

Color-Coded Oxy-Hb Status at a Given Time

Image Rendered with Interpolation Processing

Fig. 6 2D Image of Time-Series Data for Each Channel

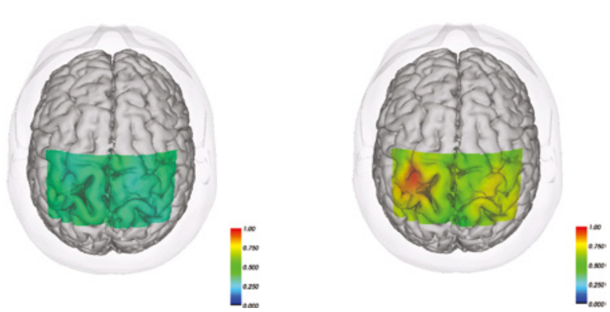


Fig. 7 Comparison of Oxy-Hb at Rest (left) and when Tapping Right Finger (right)

Optical Brain-Function Imaging

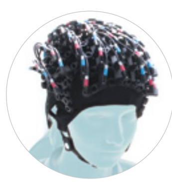
Features of Optical Brain-Function Imaging

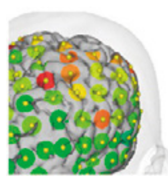
- **Using near infrared light is safe, and the restraint level is low.**
  It allows measuring brain activity status in a daily environment.
- **Flexible adjustable curved surface holder (FLASH) can be used.**
  It allows fitting a wide range of head curvatures. It is suitable for both children and adults.
- **Wide range of optional products available.**
  Statistical processing software is included standard with systems, in addition to a wide assortment of optional products are available to help facilitate cutting-edge brain-function research, such as a simultaneous EEG measurement system, MRI fusion software, and a real-time data transfer function.

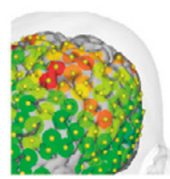
Note: "FLASH" is an acronym for Flexible Adjustable Surface Holder
Patent No. 4254420

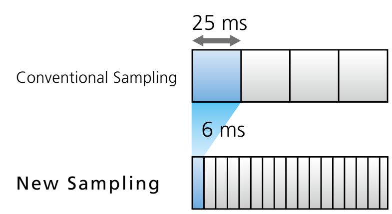
Higher Spatial and Temporal Resolution

- **Accepts up to 40 sets—2.5 times more than before (142 channels max.).**
- **Spatial resolution doubled with high-density measurements.**
- **High temporal resolution (6 ms for 1 channel: previously 25 ms) system captures rapid cerebral blood flow signals.**


Multi-Channel Measurements


Normal Distribution


High-Density Distribution




functional Near-Infrared Spectroscopy System for Research
LABNIRS

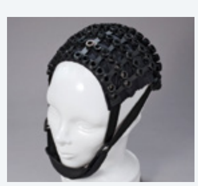
LABNIRS Options

- MRI fusion software
- Real-time data transfer software
- 3D position measurement system
- Video recording system
- Stimulus presentation system

Holder: FLASH*1 (Flexible Adjustable Surface Holder)

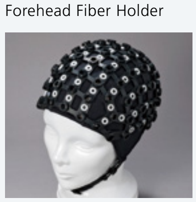
*1 Patented in Japan 04254420
*2 Supports high-density, short-distance measurements

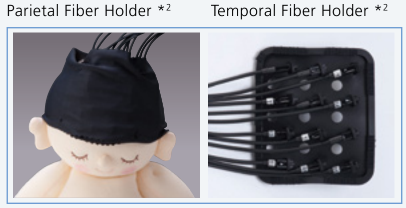

Forehead Fiber Holder


Parietal Fiber Holder *2


Temporal Fiber Holder *2


Whole-head Fiber Holder


EEG simultaneous measurement Fiber Holder


Holder set for newborns

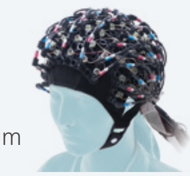

Holder Kit

Data

Various Brain-Function Measurements Using the LABNIRS

(1) Simultaneous EEG and fMRI Measurement

By using the EEG simultaneous measurement holder (optional) and creating a system that comprises the LABNIRS and an EEG (Active Two system from BioSemi), a maximum of 133 fNIRS channels and 64 EEG channels can be measured simultaneously. Fibers can be extended (optional) for simultaneous fMRI measurements.



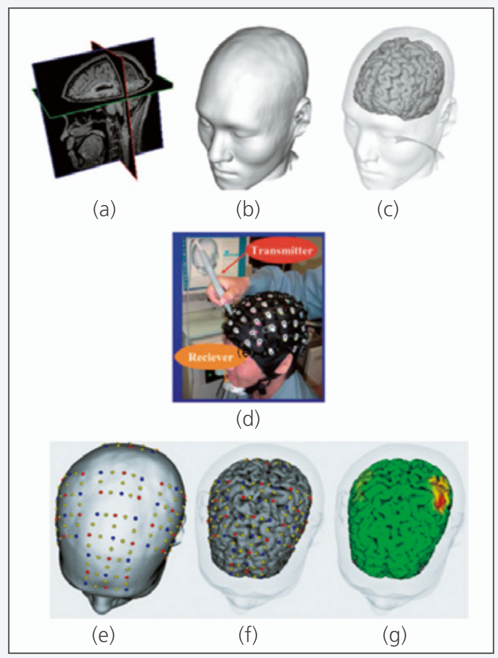
Holder for simultaneous EEG measurements

(2) Overlay with MRI Image

Overlaying the fNIRS data on an MRI image of the brain shape enables positioning the fNIRS functional image information more precisely.

—Workflow—

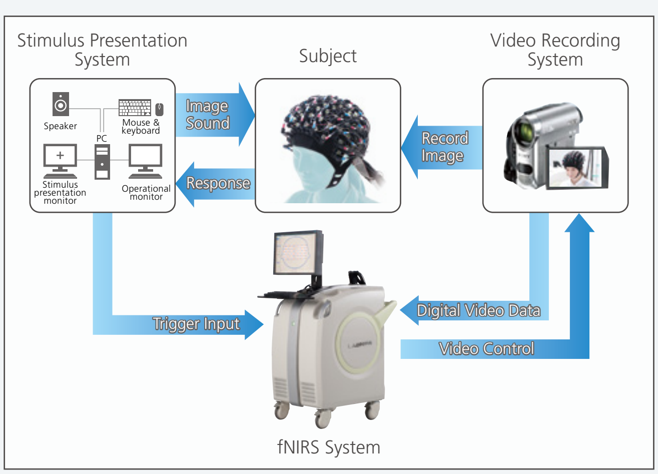
1. Import the DICOM image (TI-enhanced image) from the MRI (a).
2. Use the MRI fusion software to extract 3D scalp data (b).
3. Similarly, automatically extract the brain surface data to build 3D brain surface data (c).
4. Entering the reference points (nasion cz, and left & right preauricular points) and prove position (d).
5. Estimate the measurement position on the brain surface to overlay the fNIRS data (e) to (g).

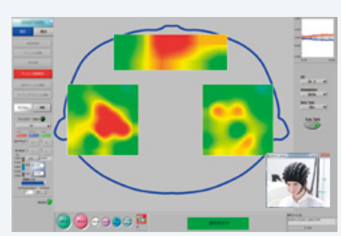


Reference:
Okamoto, M., H. Dan, *et al.* (2004) "Three-dimensional probabilistic anatomical cranio-cerebral correlation via the international 10–20 system oriented for transcranial functional brain mapping." *NeuroImage* 21 (1): 99–111.

(3) Stimulus Presentation and Video Recording System

fNIRS measurements can be linked to a stimulus presentation system using a computer and video recording system.





Example of Brain Measurement Data during Imposed Task

References:
Kohno, S., Ishikawa, A., *et al.* (2006) "Application development of functional near-infrared imaging system." *Shimadzu Review* 63 (3/4): 195–200.
Ishikawa, A., Kohno, S., *et al.* (2007). "Application development of functional near-infrared imaging system II." *Shimadzu Review* 64 (3/4): 177–183.

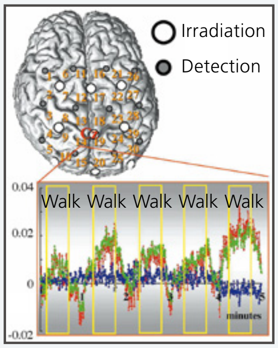
Neurorehabilitation

Example of Brain-Function Imaging Research: Neurorehabilitation Application Research

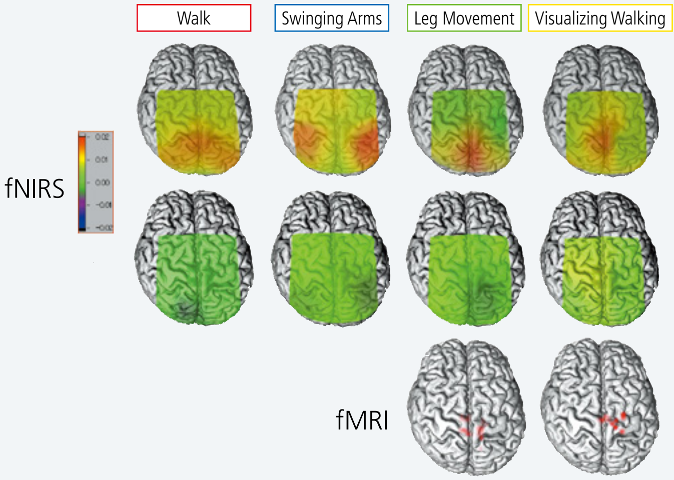
Data

In recent years, progress has been made in researching the use of fNIRS in neurorehabilitation applications, such as during or after a stroke.

PET and fMRI systems require the subject to be at rest, but fNIRS systems can measure brain function even while the subject is performing tasks that involve body movement. Therefore, it can be used to obtain information about cerebral activity associated with walking or other movement.



fNIRS Measurement of Brain Activation while Walking on a Treadmill



Brain Activity for Healthy Person during Walking and Related Tasks

The above shows the brain activity measured while walking on a treadmill. It shows an increase in Oxy-Hb associated with walking, inner side of the primary sensorimotor cortex, near the center. fNIRS is able to measure brain activity during dynamic movements assigned as tasks, such as walking or arm swinging, which cannot be measured using fMRI and PET. It can also be used to assess brain activity at the bedside. fNIRS is being used in research to evaluate brain activity during hemiplegic gait by stroke subjects, to improve asymmetry in the activity of the sensorimotor cortex, increase activity in the premotor cortex, improve walking, etc.

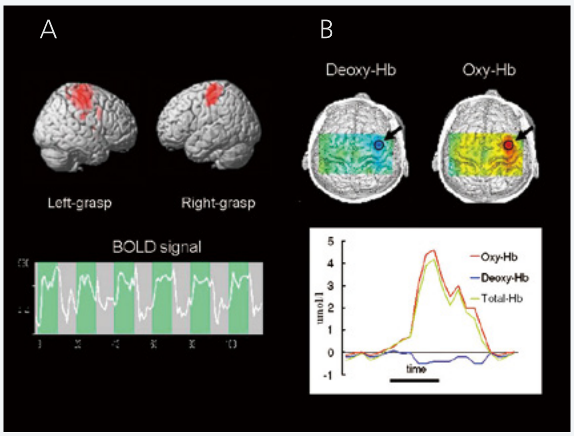
(Data provided by: Mr. Ichiro Miyai, Morinomiya Hospital, Omichi-kai Medical Corporation)

Reference: Miyai, I., (2004). "Application of fNIRS in Neurorehabilitation." *MEDICAL NOW*, No. 52: 33–36.

Comparison of fNIRS and fMRI

Example of Brain-Function Imaging Research: Comparison of fNIRS and fMRI

Data



Comparison of BOLD-fMRI (A) and fNIRS (B)
for Normal Healthy Subject

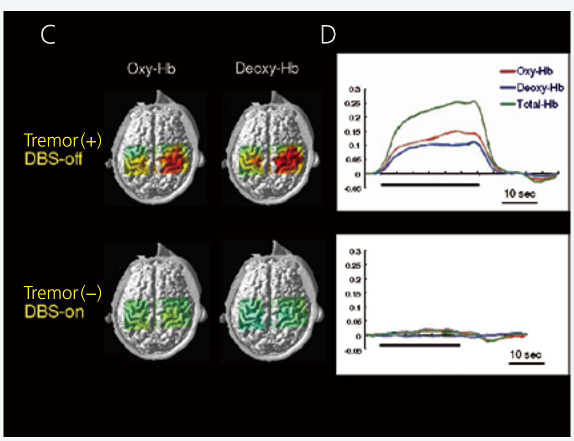
A: Measurement by fMRI

Clearly shows activity in motor cortex for opposite side due to exercise (grasping). The lower BOLD* signal shows an increase during the task (blue).

B: Measurement by fNIRS

Displays results from 2D mapping (overlaid on MRI image) of Deoxy-Hb and Oxy-Hb during exercise. The lower graph shows the change in Oxy-Hb and Deoxy-Hb in the motor cortex (marked with circles). It shows how Oxy-Hb and Total-Hb increase and Deoxy-Hb decreases during the task (40 sec).

* BOLD: Blood Oxygen Level Dependent



fNIRS Measurement of Change in
Active Brain Oxygen Metabolites in Tremor Subject

Since fNIRS is not affected by electrical noise or magnetic fields and has few limitations on patient posture during measurements, it can be used to measure brain function in cases where BOLD-fMRI cannot be used, such as on subjects being treated with deep brain stimulation (DBS) using a metal electrode.

C: fNIRS Image (overlaid on MRI image) of Essential Tremor Subject Being Treated with DBS

1. With Electrical Stimulation of DBS OFF (upper graph)
   Oxy-Hb increased significantly and Deoxy-Hb also increased, primarily in the right motor cortex, when a strong tremor occurred in the upper left extremity during a finger-to-finger test.
   (The increase in Deoxy-Hb indicates an abnormal enhanced release of oxygen metabolites.)
2. With Electrical Stimulation of DBS ON (lower graph)
   The tremor did not occur during the finger-to-finger test and the increase in Deoxy-Hb disappeared.

D: Change in Oxy-Hb, Deoxy-Hb, and Total-Hb Levels During Movement Task

Since fNIRS can measure not only Deoxy-Hb, but also changes in Oxy-Hb and blood flow, it is especially well suited to imaging brain function in subjects where brain oxygen metabolite activity and hemodynamics are not normal. Currently, BOLD-fMRI is the primary method used to image brain function, but using it in conjunction with fNIRS allows accurately imaging brain function.

(Data provided by: Mr. Kaoru Sakatani, Department of Neurological Surgery, Nihon University School of Medicine)

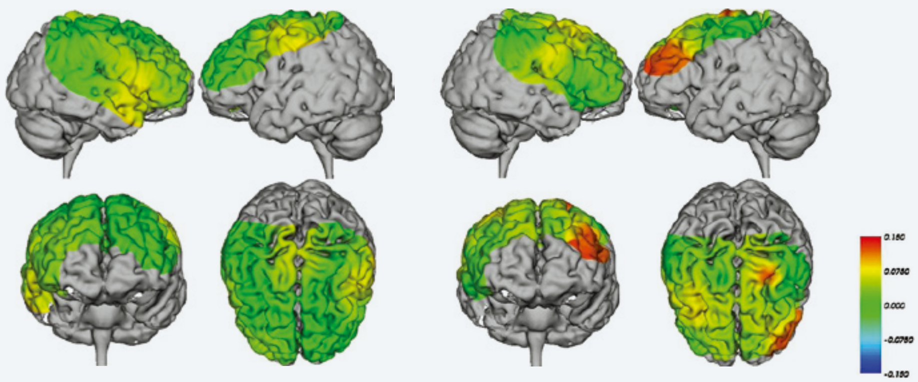
Reference:
Sakatani, K., (2006) "Imaging Brain-Function of Patients with Encephalopathy: Comparison of fNIRS and fMRI," *MEDICAL NOW*, No. 59: 44–46.

Brain Activity during Motor Control

Data

In rehabilitation-related occupations, such as physical therapy, occupational therapy, and speech therapy, important aims include adaptive motor learning and recovery of motor function in patients. The ability of fNIRS to record brain activity during exercise and movement has resulted in its rapid adoption in the field of rehabilitation research.

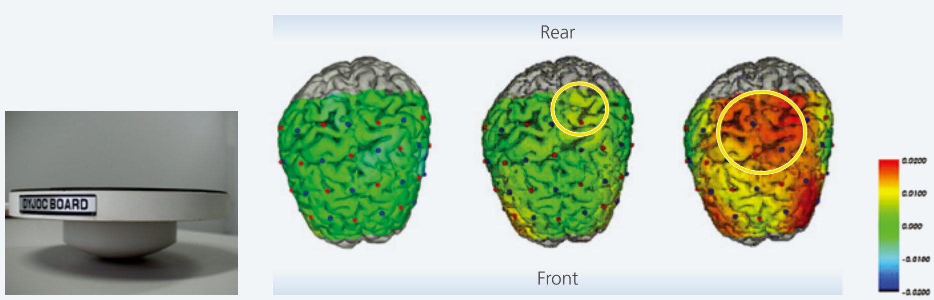
The diagrams below show brain activity during basic limb movements (walking, upright posture control, arm reaching movements, and lower-limb muscle force control).



A B

Fig. 1 Brain Activity during Lower-Limb Locomotion (Walking on a Treadmill)

A: Brain images when walking at 4 km/hour. They confirm a slight increase in Oxy-Hb concentration-length (Oxy-Hb concentration multiplied by the path length) on both sides of the primary motor cortex compared to the resting state. They also show an increased Oxy-Hb concentration-length in the pre-motor cortex.
B: Brain images when avoiding obstacles at 4 km/hour walking speed. The Oxy-Hb concentration-length when walking at 4 km/hour is subtracted from the Oxy-Hb concentration-length while avoiding obstacles at 4 km/hour walking speed. The images confirm an increase in Oxy-Hb concentration-length in the right pre-motor cortex and left pre-frontal cortex (near the dorsolateral cortex).



A B C D

Fig. 2 Brain Activity during Upright Posture Control

A: Wobble board used. B: Brain images when maintaining posture with feet together and eyes closed. The Oxy-Hb concentration-length in the reference state (maintaining upright posture with feet together and eyes open) is subtracted. C: Brain images when maintaining posture while standing on right leg. The reference state is subtracted. They confirm an increase in Oxy-Hb concentration-length in the right medial primary motor cortex and right pre-frontal cortex. D: Brain images when maintaining upright posture on a wobble board. They confirm an increase in Oxy-Hb concentration-length in the left and right primary motor cortex, supplementary motor cortex, and pre-frontal cortex.

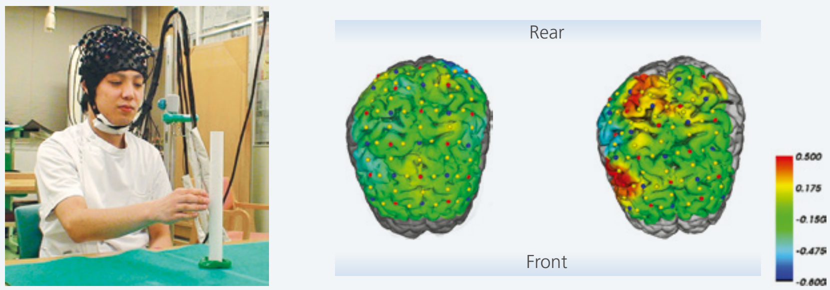


Fig. 3 Brain Activity during Arm Reaching Movements

A: Photograph of test. B: No prism glasses. C: Wearing prism glasses. Cases of unilateral spatial neglect often occur where the subject is unable to concentrate on the left half of the visual field due to damage to the right hemisphere parietal lobe. A method known as prism adaptation is used for rehabilitation in such cases. This test was performed for the basic verification of the effects of the method during arm reaching movements. Image C confirms an increase in Oxy-Hb concentration-length in the right lateral pre-frontal cortex and parietal lobe in comparison with image B.

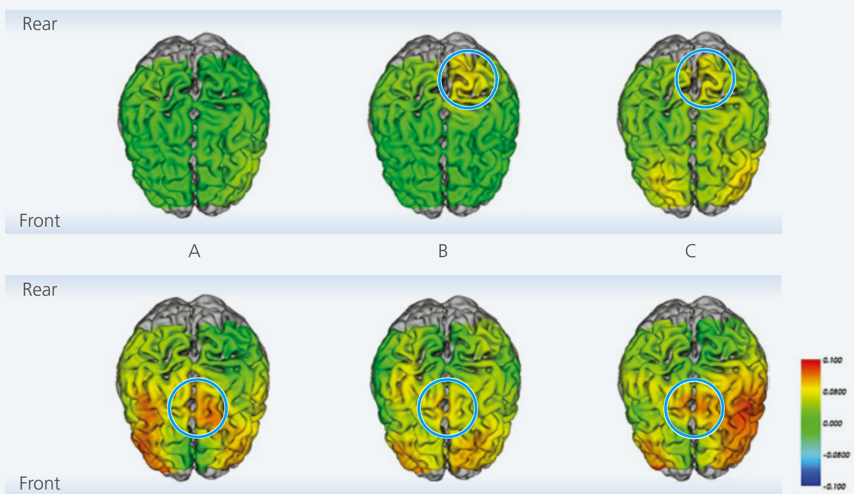


Fig. 4 Brain Activity for Muscle Force Control during Right Knee Extension Movements

A: Brain image during Incremental exercise to 20 %MVC (maximal voluntary contraction). (The resting state is subtracted.) B: Incremental exercise to 40 %MVC. An increase in Oxy-Hb concentration-length is confirmed in the left medial primary sensorimotor cortex. C: Incremental exercise to 60 %MVC. An increase in Oxy-Hb concentration-length is confirmed in the left medial primary sensorimotor cortex and left and right pre-frontal cortex. D: Decreased exercise from 20 %MVC. E: Decreased exercise from 40 %MVC. F: Decreased exercise from 60 %MVC. Greater Oxy-Hb concentration-length is confirmed in comparison with incremental exercise in the left and right pre-frontal cortex and supplementary motor cortex.

(Data supplied by: Shu Morioka, MD, PhD, Department of Neurorehabilitation, Graduate School of Health Science, Kio University)

References:

Nobusako, S., Hiyamizu, M., Maeoka, H., Morioka, S.: Neurorehabilitation and Brain Function Imaging—Walking (1), *Physiotherapy* 27: 274–282

Hiyamizu, M., Maeoka, H., Fujita, H., Morioka, S.: Neurorehabilitation and Brain Function Imaging—Upright Posture Control (2), *Physiotherapy* 27: 387–392, 2010

Taniguchi, H., Matsuo, A., Maeoka, H., Morioka, S.: Neurorehabilitation and Brain Function Imaging—Arm Reaching Movements (3), *Physiotherapy* 27: 499–504, 2010

Nobusako, S., Takebayashi, H., Hiyamizu, M., Maeoka, H., Morioka, S.: Neurorehabilitation and Brain Function Imaging—Muscle Force Control (5), *Physiotherapy* 27: 706–712, 2010

Simultaneous Measurement with EEG

Data

Application Example of Simultaneous Measurement with Electroencephalography (EEG)

More recently, to take advantage of superior spatial and temporal resolution characteristics, there has been interest in simultaneous measurement methods that combine noninvasive brain measurement methods.

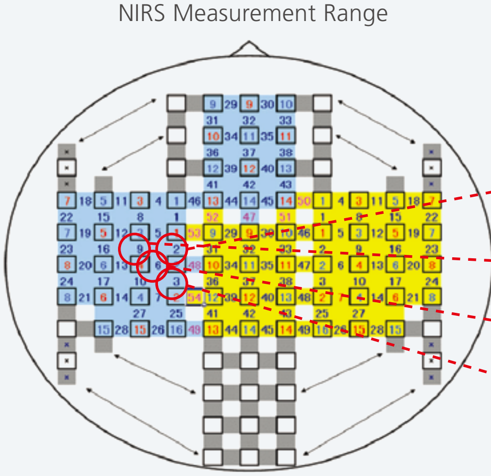
Simultaneous measurement with fNIRS and EEG was used to investigate the relationship between neural activity and the hemodynamic response of the somatosensory cortex to electric stimulation of the median nerve*.

* The median nerve extends from the brachial plexus and runs roughly down the center of the abdominal side of the upper extremities.

Fig. 1 Relative Positions of NIRS and EEG Probes

The whole-head holder (Fig. 1) includes EEG sockets ( ) located midway between the NIRS transmitter and receiver probes ( ) to align the NIRS channels (measurement points) with the position of EEG probes (Fig. 2a and 3a).

NIRS Measurement Range



Transmitters : Boxes containing blue numbers
Receivers : Boxes containing red numbers
Measurement Channels : Blue numbers
Special Channels : Red numbers

Fig. 2a Measurement Range of Transmitter and Receiver Fibers (103 channels)

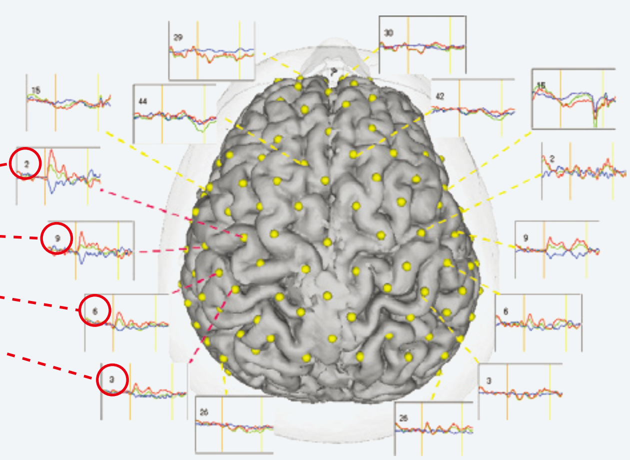
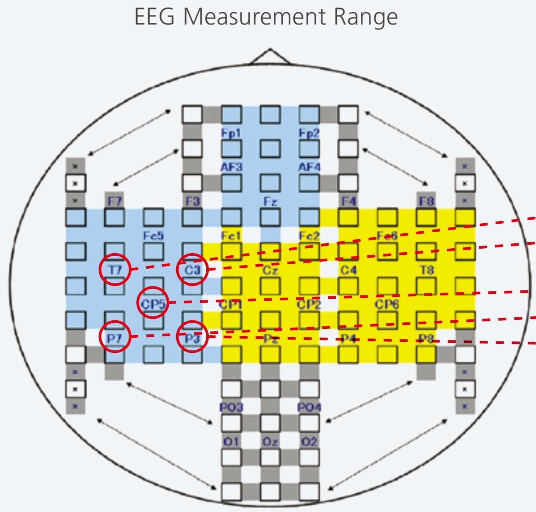


Fig. 2b Change in Oxy-Hb in Response to Electric Stimulation



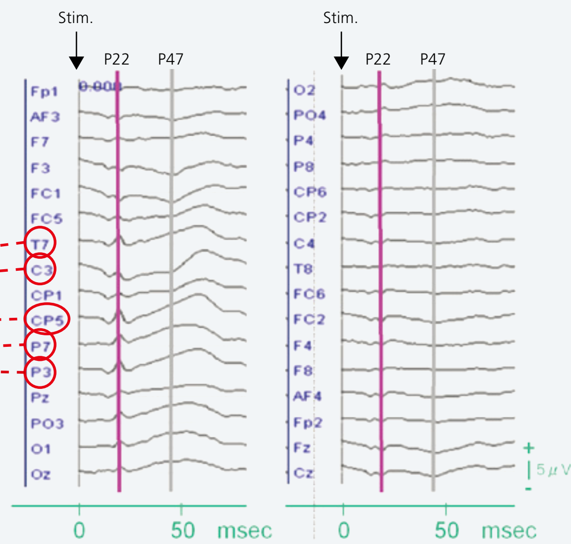
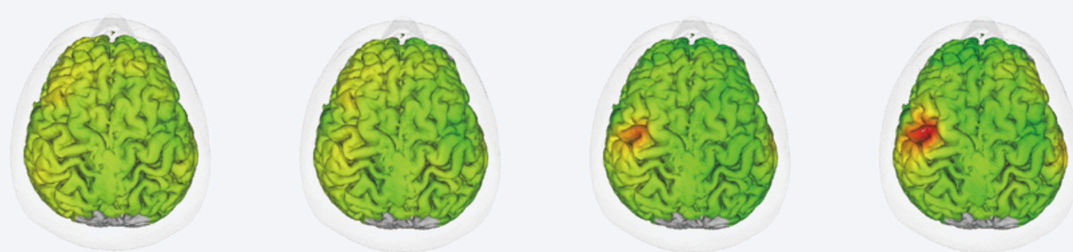


Fig. 3a Measurement Range of EEG Probes (32 channels)

Fig. 3b Somatosensory Evoked Electric Potential in Response to Electric Stimulation



0 sec 1 sec 3 sec 5 sec

Fig. 4 Brain Activity at Indicated Time (sec) Intervals After Electric Stimulation

Of all the locations where Oxy-Hb (Fig. 2b) and somatosensory evoked electric potential (Fig. 3b) were measured, the somatosensory evoked potential at P22 (positive wave at 22 ms of latency) increased in the primary somatosensory cortex of the ear (left) on the opposite side from the side that was electrically stimulated (Fig. 3a and 3b).

In addition, Oxy-Hb increased in the primary somatosensory cortex of the opposite ear from the electrical stimulation 5 seconds after the electrical stimulation (Fig. 4).

Simultaneous measurement using NIRS and EEG is especially effective for investigating the correlation between hemodynamic response and neural activity.

(Data provided by: Mr. Hisao Nishijo, Graduate School of Medicine and Pharmaceutical Sciences for Research, University of Toyama)

Reference:

Takeuchi., M, Hori, E., Takamoto, K., Tran, A.H., Kohno, S., Ishikawa, A., Ono, T., Endo, S. and Nishijo, H. (2009) "Brain cortical mapping by simultaneous recording of functional near infrared spectroscopy and electroencephalograms from the whole brain during right median nerve stimulation." *Brain Topogr*, 22, 197–214.

NIRS Signal Analysis Method

Data

Various non invasive methods are available to measure brain activity. One of these, functional magnetic resonance imaging (fMRI), has helped clarify higher order brain functions such as cognition and language. However, fMRI does not permit the subject's body, the head in particular, to move during measurements, which is problematic for brain function measurements in natural situations. At the same time, interests in near-infrared spectroscopy (NIRS) has increased in recent years. As NIRS permits brain function measurements in natural situations, it may support applications that fMRI cannot address. There is much debate about how to interpret signals obtained by NIRS, and it is problematic that no statistical signal processing method has yet been determined. Signals obtained by NIRS contain noise from the measurement instrument and effects from the subject's pulse, breathing and blood pressure fluctuations. Relative changes in NIRS signal values after the start of measurements make it difficult to compare data between subjects or to evaluate general trends during tasks.

Signal Processing by Multiresolution Analysis and Applying Standard Scores

A method is required to eliminate the signals unrelated to brain activity and to evaluate general brain activities during tasks. We have developed such a method. In the method, multiresolution analysis by discrete wavelet transform divides the NIRS signals into various frequency components, as shown in Fig. 1. The signal components corresponding to the task are then extracted and the signals are expressed as standard scores.

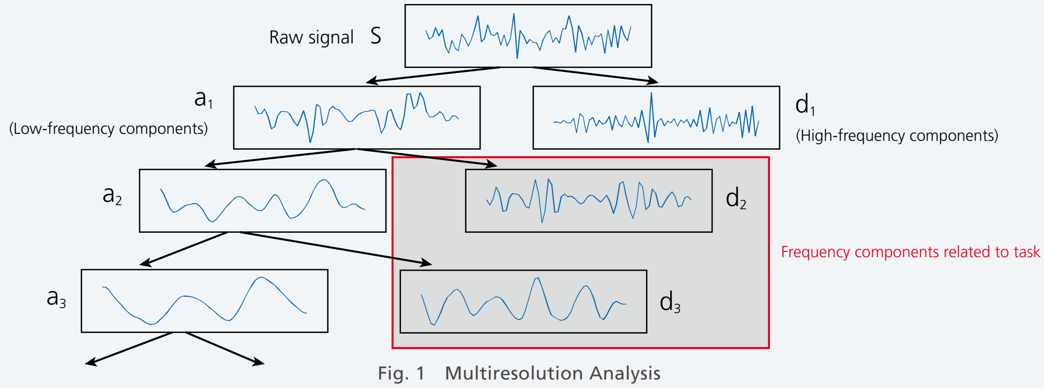


Fig. 1 Multiresolution Analysis

Fig. 2 shows a comparison between the raw signals and the signal components related to brain activity that were extracted by multiresolution analysis and reconstructed. It is apparent that the analyzed signals more clearly show the Oxy-Hb and Deoxy-Hb fluctuations.

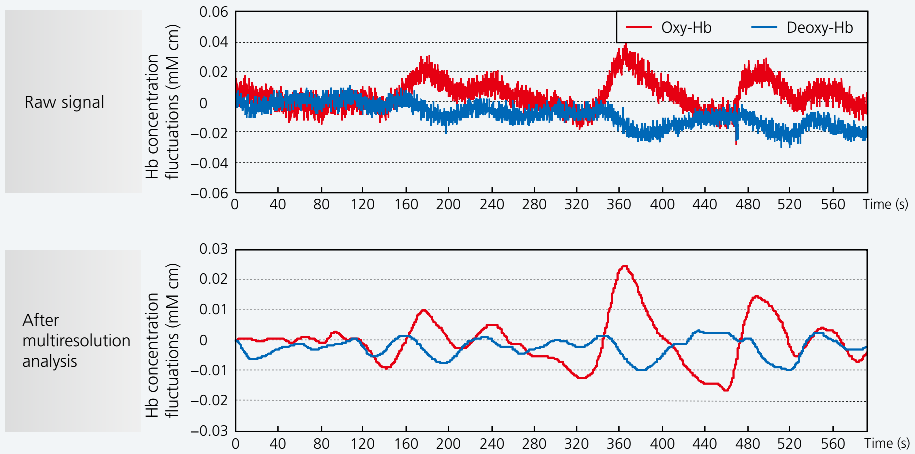


Fig. 2 Comparison of Raw Signals and Signals After Multiresolution Analysis

This example shows the simultaneous measurement of brain activity by NIRS and fMRI while performing three arithmetic tasks with different degrees of difficulty. The method we developed was then used to create brain activity images. Standard scores were applied to the NIRS signals after multiresolution analysis and the signals from the nine subjects were averaged to create brain activity images.

Fig. 3 shows comparisons between the fMRI and NIRS brain function images. Both show that the higher the degree of difficulty of the arithmetic task, the greater the activity of both lateral frontal lobes.

Low degree of difficulty

Addition of single digits with no carry-over
Example: 3 + 5

Medium degree of difficulty

Addition of three numbers
Example: 6 + 5 + 9

High degree of difficulty

Subtraction and division using decimals
Example: 72 ÷ (0.45 – 0.32)

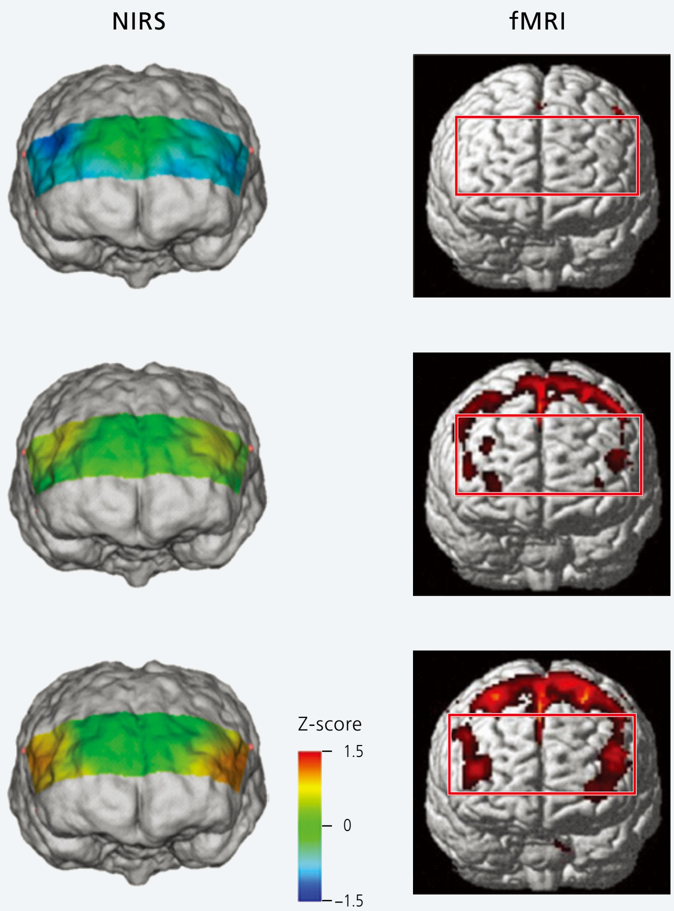


Fig. 3 Comparison of Brain Function Images by NIRS and fMRI (9 subjects)

Introduced here is a method of NIRS signal analysis using a combination of multiresolution analysis by discrete wavelet transform and applying standard scores. Simultaneous NIRS and fMRI brain function measurements were made while performing arithmetic tasks. Comparison of the fMRI results and the brain function images created by the method introduced here show similar trends.

In the future, we hope to expand application of this method to tasks that are difficult to measure by fMRI, such as brain activity measurements on car drivers, and to the development of brain-computer interfaces (BCI) for operating equipment by thoughts alone.

(Data supplied by: Prof. H. Tsunashima, Department of Mechanical Engineering, College of Industrial Technology, Nihon University)

Investigating Inner Speech

Data

NIRS signals from the head surface were used to estimate the time when the subject made inner speech without vocalization and to guess a number between 1 and 5 reechoes by the subject in his/her mind.

Two separations between transmitter and receiver optical fiber probes (7 and 18 mm spacing), as shown in Fig. 1, were used to measure the NIRS signals across the entire left and right forehead. Simultaneous measurements of the scalp blood flow and electromyograms were performed to evaluate the effects of skin blood flow and muscle blood flow on NIRS signals.

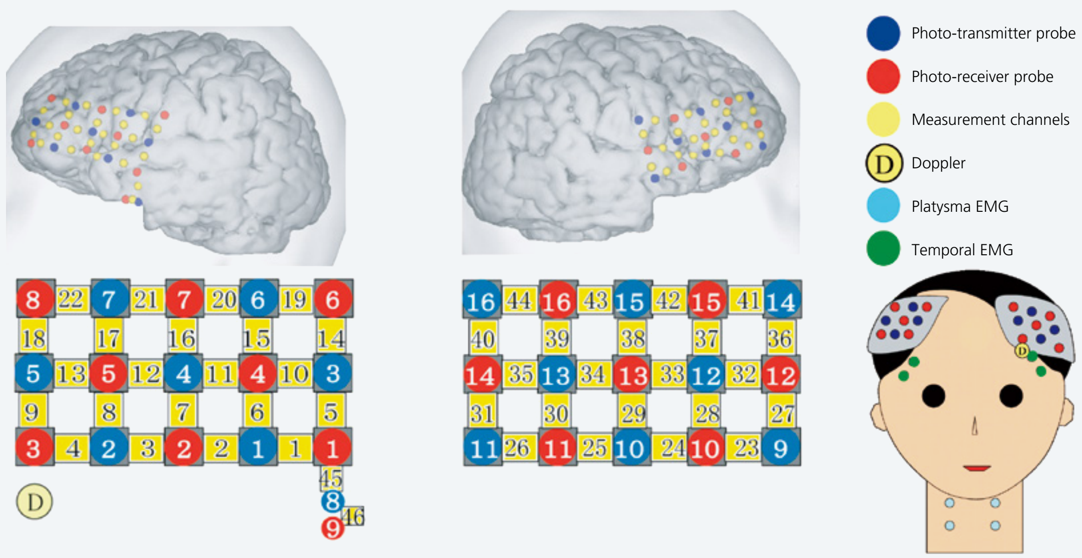


Fig. 1 Multiresolution Analysis

The probe channel positions are projected onto the MRI brain surface image. Probes are placed at 18 mm spacing in a 3×5 arrangement over the entire left and right forehead (44 ch), and at 7 mm spacing on the left forehead (1 ch).

Fig. 2 shows typical NIRS signals when the subject recites a tongue twister internally without vocalization when the chosen number is read. Multiple channels containing Broca's area (representative channel 11) show a transient increase in Oxy-Hb and Total-Hb concentrations when the chosen number 3 is read.

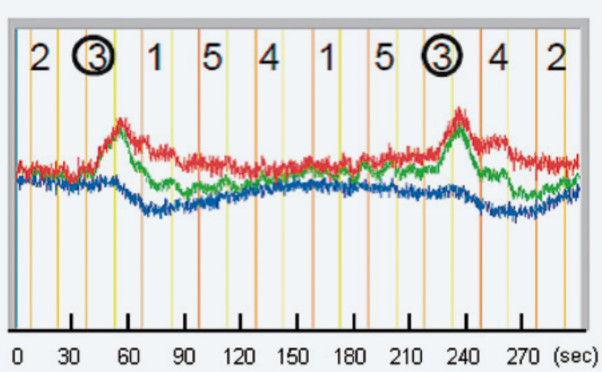


Fig. 2 Typical NIRS Waveforms Blood Flow Fluctuations in Broca's Area (representative channel 11).

NIRS waveform results from four subjects were visually evaluated by five researchers. They were able to determine the number chosen by the subject with 73 % accuracy.

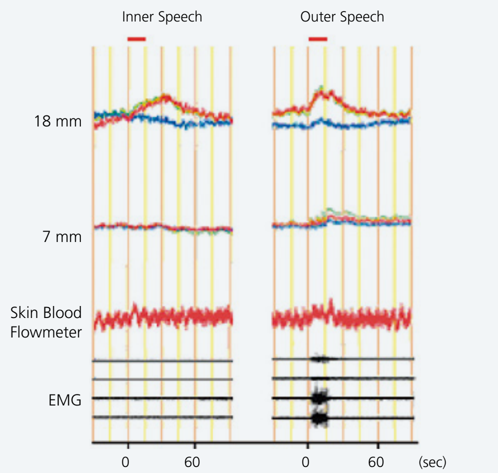


Fig. 3 NIRS Waveforms, Skin Blood Flow Fluctuations, Electromyogram during Inner Speech and Outer Speech

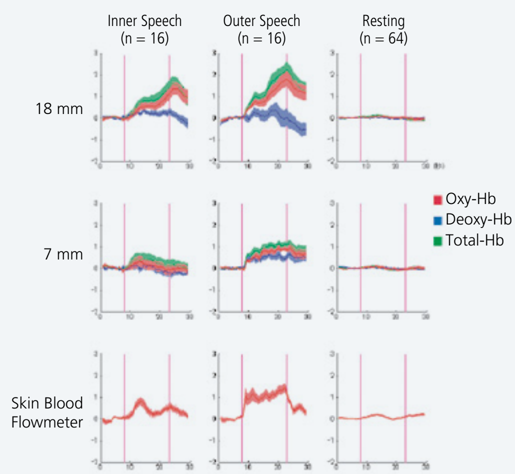


Fig. 4 NIRS and Skin Blood Flow Average Waveforms during Inner Speech, Outer Speech, and Resting

Shadow width ±1S.E. Resting shows the average waveform when a number different from the pre-chosen number is read.

The large changes in the electromyograms of the left and right platysma and temporal muscles that occur under outer speech conditions when a tongue twister is recited out loud indicate activity in these muscles.

Increased skin blood flow measured by the Doppler skin blood flowmeter can be observed throughout the outer speech period. NIRS measurements at the short probe spacing (7 mm) also indicate that Oxy-Hb and Total-Hb concentrations increase continuously during the outer speech period (Fig. 3).

Conversely, no changes in the platysma and temporal electromyograms are apparent with inner speech. This provides objective evidence that no vocalization occurs. The short transient increases (interval approx. 5 sec, rising latency tune approx. 3 sec) were detected by the Doppler skin blood flowmeter, although not as large as for outer speech and no continuous increase in blood flow was apparent (Fig. 3).

The NIRS signals in the representative channel near Broca's area and the averaged Doppler skin blood flow signals yielded similar results (Fig. 4).

These results indicate that it is necessary to consider at least the skin blood flow and muscle activity effects when interpreting the NIRS signals during NIRS measurement tasks involving vocalization. The possibility remains that even during inner speech involving no vocalization, skin blood flow fluctuations due to autonomous nervous system activity may affect the NIRS signals. Consequently, a method to eliminate the effects of skin blood flow and muscle activity on NIRS signals is particularly important when performing measurements to measure brain functions.

NIRS measurements make it possible to estimate the time when the subject recited a tongue twister internally without vocalization and further estimate the number pre-chosen by the subject with a certain degree of accuracy. It was confirmed that the NIRS measurements with 7 mm probe spacing produced data reflecting the skin blood flow fluctuations and that the NIRS measurements with 18 mm probe spacing produced data reflecting brain blood flow fluctuations independent of the skin blood flow fluctuations.

The ability to distinguish between brain activity-derived NIRS signals and skin blood flow signals during inner speech promises future applications of NIRS measurements to BMI.

(Data supplied by: Shigeru Kitazawa, MD, PhD, Juntendo University School of Medicine

Reference:

Iwano, T., Takahashi, T., Takigawa, J., Kawagoe, R., Shibuya, S., Kitazawa, S. (2010) "Detection of inner speech using near infrared spectroscopy", *Shimadzu Review*, Vol. 66, No. 3, 4

Language Processing Functions

Data

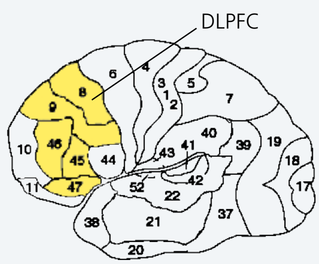
Semantic Processing and Brain Functions in Chinese/Japanese Bilingual Subjects

There are some isomorphic words that are written the same in Japanese and Chinese but have different meanings. For example, 汽車 means “automobile” in Chinese but “steam train” in Japanese. We were able to confirm differences in brain function between Chinese/Japanese bilingual subjects (first language (L1): Chinese, second language (L2): Japanese) and Japanese monolingual subjects (first language: Japanese) during the semantic processing of isomorphic words.

fNIRS measurements on the Chinese/Japanese bilingual subjects revealed lower activation of semantic information in the non-target first language during processing targeting the second language in which the subject has a lower degree of proficiency.

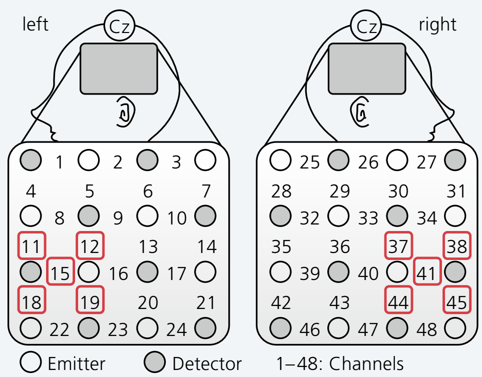
Measurement Positions

12 bilingual and 12 monolingual subjects were measured. fNIRS measurements were performed using 48 channels on the left and right side of the dorsolateral prefrontal cortex (DLPFC), which contains Brodmann’s areas 9, 45, and 46 that are involved with language and communication.



Muzur *et al.* (2002)

Arrangement of 48 Channels

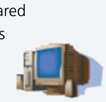


Channels presumed to be positioned on DLPFC (BA 45, 46, and 9)

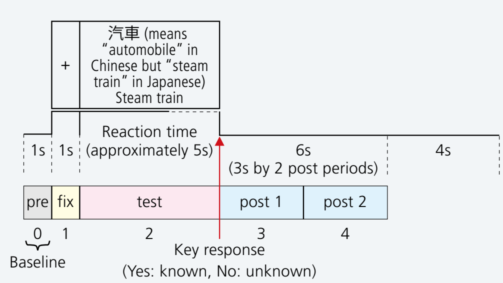
Data Acquisition Intervals

Japanese/Chinese isomorphic words were visually presented together with one of four types of pictures corresponding to a meaning that is Japanese-specific, Chinese-specific, shared in Japanese and Chinese, or does not exist in Japanese or Chinese. The bilingual and monolingual subjects were asked to determine whether the picture represents the meaning in Japanese of the presented Japanese/Chinese isomorphic word. There are three data acquisition intervals: the “test” interval when the evaluation is performed, the “post 1” interval of hypothesized reduced searching for semantic information in the non-target language (L1, Chinese), and the “post 2” interval of hypothesized concentration on the meaning in the target language (L2, Japanese). The Hb concentration changes in each interval were compared between the bilingual and monolingual subjects.

Yes / No Responses to Four Meanings

		Japanese	
		Exists	Does Not Exist
Chinese	Exists	Shared (e.g., 温泉 (means “hot spring” in Japanese and Chinese)) 	Chinese-specific (e.g., 汽車 (means “automobile” in Chinese but “steam train” in Japanese)) 
	Does Not Exist	Japanese-specific (e.g., 汽車 (means “automobile” in Chinese but “steam train” in Japanese)) 	Unshared (e.g., 温泉 (means “hot spring” in Japanese and Chinese)) 
Correct response		Yes (known)	No (unknown)

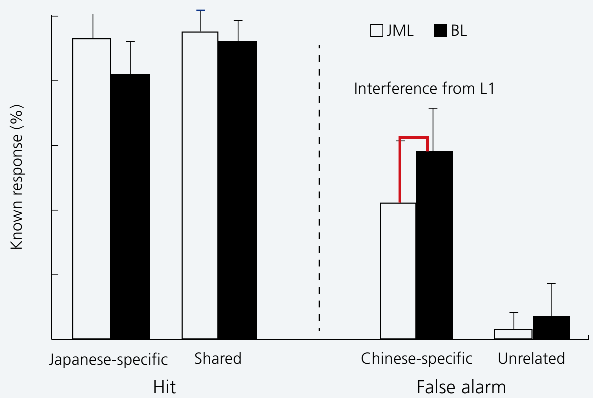
fNIRS Measurement Intervals



Results

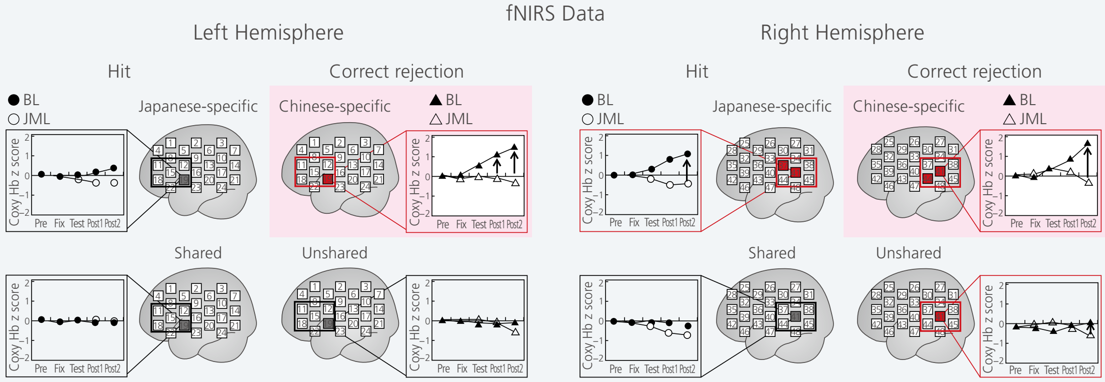
When a Japanese/Chinese isomorphic word was presented to the bilingual subjects together with a picture representing the meaning in the non-target language (L1, Chinese), the false response rate (proportion falsely identified as the Japanese meaning) was higher than in the monolingual subjects. This result shows that the non-target language (L1) processing seems to interfere with the target language (L2) processing in bilingual subjects.

Yes Response Rate



Two-way analysis of variance on the subject groups (bilingual, monolingual) and the data acquisition intervals (test, post 1, post 2) revealed that, unlike the monolingual subjects, the bilingual subjects exhibited significant activation of the left DLPFC when evaluating a Japanese/Chinese isomorphic word presented with a picture showing the meaning specific to the non-target language (Chinese). This result suggests that the left DLPFC activated to inhibit interference from the non-target language (Chinese). Unlike the left DLPFC, the right DLPFC activated under a wide-range of conditions (Japanese-specific, Chinese-specific, does not exist in Japanese or Chinese) that require target language (Japanese) processing. Attention must be paid to the activation of the right DLPFC to determine whether the subject understands the meaning in Japanese.

fNIRS Data



For semantic processing of the target language (L2) by bilingual subjects, fNIRS measurements clearly reveal that the left DLPFC is related to the reduced L1 activity in the early processing stage (post 1) and the right DLPFC is related to maintaining attention on L2 in the late processing stage (post 2).

(Data supplied by: Hirofumi Saito, PhD, Graduate School of Information Science, Nagoya University)

Reference:
Misato Oi, Hirofumi Saito, Hiroshi Ito and Paul L. Rumme. (2010).
"Semantic judgment of Chinese–Japanese bilinguals: a near-infrared spectroscopy study" *NeuroReport* 21(2): 127–131.

Mental Disorder Research

Data

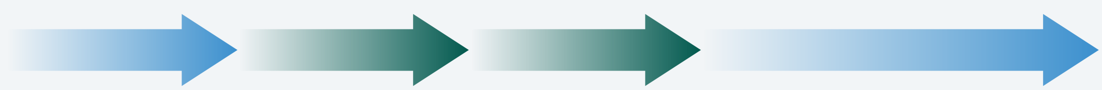
Brain Activity Changes in the Prefrontal Cortex of Subjects with Depression or Bipolar Disorder During Verbal Fluency Tasks

Cognitive impairment and associated functional disorders of the frontal lobe are known characteristics in depression subjects. Verbal fluency tasks are widely used in brain-function research as one of the most sensitive methods of determining cognitive impairment.

fNIRS measurements of Oxy-Hb concentration using 42 prefrontal cortex channels were conducted on 14 bipolar disorder subjects, 39 depression subjects, and 24 healthy subjects performing verbal fluency tasks. The new task presentation method and data analysis method found significantly lower Oxy-Hb concentration in the depression and bipolar disorder groups compared to the healthy group, as well as significant differences in the hemoglobin waveforms between the depression and bipolar disorder subjects.

Task Presentation Method

Pre-test rest (30 sec.); Recall and Japanese words beginning with “*ka*” (30 sec.); hemoglobin; Recall and say Japanese words beginning with “*no*” (30 sec.); Post-test rest (70 sec.)

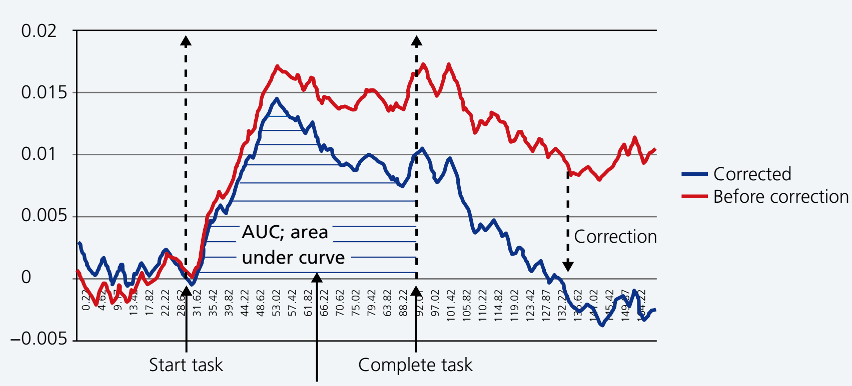


(In Japanese, words beginning with “*ka*” are the most common, while words beginning with “*no*” are the least common.)

Data Analysis Method

The moving-average method is used to reduce the noise components and baseline-shift correction is applied to the changes in Oxy-Hb concentration. The following two index values are calculated for the average waveform data for all 42 channels, and the p values are calculated between the subject groups and healthy group.

- Signal integrated value over the 60 sec. task time ((1) AUC: area under the curve)
- Time to reach half the signal integrated value during the task ((2) WC: weighted center)



Meaning of AUC and WC Indexes

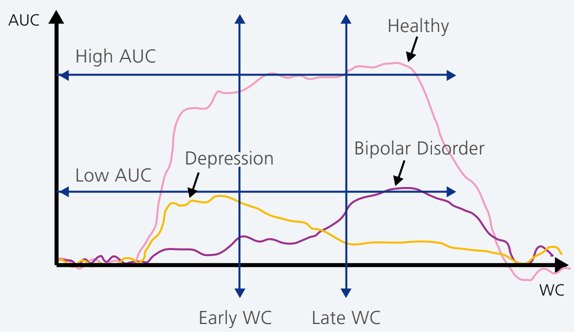
Results

The average Oxy-Hb in both sides of the pre-frontal cortex showed different patterns in the three groups.
In comparison with the healthy subjects, AUC is characteristically low in the bipolar disorder and depression subjects, and significant differences in WC are apparent in their waveforms. (See the diagram below.) With depression, heightened AUC occurs early in the verbal fluency task but is not maintained and drops, and the low state continues. However, AUC increases later in the case of bipolar disorder. The peaks are clearly lower than in healthy subjects.

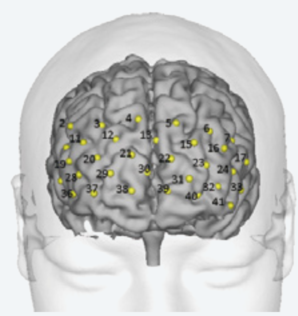
Group Comparison of Two Indexes Using Measurement Channel Average Values

	Bipolar disorder group (n = 14)	Depression group (n = 39)	Healthy control (n = 24)	Group Comparison p Value
AUC	2.9 ± 3.6	1.8 ± 2.5	5.5 ± 3.2	p < 0.001
WC	34.2 ± 12.8	25.3 ± 14.8	33.9 ± 5.2	p = 0.01

Schematic View of Differences in AUC and WC Determined from Averages of Healthy, Depression, and Bipolar Disorder Groups



Measurement Channel Positions



Bipolar disorder and depression were distinguished by discriminant analysis using the AUC parameter conventionally used in research to express overall activity and the new WC parameter that reflects the temporal activity of the cerebral cortex. Values of 0.71 sensitivity and 0.46 specificity were achieved in the detection of bipolar disorder.

Discriminant Analysis of Bipolar Disorder

		Disease Diagnosis	
		Bipolar Disorder	Depression
Discriminant Analysis	Bipolar Disorder	10	21
	Depression	4	18

These results suggest that even a diagnosis of long-term depression may occasionally be altered to a diagnosis of bipolar disorder.

Applying the task presentation method and data analysis method introduced here to fNIRS measurements may provide an effective monitoring tool for brain function evaluations related to mental disorders in the future.

(Data supplied by: Shinji Shimodera, MD, PhD, Department of Neuropsychiatry, Kochi Medical School, Kochi University)

Reference:
Shimodera, S., Imai, Y., Kamimura, N., Morokuma, I., Fujita, H., Inoue, S., Furukawa, T. A. (2012).
"Near-infrared spectroscopy of bipolar disorder may be distinct from that of unipolar depression and of healthy controls." 4(4): 258–265.

Versatile Application Fields

Application Range Has Grown to Meet the Diverse Needs of Research.

Since the beginning of the current century, brain science research is accelerating more and more. Research is no longer limited to basic research, but is now available for a wide variety of applications. As appropriate instruments, experiments and data is analyzed, are designed according to various research objectives, brain science will surely continue to develop. In that context, fNIRS provides a key to bringing brain science to additional new fields. We hope Shimadzu's LABNIRS will be helpful for your research and also contribute to the further development of brain science.

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