SHIMADZU
Excellence in Science

ADVANCED HEALTHCARE

Shimadzu Advanced Healthcare
—Current Status and Future Outlook—

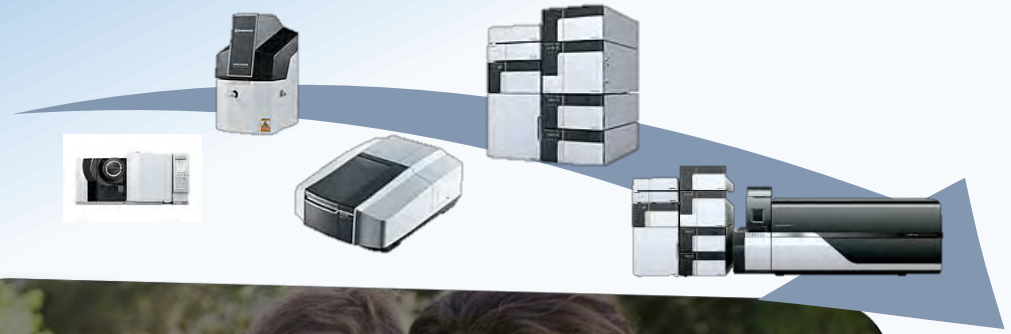
Creating the Future of Healthcare with Partners
～ SHIMADZU Advanced Healthcare ～

- Pioneering Partnerships for Advanced Healthcare -

Shimadzu Advanced Healthcare

- Supply products and services that offer new added value by integrating analytical/measuring technology with medical imaging technology.
- Provide cross-categorical support for the entire series of healthcare stages, starting with routine health management and extending to diagnostics, treatment, and prognosis management.

Analytical and Measuring Technologies



Advanced Medical Diagnostic Imaging Technologies

- Fluoroscopy systems
- Angiography systems
- General-radiography systems
- PET systems
- Near-infrared light application systems

Medical Diagnostic Imaging Technologies

Advanced Analytical and Measuring Technologies

- Chromatography systems
- Mass spectrometry systems
- Photometric analysis systems
- Surface analysis and observation systems
- Life science-related analysis systems

Platform for Health Promotion that Underlies Advanced Healthcare

With a particular focus in three areas of disease—dementia, cancer, and lifestyle diseases, Shimadzu is implementing advanced healthcare measures based on a platform for improving health that spans the entire scope of healthcare, from routine health management to prognosis management.

	Routine Health Management	Ultra Early Examination	Diagnosis	Treatment (treatment support)	Prognosis Management
Cancers	**(3) Health management business** Health management Recording/ managing daily activity logs Diet Exercise Sleep	**(2) Next-generation examination business** Disease marker analysis (mass spectrometry)	**(1) Integrated analytical-medical systems** Diagnostic imaging (PET, mass spectrometry)	**(1) Integrated analytical-medical systems** Cancer photoimmunotherapy (treatment support) Support for acquiring blood samples from adrenal veins (X-ray, mass spectrometry)	**(2) Next-generation examination business** Biomarker analysis (mass spectrometry)
Lifestyle Diseases			Bone mineral density measurement/angiographic diagnostic imaging (X-ray)		Medication management (mass spectrometry)
Psychiatric/ Neurological Disorders			Initial consultation by specialist	**(2) Next-generation examination business** Assessment of functional improvements for mild cognitive impairment (near-infrared imaging system)	Brain function rehabilitation (near-infrared imaging system)
Healthcare Systems	Healthcare systems for comprehensive support Disease prevention/health improvement by behavioral changes				

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Preventing and Living with Dementia

Currently, Shimadzu is considering how best to contribute toward building a kinder society where people can live a rich life without fear if they develop what is called “dementia” or even if they are still in the “mild cognitive impairment” (MCI) stage.

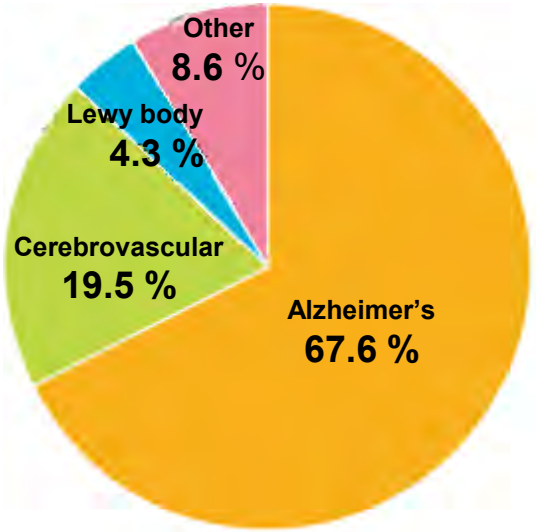
Dementia and Alzheimer's Disease

- **Dementia (symptoms)**
  - Dementia refers to impairments in ability to recognize or decide things that interfere with living in society.
  - Alzheimer-type dementia (Alzheimer's disease) is one type of dementia. Other types of dementia include vascular dementia, Lewy body dementia, and frontotemporal dementia.

- **Dementia Patients (units: 1,000 people)**

	2015	2030	Increase (%)
World*1	46,780	74,690	160
Japan*2	5,170	7,440	144

*1: World Alzheimer Report 2015
*2: Based on 2014 grants-in-aid for special scientific research from the Ministry of Health, Labour and Welfare



- **Alzheimer-type dementia accounts for about 68 %. There is still no treatment method (drug) for the root causes.**

Advanced Healthcare for Brain Disorders

- **Offer various series of advanced healthcare products for applications ranging from from Ultra-Early Diagnosis to treatment, and prognosis management.**
- **Contribute to researching and developing prevention and treatment of root causes related to brain disorders by enabling visualization of the status of the brain and mind.**

Ultra-Early Diagnosis and Prevention

Notice and prevent dementia before it develops.

Technology for non-invasively monitoring brain function as easily as routine activities

- Near-infrared brain function imaging system (fNIRS) used to assess cognitive functions
- Technology for predicting beta-amyloid plaque levels in the brain by MALDI measurement of beta-amyloid peptide markers in the blood (amyloid MS)

Diagnosis, Examination, and Treatment

Improve performance of medical checkups and diagnoses.

Technology for detecting brain structure or variations in blood flow or detecting biomolecular or chemical reactions associated with abnormal conditions or while maintaining a normal state

- fNIRS used to assist in distinguishing depression
- Technology for predicting beta-amyloid plaque levels in the brain by MALDI measurement of beta-amyloid peptide markers in the blood
- Technology for assessing dementia risk based on protein markers in the blood
- Dedicated brain PET system intended for high sensitivity and high resolution

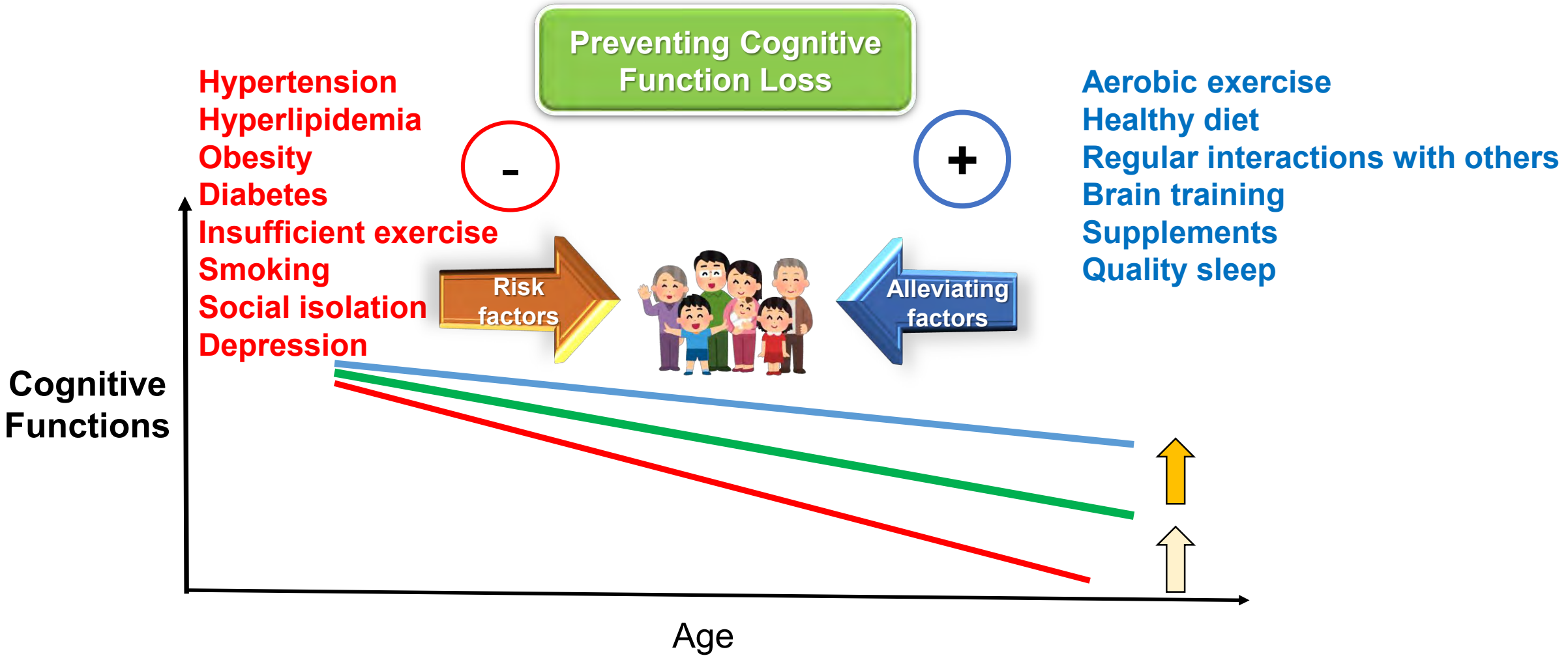
Prognosis Management

Improve rehabilitation efficiency.

Technology for assessing the recovery level of lost motor functions by measuring brain activity while imagining exercise

- Using fNIRS to detect and provide feedback from brain activity in stroke patients as they imagine moving their body

Risk Factors and Alleviating Factors Related to Cognitive Function Loss



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Routine Health Management

Control exercise, diet, sleep, and other factors.

Systems for continuously monitoring health in an easy and fun manner and then suggesting individualized methods for improving health

- Platform for improving health
- Start with dementia prevention and then expand to other packages (such as mental health or lifestyle diseases).

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Platform for Improving Health: Dementia Prevention Package

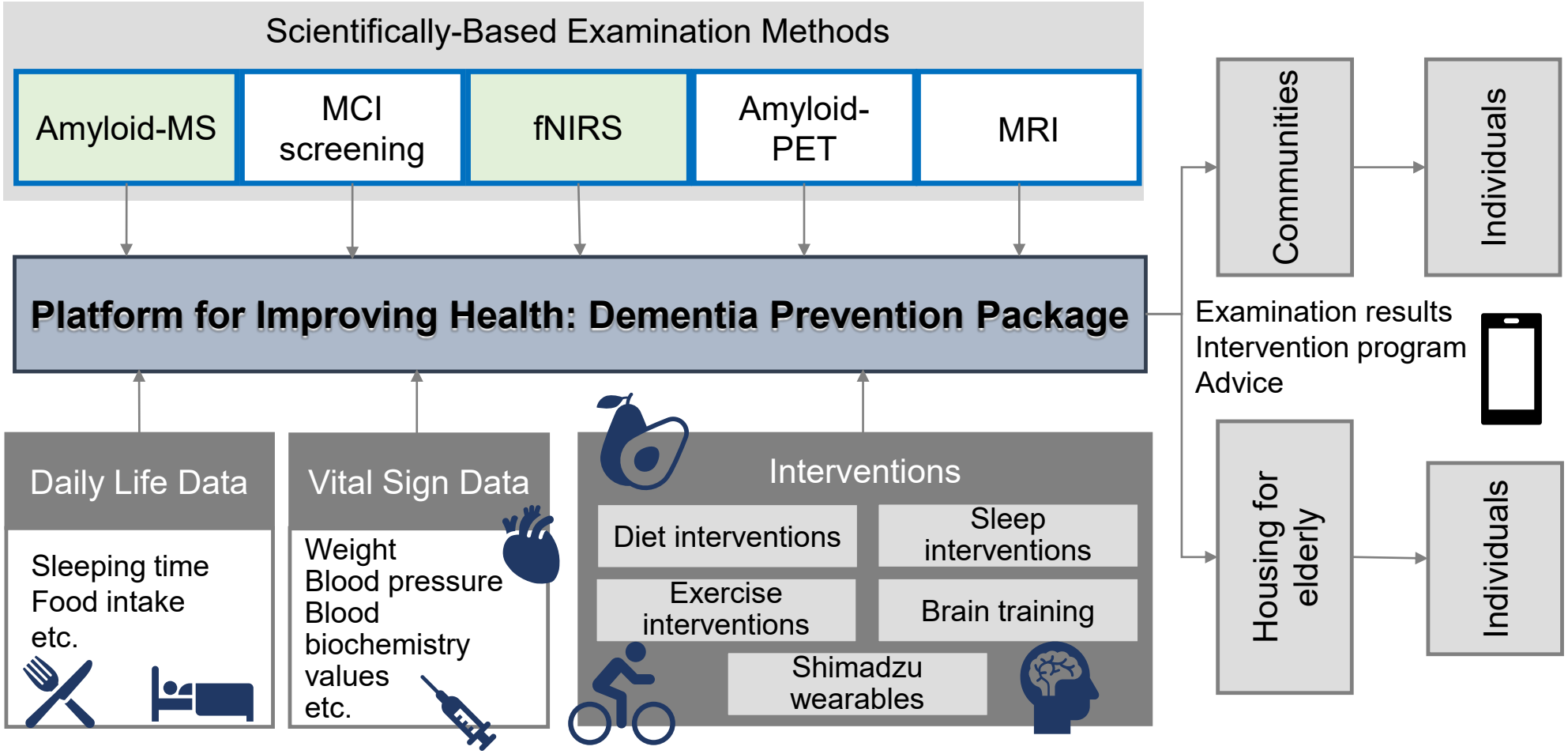
- Use the various scientifically-based examination methods in which Shimadzu has been involved to offer a software application that records data from daily life and encourages behavioral changes to seamlessly offer optimal interventions for preventing/delaying dementia.

Value Provided to Medical Institutions

- Screen for dementia (high-risk groups)
- Confirm effectiveness of interventions.
- Measures for preventive medicine and early treatment

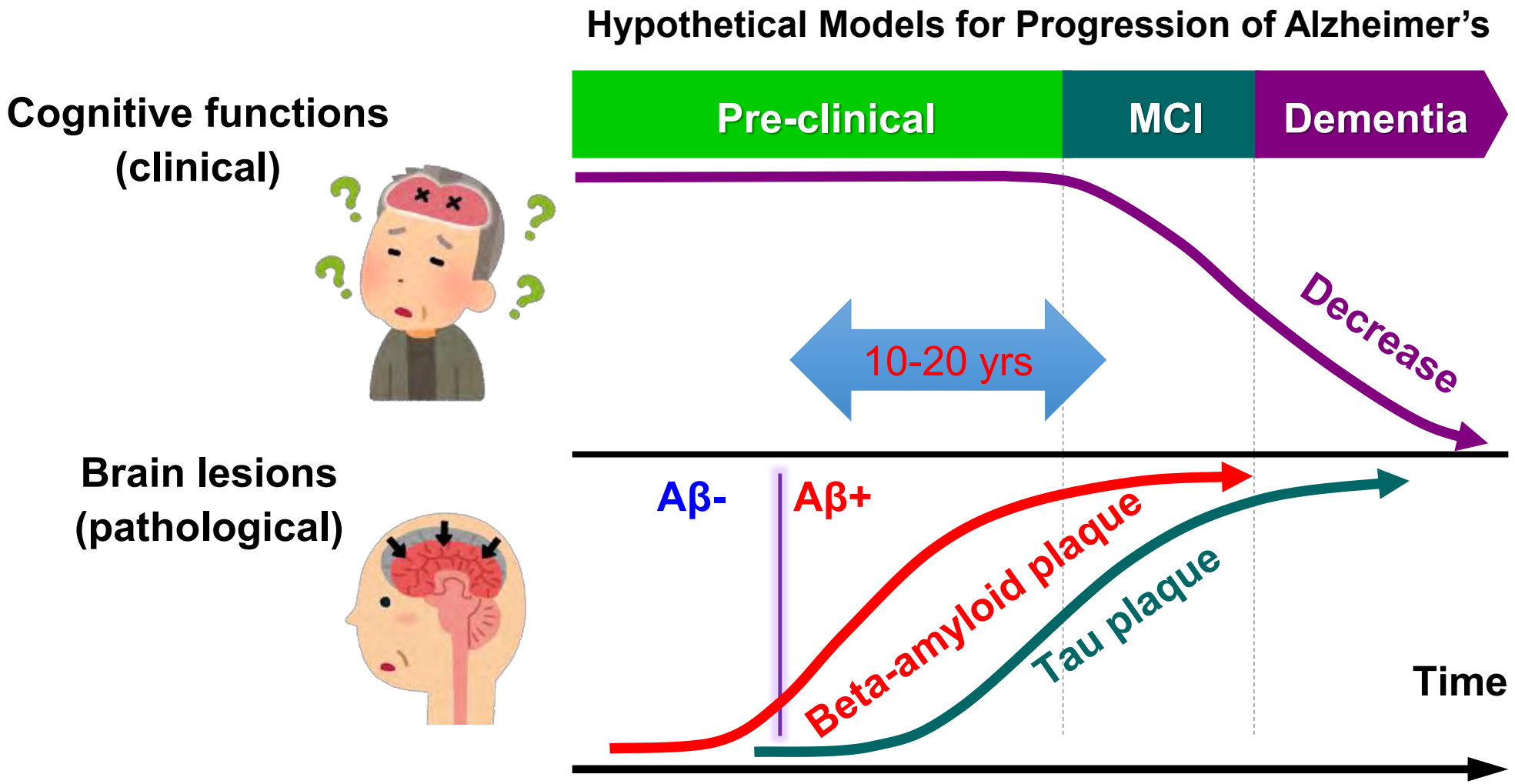
Value Provided to Regions

- Contribution to building communities with high citizen satisfaction levels
- Creation/operation of gathering places or other systems for promoting healthy behavioral changes



Amyloid-MS

Hypothetical Models for Progression of Alzheimer's



Lesions in the brain must be discovered before cognitive function decreases.

Detecting Changes in the Brain (Amyloid Plaque Levels)

Existing Methods

PET examination
(high cost and few facilities)

or

Cerebrospinal fluid test
(invasive)

Predict presence of brain changes (abnormal amyloid plaque levels)

Normal

or

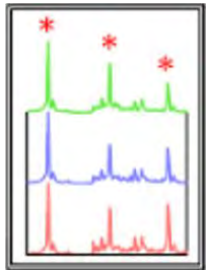
Abnormal

If Blood Biomarkers are Used

Blood plasma

…

MALDI-MS



Blood test
(minimally invasive, inexpensive, and capable of large-scale examinations)

Target: Beta-amyloid in blood plasma

But...

- Blood plasma contains only extremely tiny quantities of beta-amyloids (1/100 of level in cerebrospinal fluid).
- They could not be detected by MS, of course, or by ELISA either.

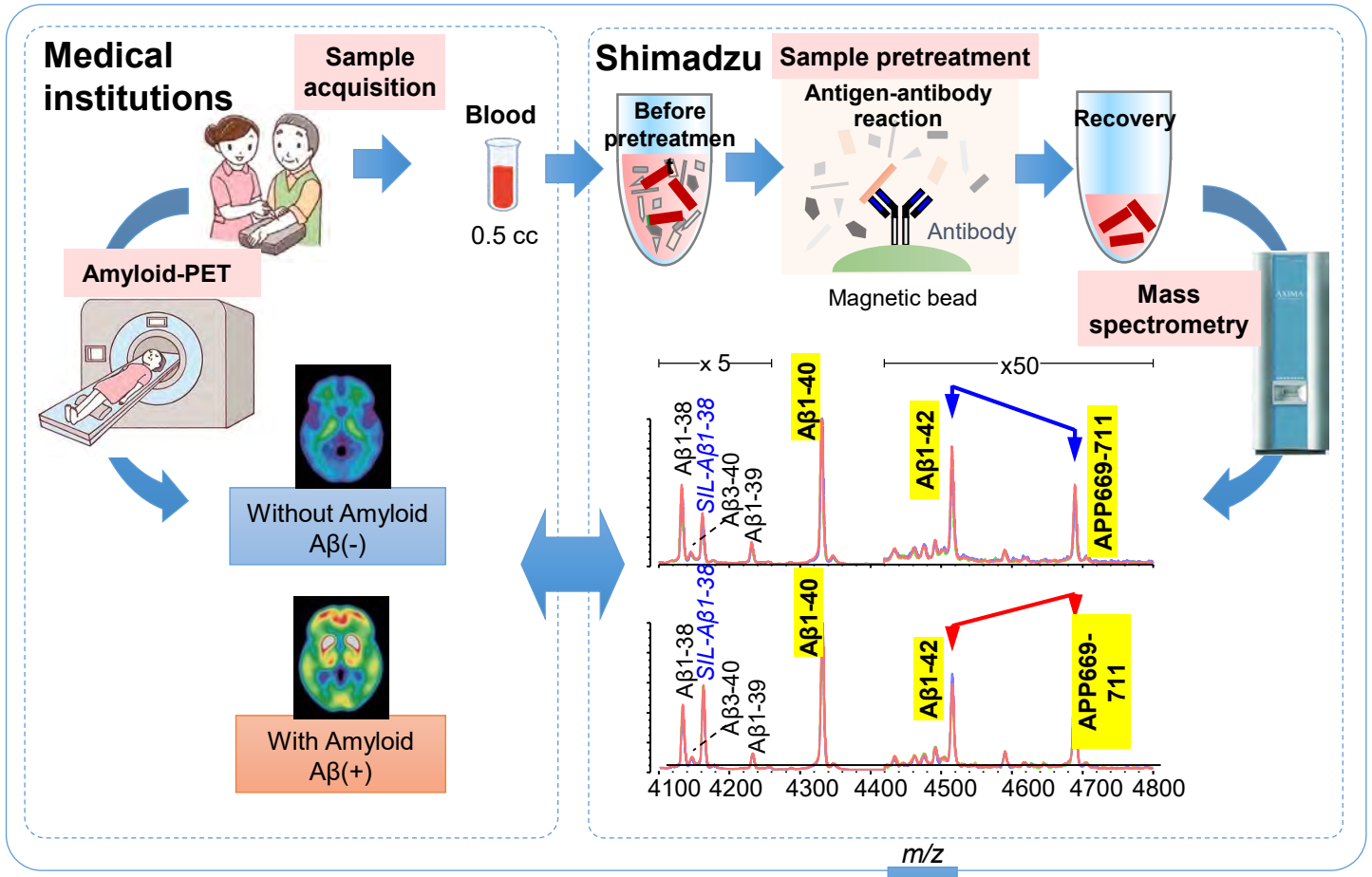
Press Release (January 31, 2018)
Method Established for Predicting Brain Changes (Amyloid Plaques) from 0.5 cc of Blood

Healthcare institutions in Japan
1. National Center for Geriatrics and Gerontology (NCGG)
2. Tokyo Metropolitan Geriatric Medical Center
3. Kindai University

Search

Healthcare institutions in Australia
Florey Inst. (AIBL)
1. Melbourne
2. Perth

Verification



Results

■ **Using identical composite biomarkers and decision criteria (cutoff values), samples from both Japan and Australia indicated high accuracy (percentage of correct amyloid plaque levels).**

Combined

Two types of biomarkers

$APP_{669\text{-}711}/A\beta_{1\text{-}42}$, $A\beta_{1\text{-}40}/A\beta_{1\text{-}42}$

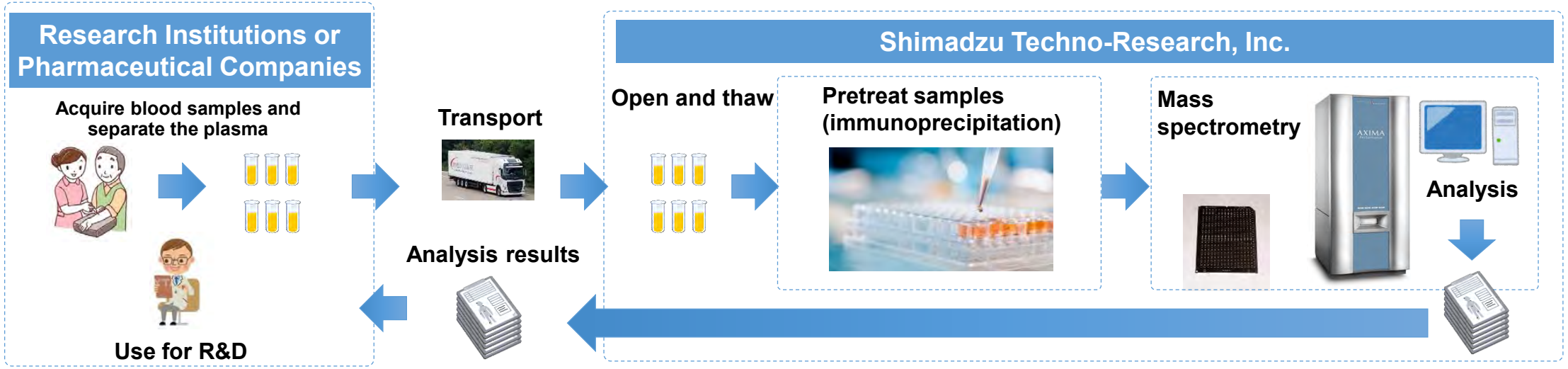
New

Composite biomarker

Amyloid MS Contract Analysis Service
(Started August 2018)

Applications
- Pharmaceutical companies (for developing drugs to treat Alzheimer's)
- Pharmaceutical research institutions

Purpose of Data Analysis
- Patient recruitment for clinical trials (as substitute or supplement for PET or CSF analysis)
- Other clinical research



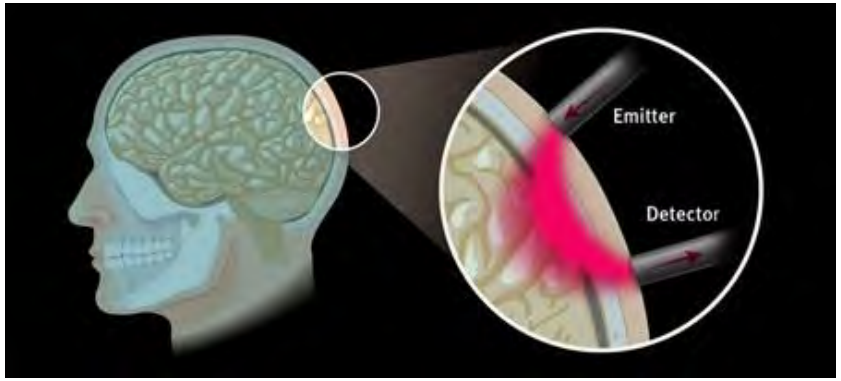
fNIRS

Measurement Principle of fNIRS

fNIRS (functional Near-Infrared Spectroscopy) systems use near-infrared light to safely measure the oxygen level in biological tissue without harming the body. They are used to measure brain activity.

LABNIRS
Near-Infrared Brain Function Imaging System

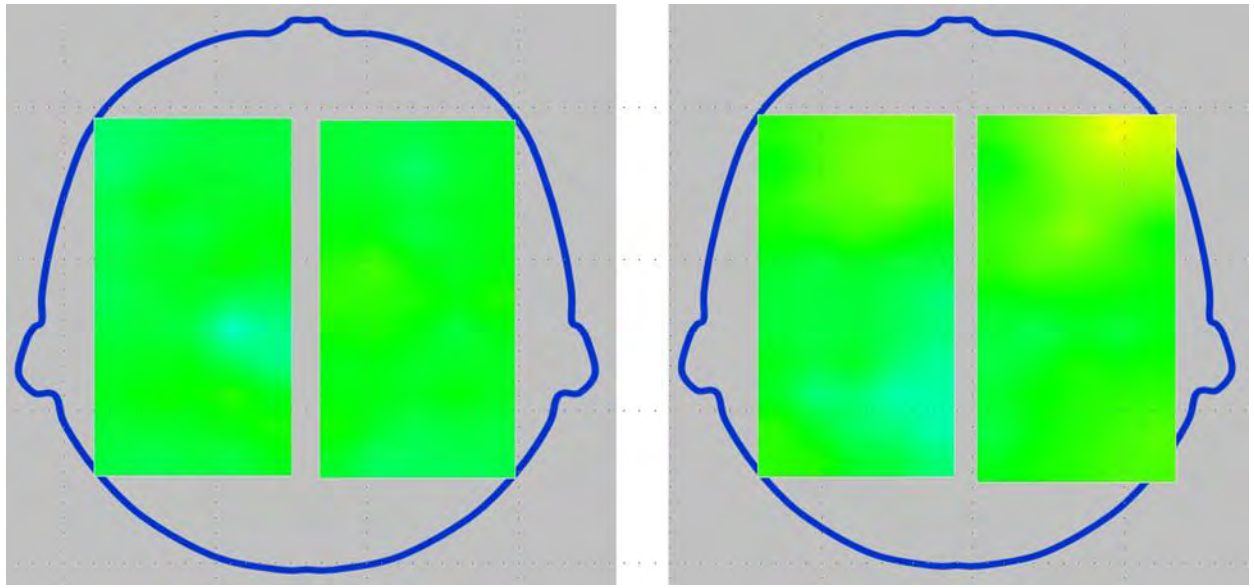
Illustration of Near-Infrared Light Measuring the Brain Surface



What is fNIRS?
fNIRS (functional near-infrared spectroscopy) measures the oxygen level of blood flowing through the surface layer of the brain by measuring how much near-infrared light it absorbs. When neural activity in the brain consumes oxygen, the body increases blood flow in an effort to deliver more oxygen. fNIRS systems can visualize the status of brain activity by measuring the changes in blood oxygen levels.

Specific Example of fNIRS Testing Method and Application

Brain activity is measured by fNIRS as the subject performs a successive subtraction calculation problem.
Overall cognitive function levels are quantified numerically by analyzing the blood flow ratio.



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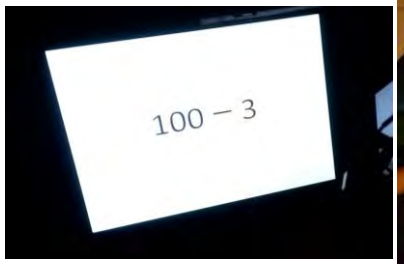
MCI

t30

Normal

Starting with 100, successively subtract 3. Next, successively subtract 7 from 100.

"97, 94, 91, 88, 85..."



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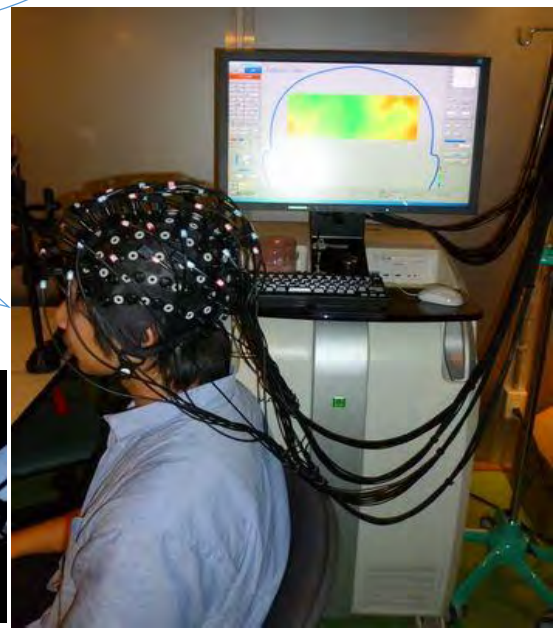

Performing fNIRS measurements

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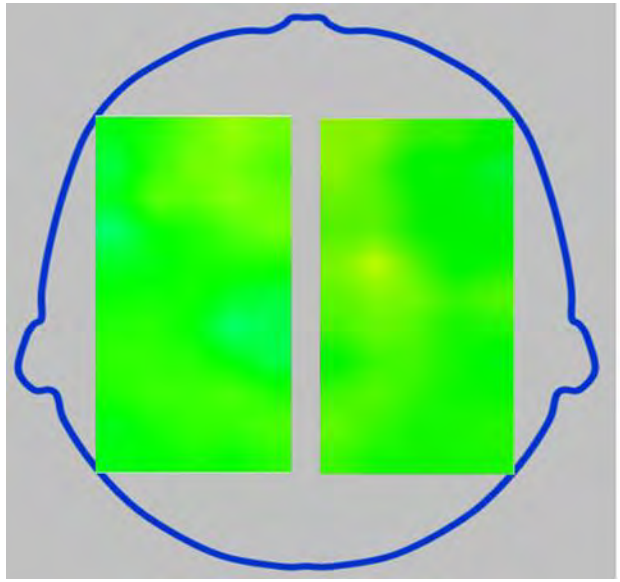

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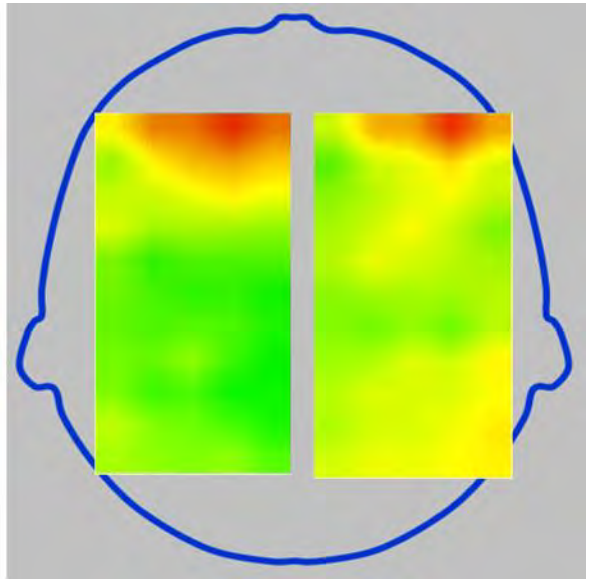

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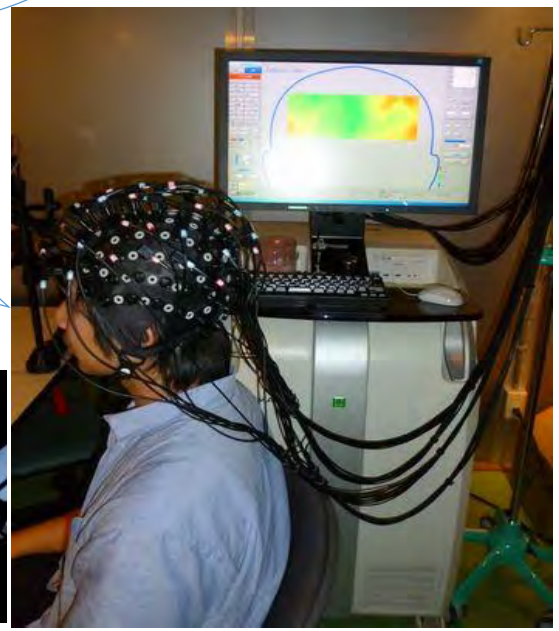

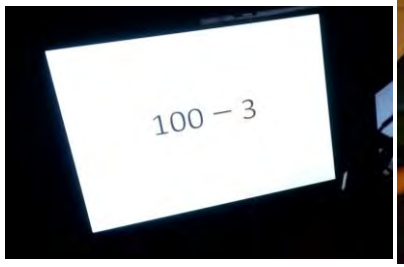

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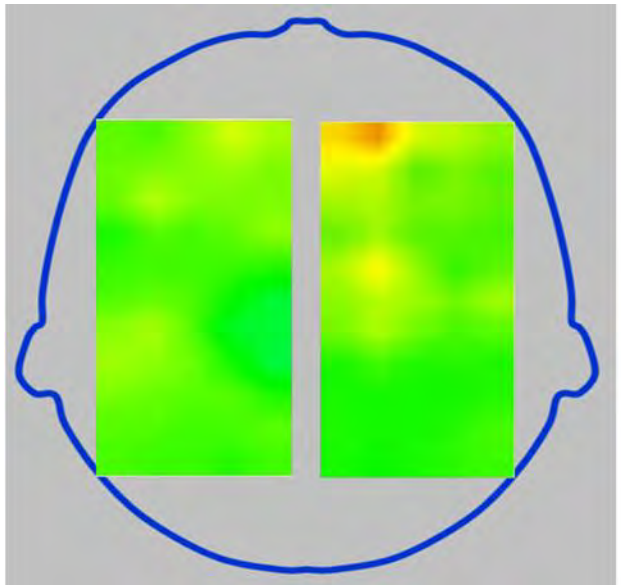

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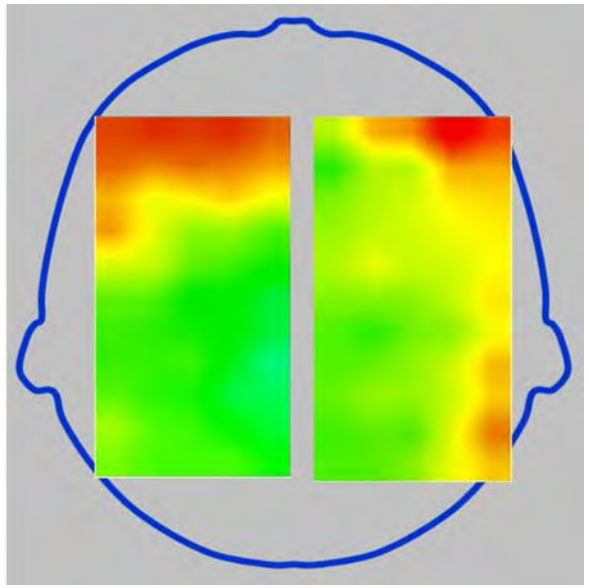

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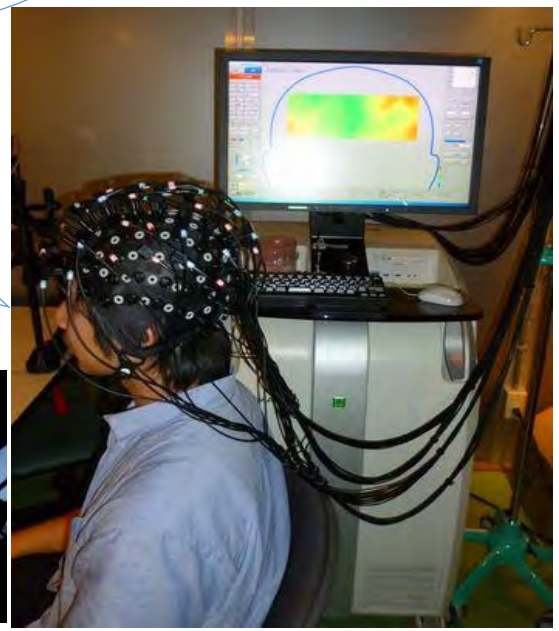

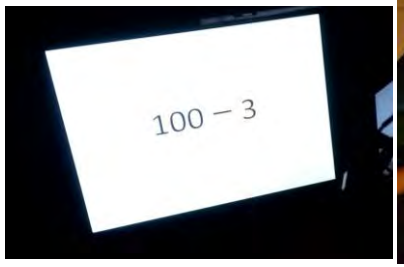

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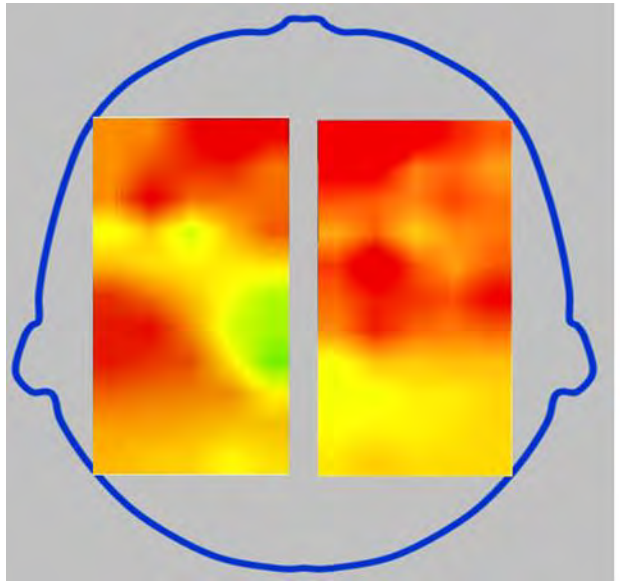

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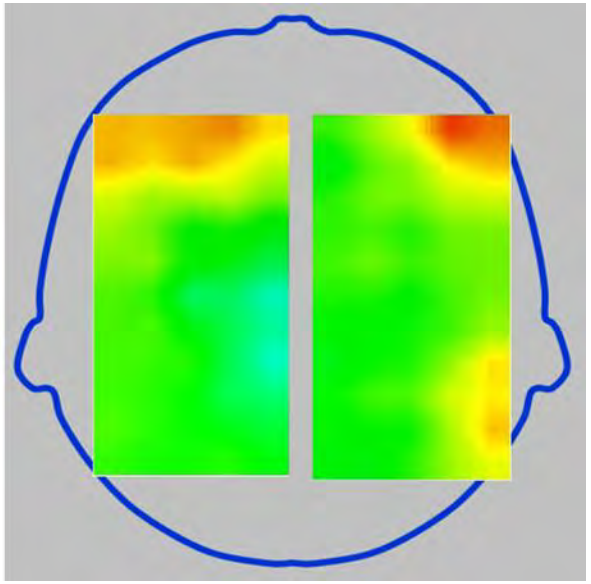

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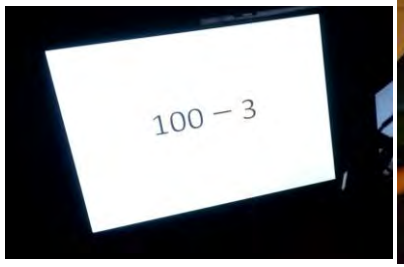

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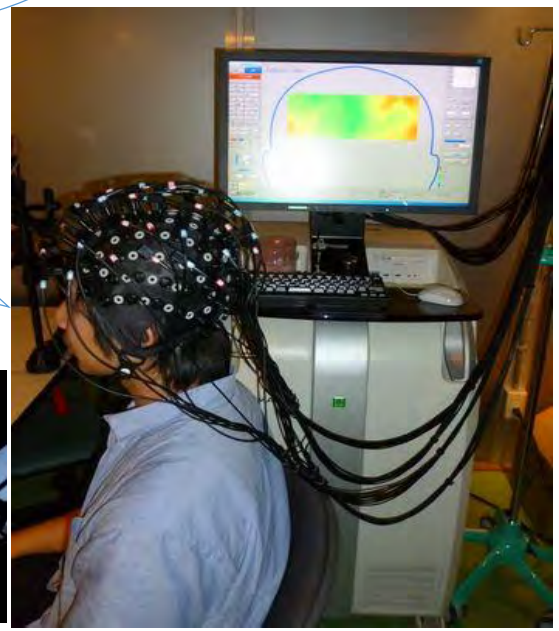

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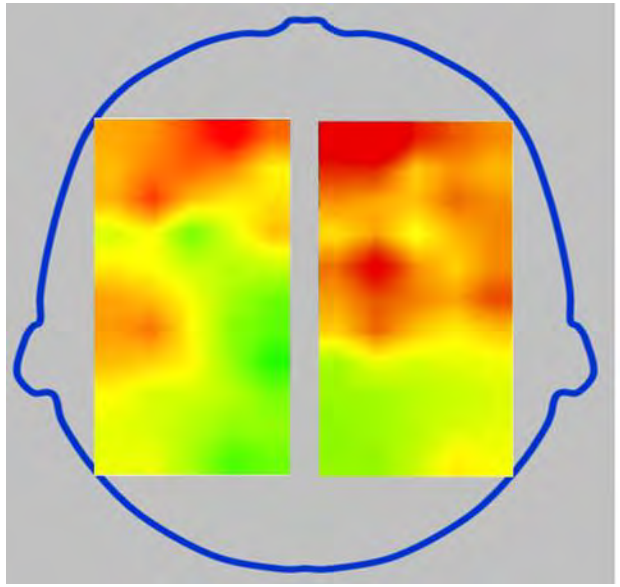

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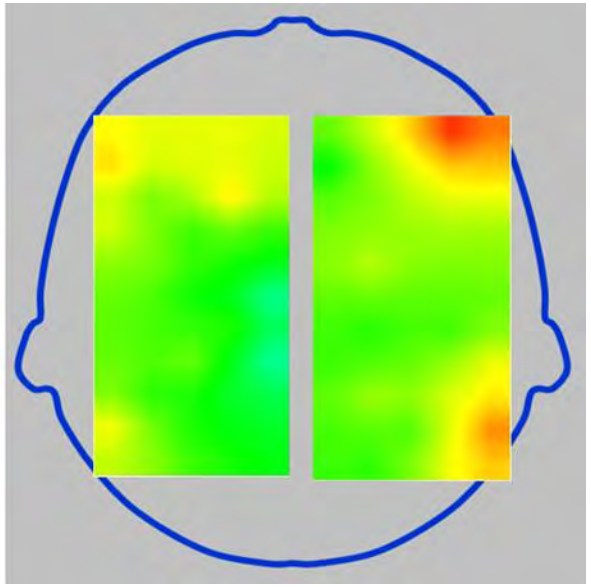

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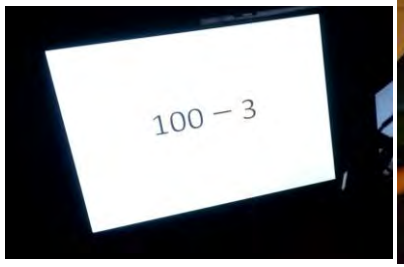

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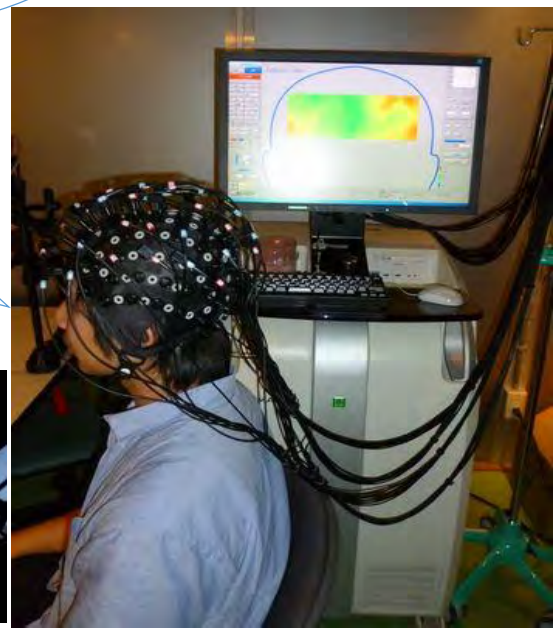


Performing fNIRS measurements

Social Participation and Maintaining Healthy Activities of Elderly

Shimadzu: Visualize brain activity by fNIRS

Local government ↔ Cooperation ↔ Vendor

Citizen-led

Gathering Place

Prevention/health improvement

Exercise, brain training, and health advice

(public welfare facilities, community centers, and businesses)

fNIRS trial session

National participation goal:
4.9 % now → 8 % by 2025

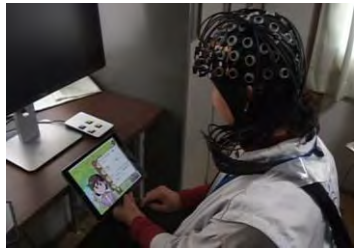
PR

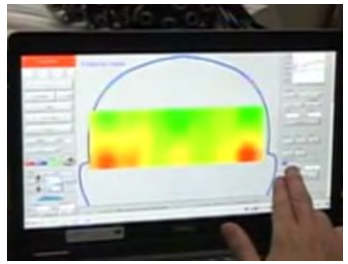
Citizens with MCI: 5 million

Social withdrawal countermeasures

Using Shimadzu's fNIRS brain function imaging system to visualize the brain can increase motivation

Visualizing brain activity by fNIRS





View video

My brain is functioning properly.

In future, visualize prevention effectiveness.

Dementia portal site/app

Future:
Results viewable anytime on a smartphone

Measures for Dementia Prevention Intended by Shimadzu

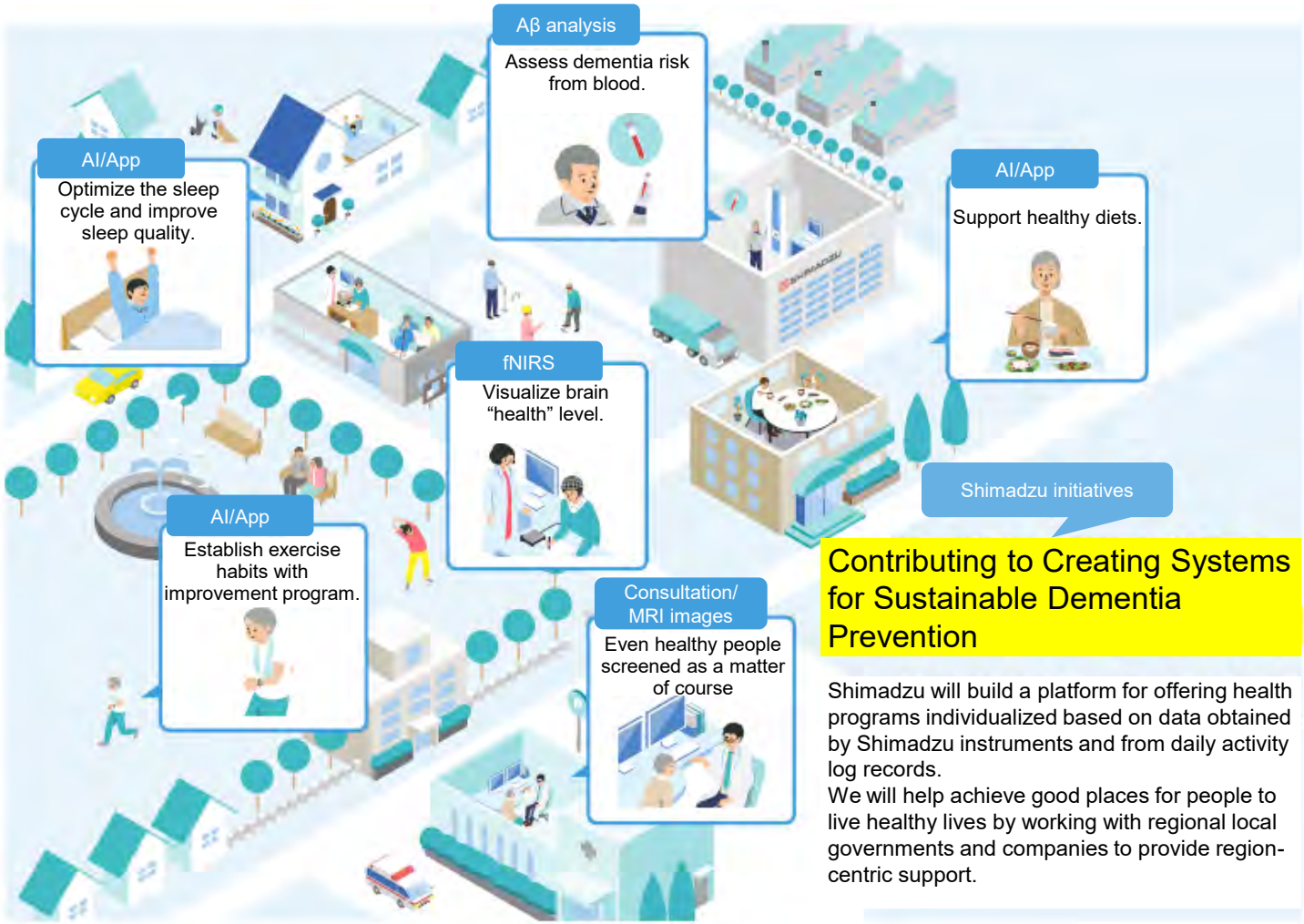
Longevity-Based Society

As societies throughout the world continue to age, it has become increasingly important to extend our healthy life expectancy*1. As our lifestyles have evolved, the number of patients with lifestyle diseases or diseases closely associated with lifestyle habits, such as cancer and mental/neurological disorders, has increased each year as well.

Given that people are staying healthy longer as the average life span increases, it is important to provide broad healthcare for all the disorders caused by lifestyle habits, from a perspective of prevention.

This shows some of the systems for sustainable dementia prevention that Shimadzu is trying to create.

*1: “Healthy life expectancy” refers to how long people can live without daily activities being restricted by health issues.



Contributing to Creating Systems for Sustainable Dementia Prevention

Shimadzu will build a platform for offering health programs individualized based on data obtained by Shimadzu instruments and from daily activity log records.
We will help achieve good places for people to live healthy lives by working with regional local governments and companies to provide region-centric support.

Shimadzu R&D Areas and R&D Strategy

Strengthening R&D Functions: Newly Constructed Facilities

- Following the Healthcare R&D Center, Shimadzu intends to expand/improve the Technology Research Laboratory and is building a new Shimadzu Tokyo Innovation Plaza.
- Make comprehensive significant improvements to technical capabilities, from product development to basic research and application development.
- At each research institution, engage in open innovation more actively and strive to create innovative results.

Developing Products/Services and Incubating New Businesses

Healthcare R&D Center (within Sanjo Works in Kyoto city)

This center consolidates life science engineering units in one location. It provides a joint research environment and promotes collaboration with advanced partners in various academic, corporate, or other fields. It also enables closer cooperation between Analytical & Measuring Instruments and Medical Systems segments for creating new added value. Completed in February 2019.

Strengthening Basic Research

Technology Research Laboratory and SHIMADZU Future Collaboratory (Seika-cho, Kyoto)

Significantly expands/improves the development function for basic research fields. It will also pursue developing advanced technologies, such as based on the five senses, innovative biotech, and AI. It will also actively engage in open innovation. Scheduled for completion in October 2020.

Accelerating Application Technology/Software Development

Shimadzu Tokyo Innovation Plaza (inside King Skyfront in Kawasaki city, Kanagawa prefecture)

This plaza will develop advanced analytical techniques and software applications. Taking advantage of its location near central Tokyo and Haneda Airport, it will even serve to facilitate international exchanges between researchers. Scheduled for completion in 2021.

SHIMADZU

Excellence in Science

This document contains forward-looking statements. Forecasts of future business performance that appear in this document are predictions made by the company's management team that are based on information available when these materials were prepared and are subject to risks and uncertainties. Consequently, actual results may differ materially from the forecasts indicated above. Factors that may influence actual business performance include, but are not limited to, economic conditions within and outside Japan, changes in technologies in markets, and fluctuations in exchange rates.