# Bridges between Neuroscience and Society

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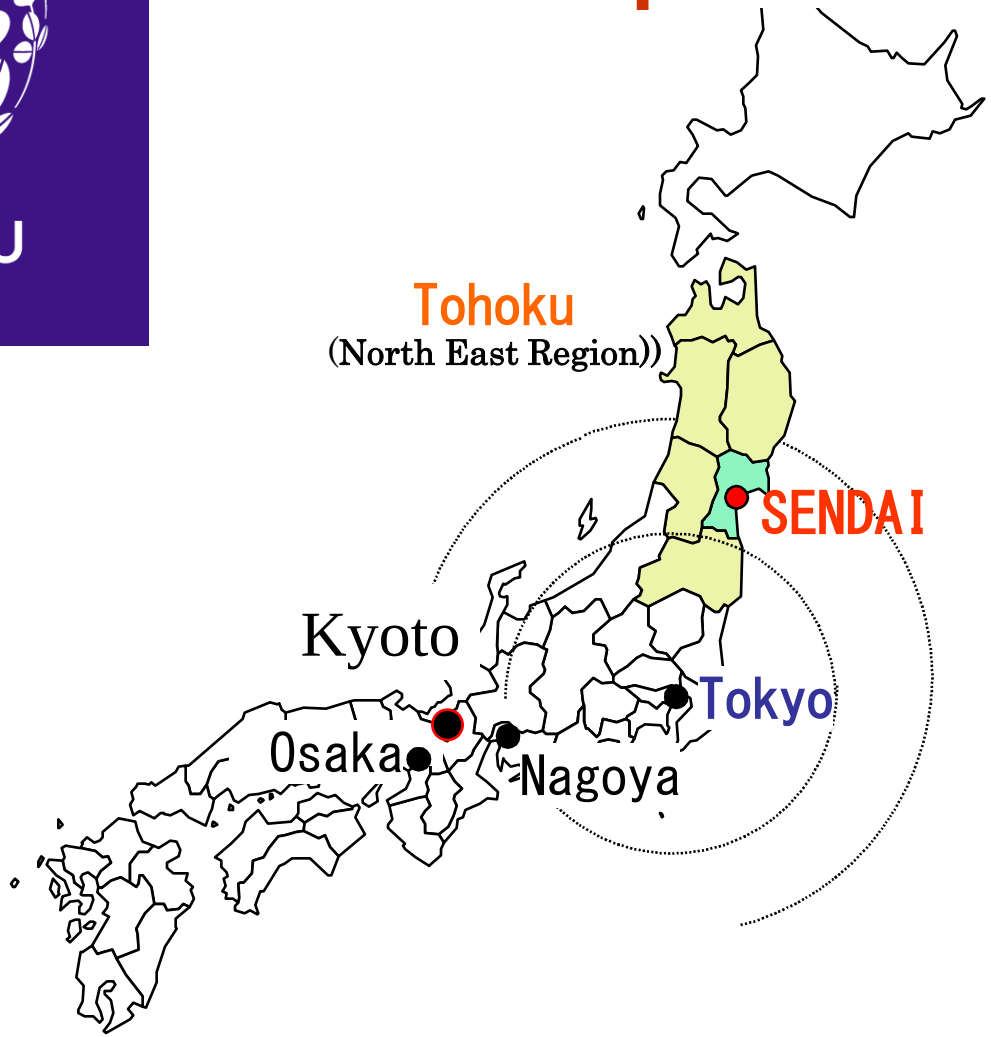
# Tohoku University

TOHOKU
UNIVERSITY

## Founded in 1907 as 3rd Imperial University



# World Ranking by Citations

| National Ranking | World Ranking | Field | Citations | Papers |
|---|---|---|---|---|
| 1 | 2 | Materials Science | 25,185 | 4,554 |
| 2 | 14 | Physics | 89,139 | 9,762 |
| 5 | 21 | Chemistry | 53,301 | 5,919 |
| 4 | 72 | all fields | 302,547 | 36,583 |

**Source: ISI Essential Science Indicators℠, Jan. 1995 – Apr. 2005**

# Number of Students and Staff

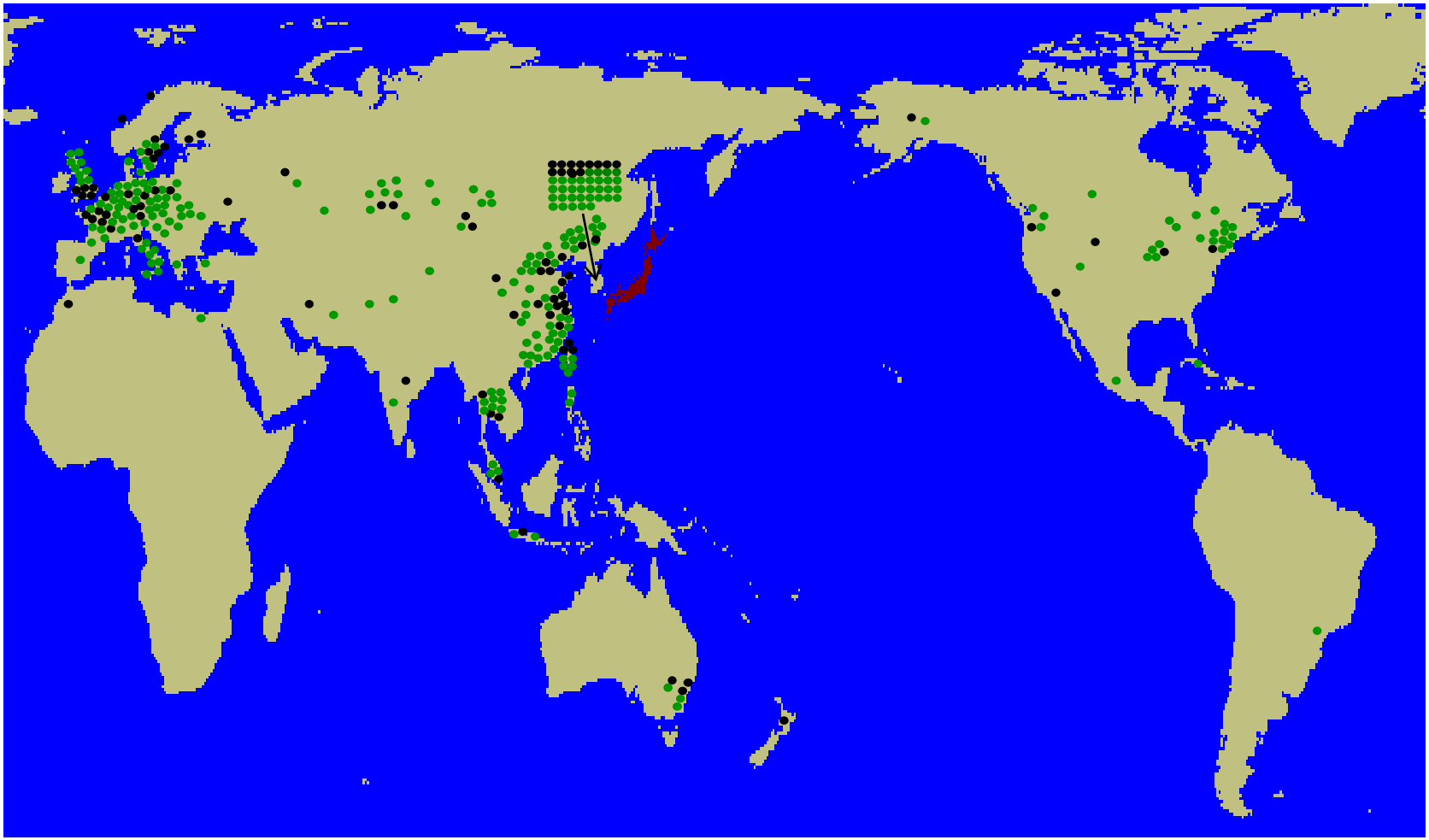
As of October, 2008

| | |
|---|---|
| **Undergraduate** | **10,953** |
| **Master** | **4,146** |
| **Doctor** | **2,748** |
| **Total** | **17,847** |

| | |
|---|---|
| **President** | **1** |
| **Executive Directors** | **7** |
| **Auditor** | **2** |
| **Faculty Members** | **2,743** |
| **Administrative and technical staff** | **2,803** |
| **Total** | **5,556** |

# Academic Exchange Agreements with Non-Japanese Universities

- ● : **Agreement on the University Level － Total of 87 universities**
- ● : **Agreement on the Department Level － Total of 228 departments**



# Liaison Offices outside of Japan


As of April, 2008

Institute of
Development, Aging and Cancer (IDAC),
Tohoku University

# Mission and Ultimate Goal of IDAC

TOHOKU UNIVERSITY

## Mission

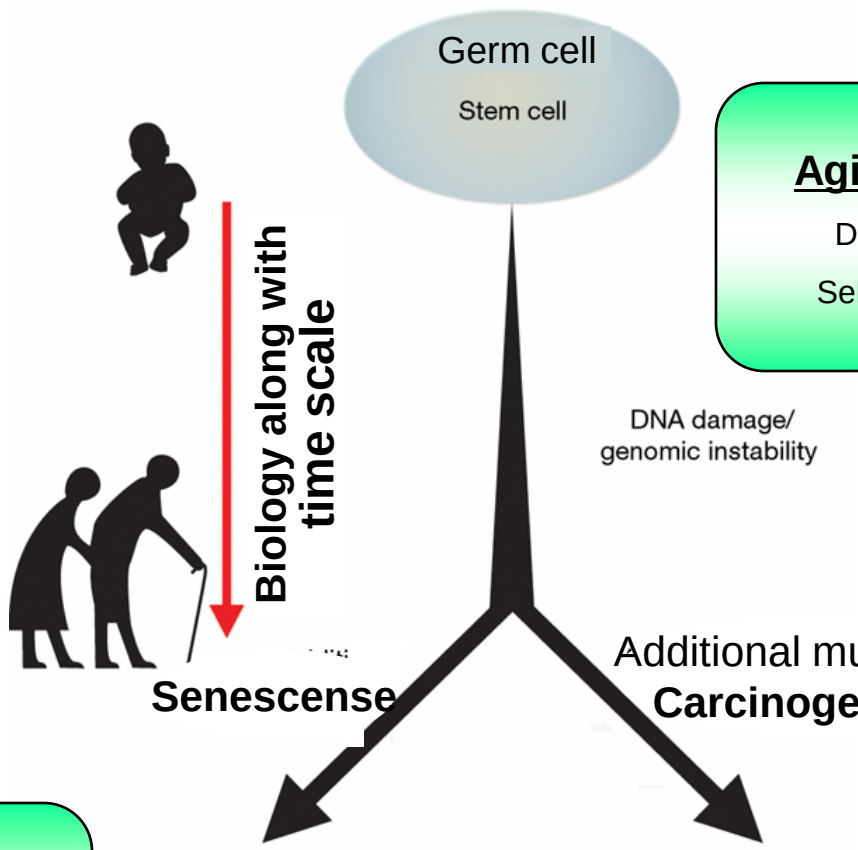
1. To investigate basic mechanisms of aging
2. To develop a novel diagnostic and therapeutic method for age-related disease such as degenerative brain diseases and cancer.

## Ultimate Goal

**To establish "Medical science in Aging"**
**(A new field of science)**
**and to create Smart Aging Society**

**Aging=whole process of life: from fertilization, development, growth and maturation, senescence to death**

# Key Research Domain at IDAC




**Aging Mechanisms**

DNA damage/repair

Self defense mechanism

**Brain developing/aging**

Neuroimaging

Diag./treat. of AD

**Basic and clinical Oncology**

Angiogenesis

Diag./treat. of cancer

# Department of Functional Brain Imaging

# Division of Developmental Cognitive Science

# Organization

Director
Prof Ryuta Kawashima

Neuronal Mass Dynamics

Assoc Prof Jorge Riera
+
4 postdocs, 4 students

Cognitive Neuroscience

Assoc Prof Motoaki Sugiura
Assoc Prof Takashi Tsukiura
Assist Prof Yuko Akitsuki
+
5 postdocs, 9 students

Language Neuroscience

Assist Prof Satoru Yokoyama
+
1 postdoc, 5 students

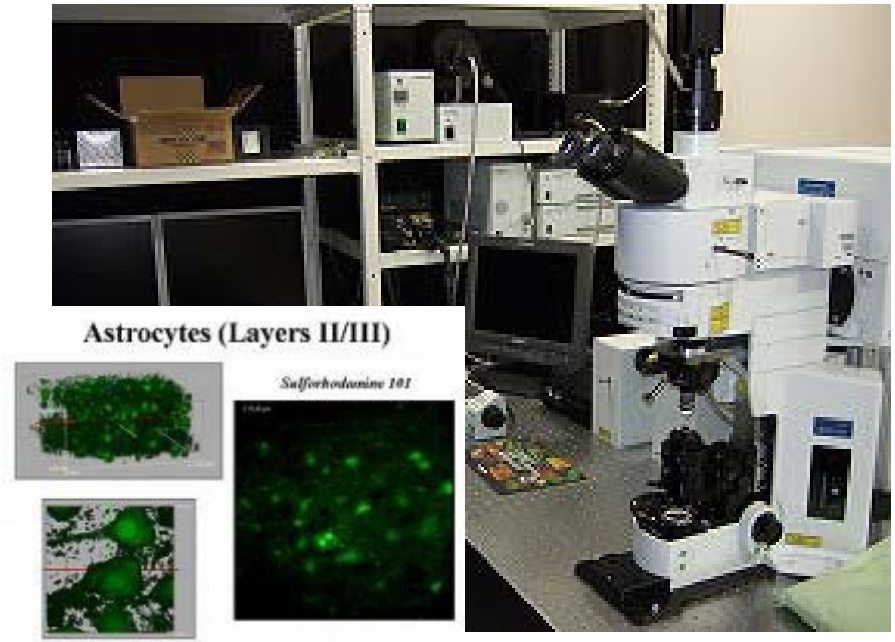
Developmental Cognitive Science

Assoc Prof Yasuyuki Taki
Assist Prof Hiroshi Hashizume
+
1 postdoc, 4 students

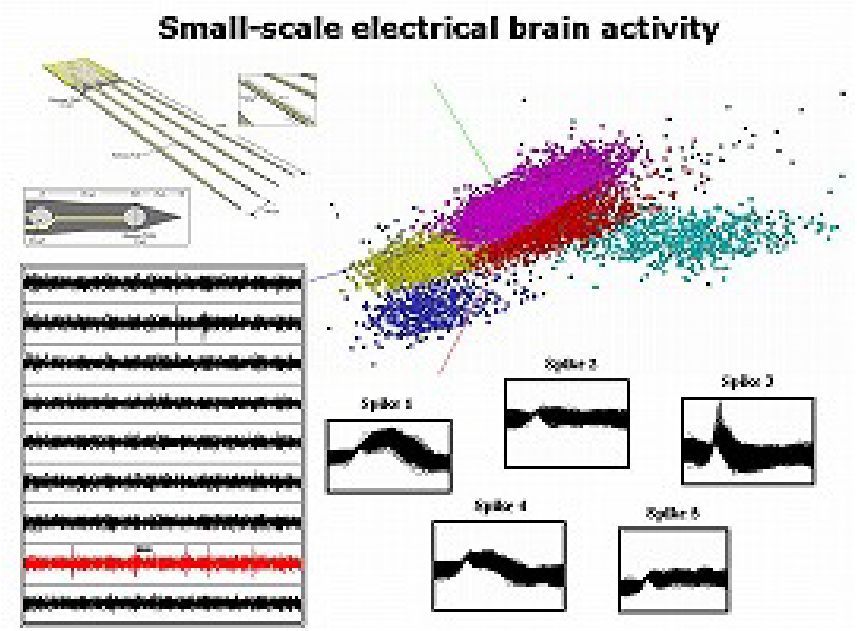
# Background: Animal Researches

Researches on the micro-architecture of the cerebral cortex to understand neuro-vascular coupling

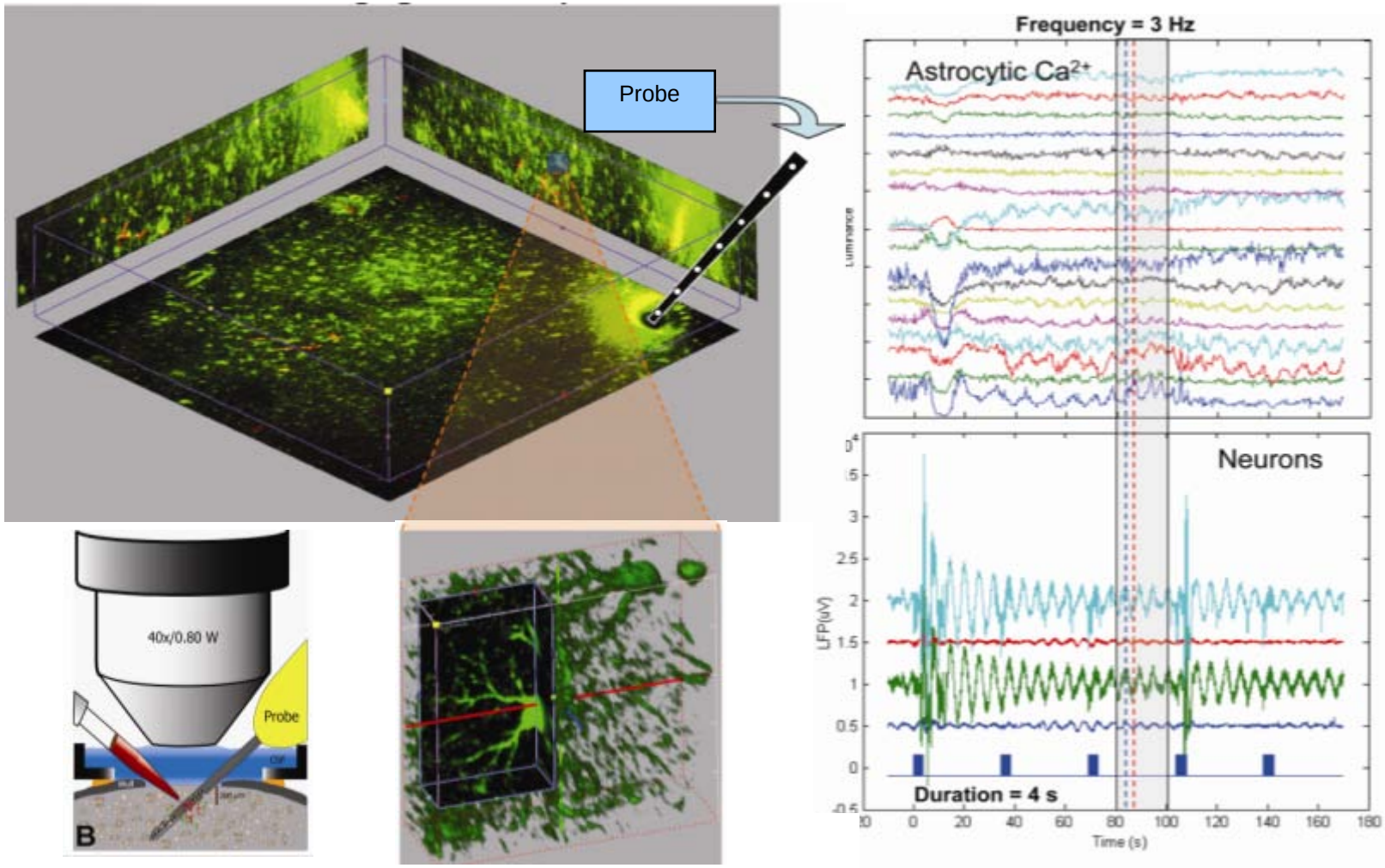
Two Photon Laser Scanning Microscope




Multi-Channel Electrophysiological Set-up

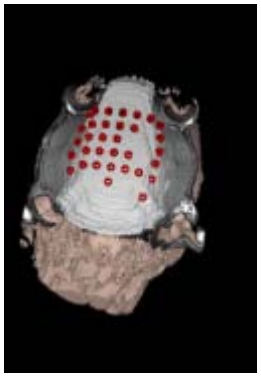


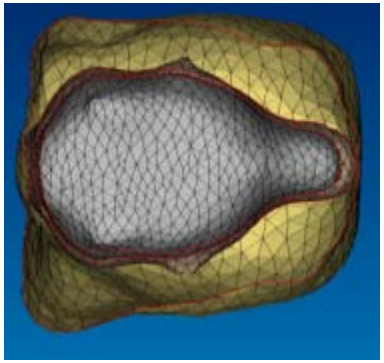
# Background: Animal Researches

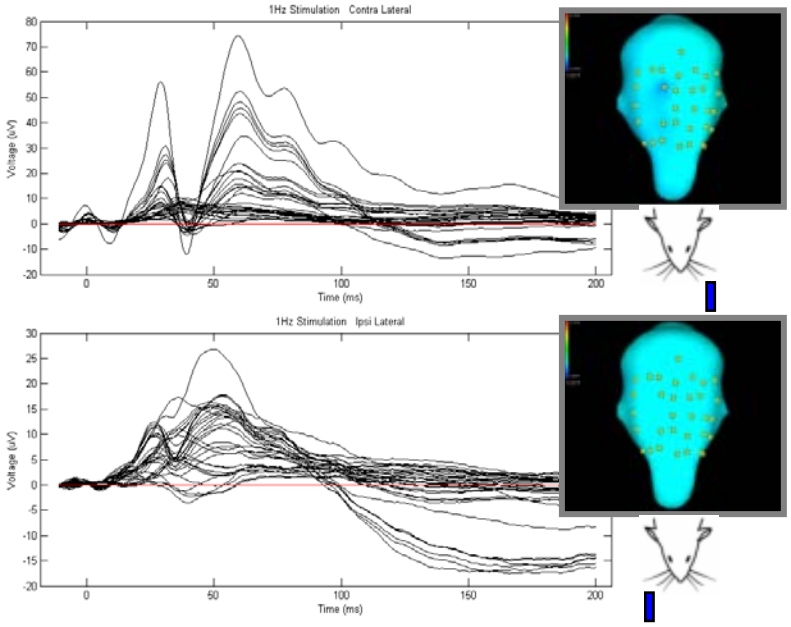


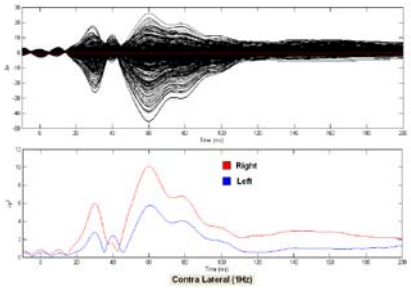

Simultaneous recoding by 2PLSM and multi-unit recording

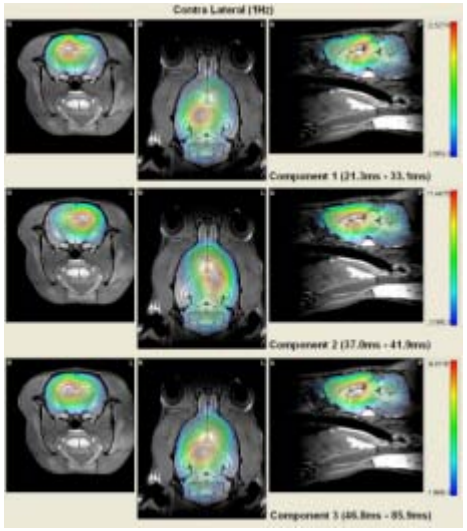
# Background: Animal Researches







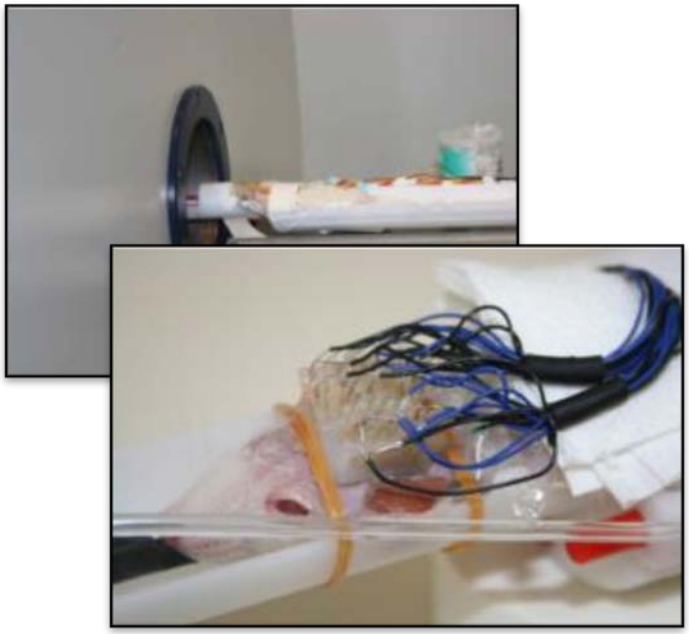



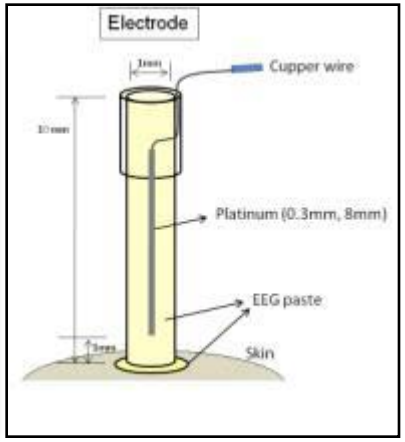



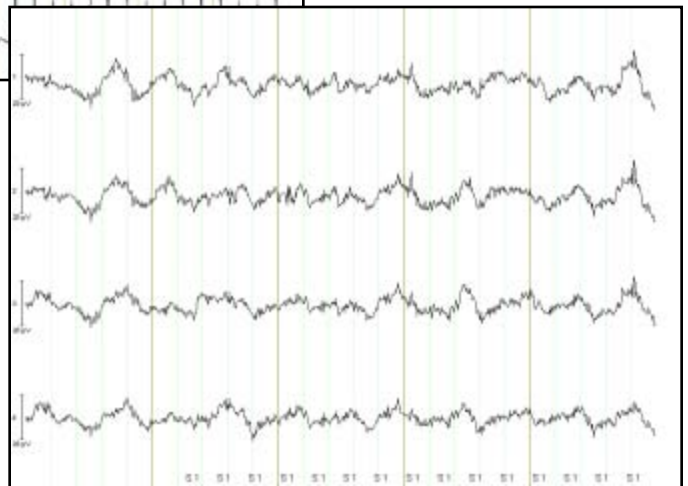

Simultaneous recoding by multi-channel EEG and multi-unit recording

# A new 7T MRI System



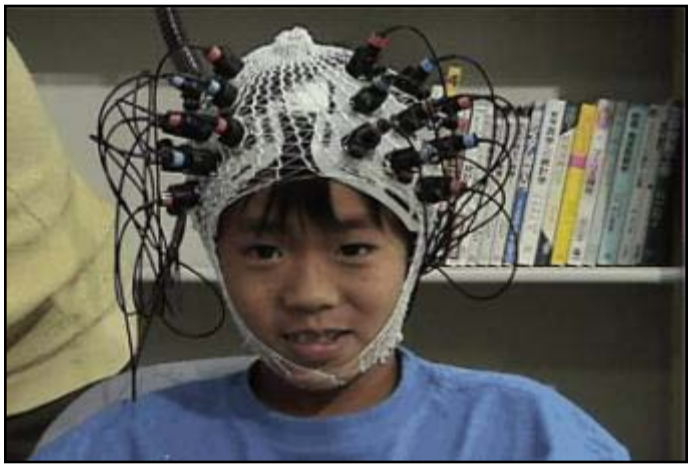


# Background: Human Researches

## Basic Brain Science using Functional Brain Imaging Techniques

Functional MRI



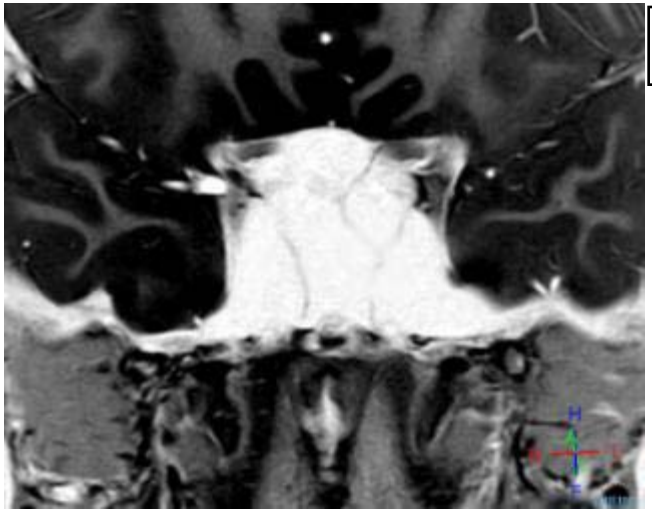
Near Infra-red Spectroscopy (NIRs)

Multi-channel EEG

The final goals of our studies are to reveal functional organization of human brain involved in higher brain function, and to figure out the relationship between brain and mind.

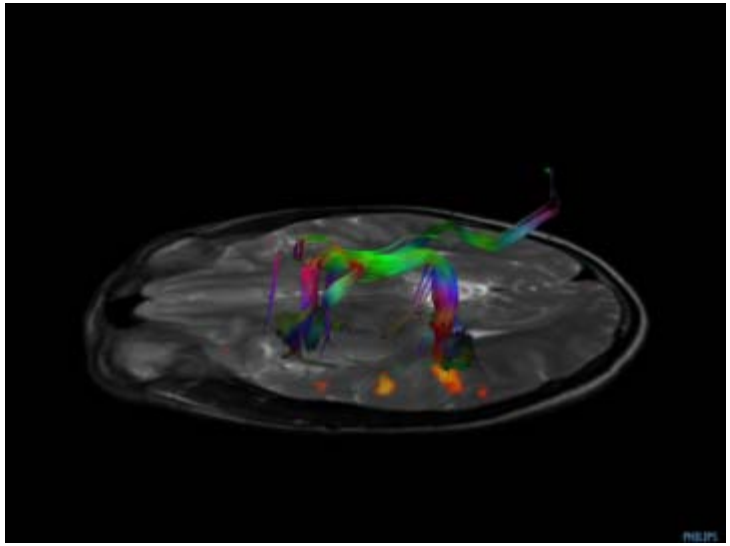
# 3T MRI system

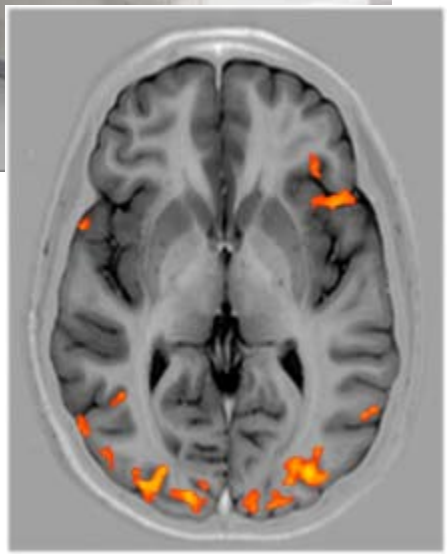
Philips Intera Achieva 3.0T Quasar Dual



Precise Anatomy

Fiber Tracking

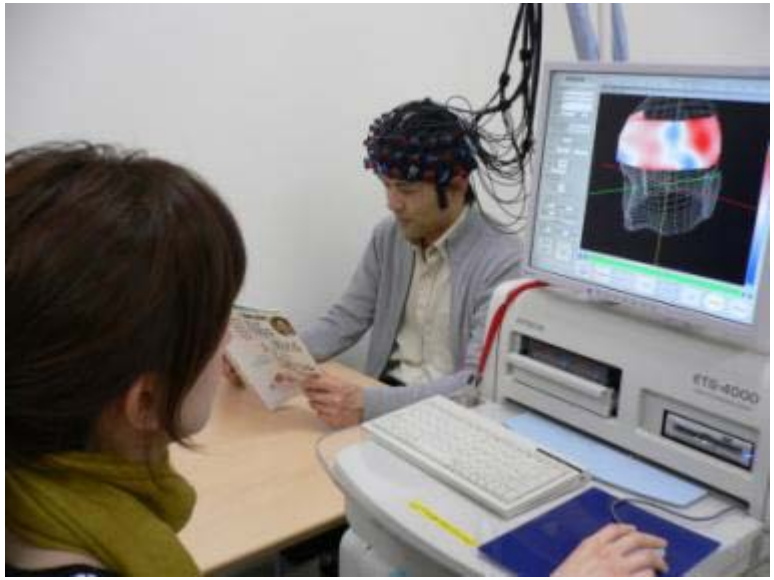




Mapping of Individual Brain Function

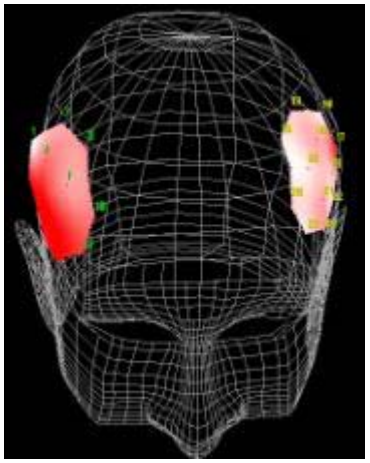
# NIRs systems

- Hitachi Medico ETG-4000, ETG-100

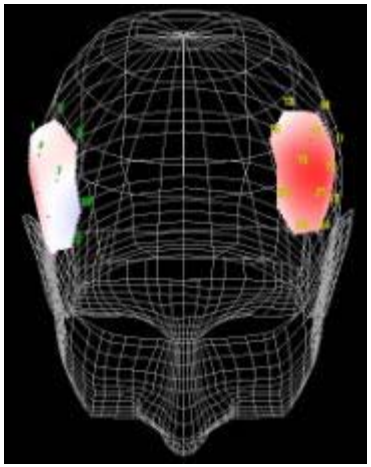



# R&D for Brain Computer Interface

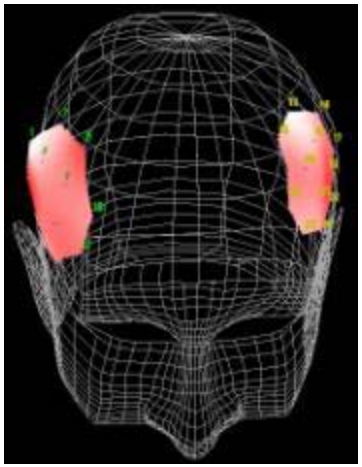
Rt on Lt off



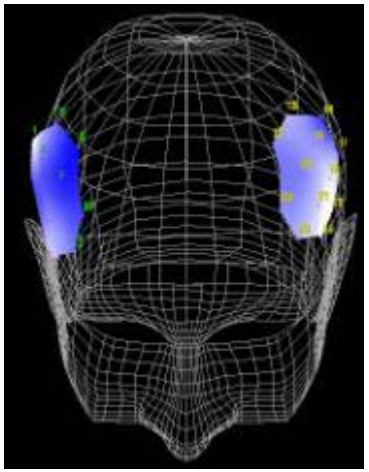
Rt off Lt on



Rt on Lt on

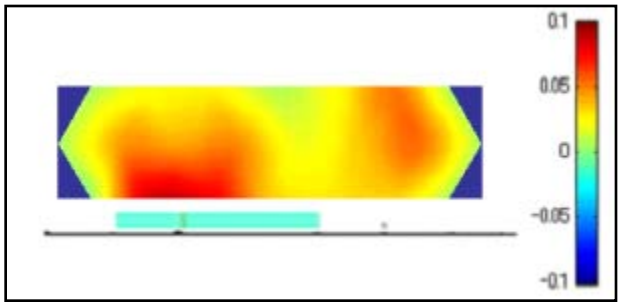


Rt off  Lt off



# Wearable NIRs System

An Experimental Model by Advanced Research Laboratory, Hitachi Ltd.

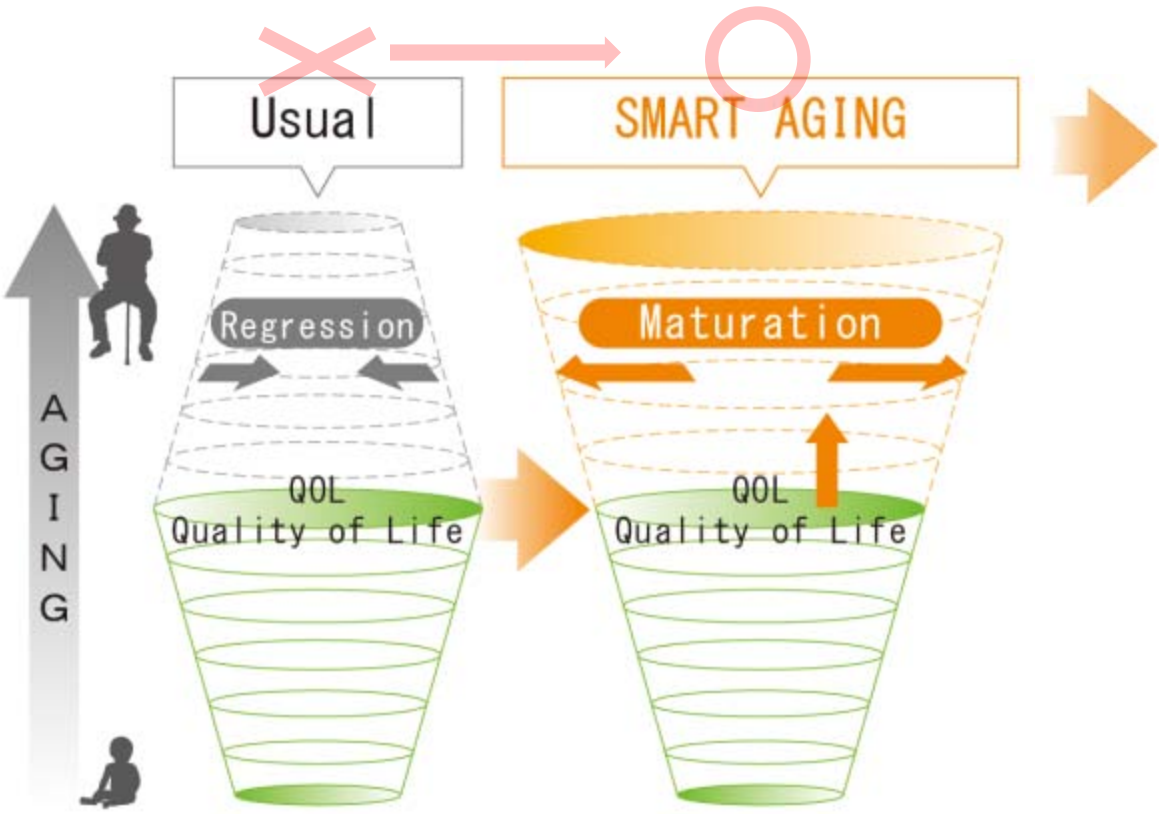



# NIRs Measurement during Driving Motorcycle

# From Anti Aging to Smart Aging: Prevention of Senile Dementia by Brain Training

# What is Smart Aging?

The concept of smart aging encompasses a positive acceptance of later stages of life as “development stages in an intellectually maturing life,” unlike negative concepts, such as anti-aging, that imply an unwillingness to accept or face later stages of life. It is a paradigm shift of the view of the aging society.




Intellectually Connected Society

**Elderly people’s energy:**
Life becomes increasingly enriched with aging

**Sharing of wisdom among generations:**
Everybody from all age brackets are consequently connected to each other, regardless of age and sex, through intellectual curiosity and can support each other

# Mental-Exercise Hypothesis

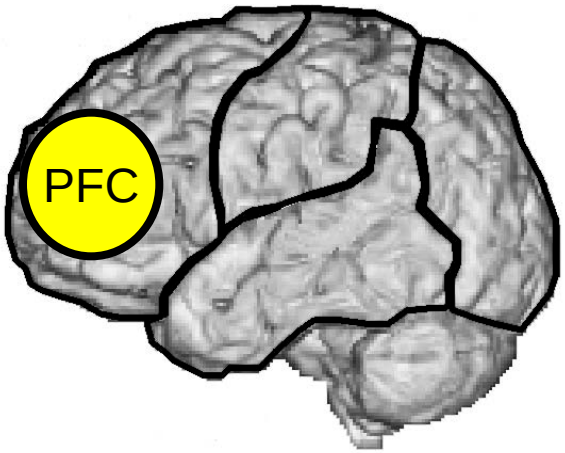
- The rate of age-related decline in measures of cognitive functioning will be less pronounced for people who are more mentally active, or, equivalently, that the cognitive differences among people who vary in level of mental activity will be greater with increased age.

# Hypothesis from Brain Science

The prefrontal cortex plays extremely important roles in keeping our daily life healthy and happy.

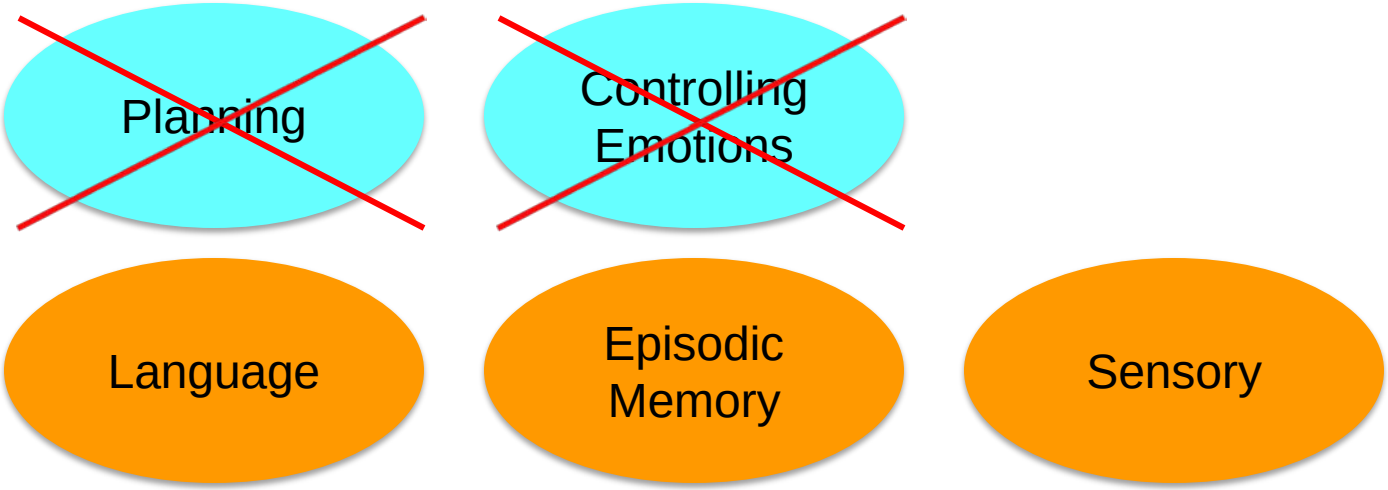
## Functions of the Prefrontal Cortex

1. Verbal and non-verbal communication
2. Logical thinking
3. Working memory
4. Control, especially inhibition for behavior
5. Control for emotion
6. Intention
7. Attention
8. Initiation
9. Learning



# Dysfunction of the Prefrontal Cortex

- Patients with PFC lesion

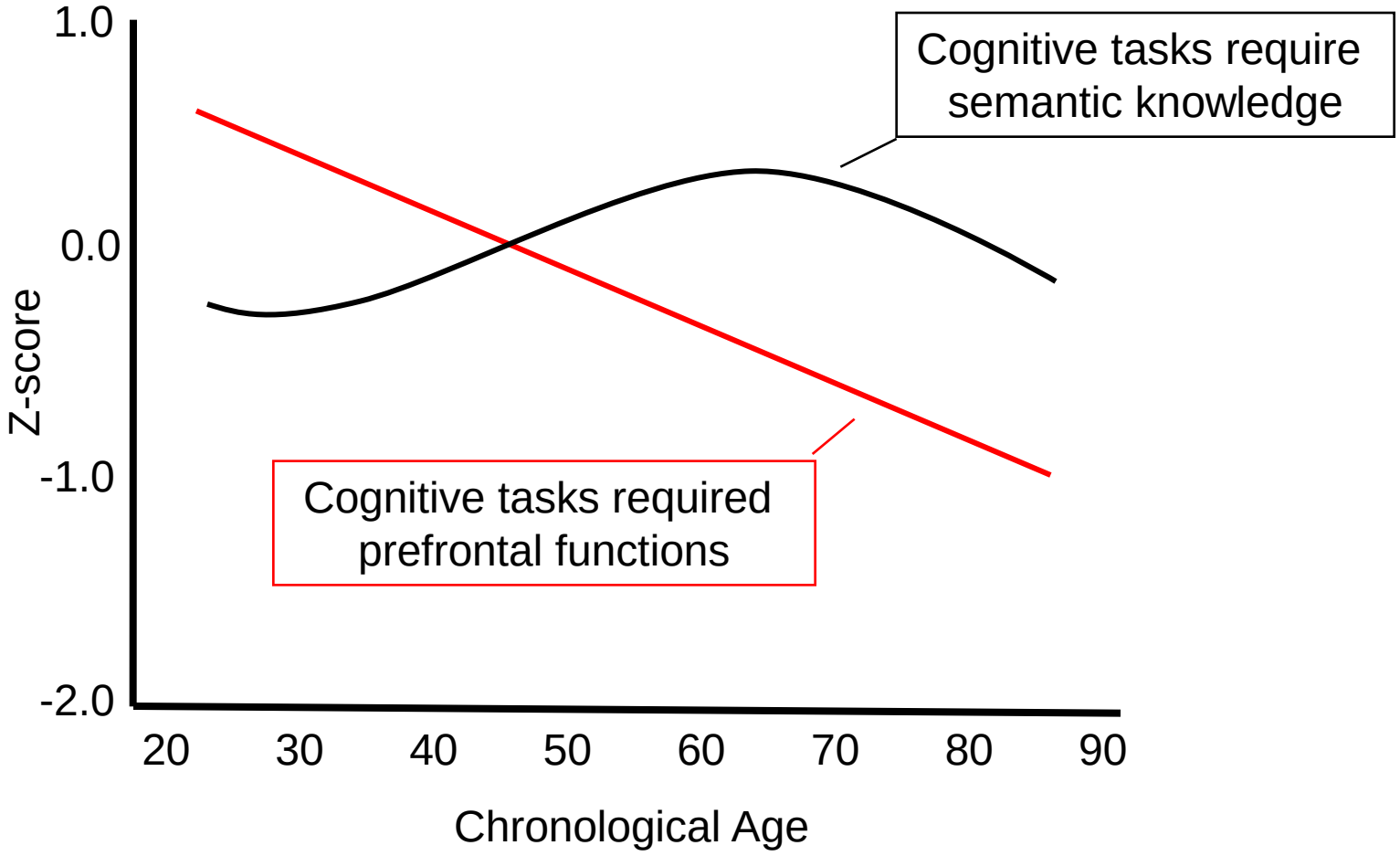



- Psychological stases
  - Feeling guilt or remorse
  - Interpreting reality
  - Lying

# Dysfunction of the Prefrontal Cortex

- Reduction of the volume of the PFC
  - Repeated stressors
  - Suicide victims
  - Criminals diagnosed as sociopaths
  - Drug addicts
- Psychiatric disorders
  - Schizophrenia
  - Depression
  - Mild Cognitive Impairment (MCI)
  - ADHD

# Changes of Neuropsychological Measures during Aging

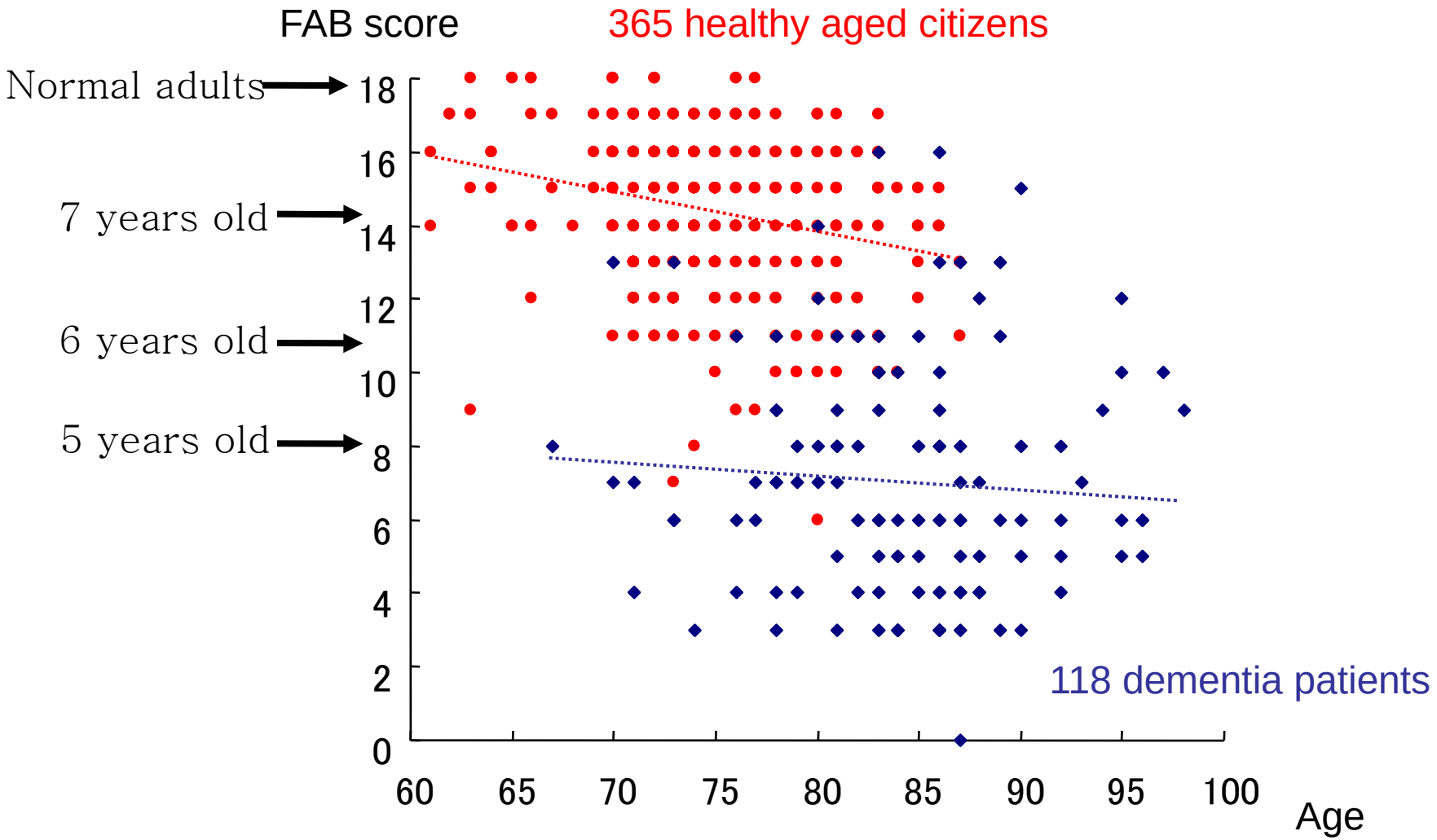



Modified from Salthouse 2006

# Frontal lobe performance inspection
# FAB: frontal assessment battery at bedside

1. Similarities(conceptualization)
   “In what way are they alike? A banana and an orange.”
2. Lexical fluency(mental flexibility)
   “Say as many words as you can beginning with the letter ‘S,’ any words except surnames or proper nouns.”
3. Motor series(programming)
   “Look carefully at what I’m doing.” fist-edge-palm
4. Conflicting instructions(sensitivity to interference)
   “Tap twice when I tap once. Tap once when I tap twice.”
5. Go/No-Go(inhibitory control)
   “Tap once when I tap once. Do not tap when I tap twice.”
6. Prehension behavior(environmental autonomy)
   "Do not take my hands."

# Relation between Prefrontal Function and Age




We assessed the prefrontal function by FAB (Frontal Assessment Battery at Bedside)

# *Learning Therapy*

To prevent or slow the progress of dementia through learning and communication

# What is Learning Therapy?

1. A therapy aimed at improving the prefrontal cortex functions of people through learning-based communications between learners and supporters.

2. Learning Therapy was developed by Dr. Ryuta Kawashima at IDAC, Tohoku Univ. in collaboration with various retirement communities.

3. Learners work with a supporter on weekly exercises involving reading, writing and mathematical calculations.

4. Versions of Learning Therapy have been developed for people with dementia and people with normal cognitive function or mild cognitive impairment.

# Two objectives of Learning Therapy

1. Dementia Care
   i. *Purpose:* to improve prefrontal cortex functions
   ii. *Target:* people with dementia
   iii. *Cognitive level of materials:* Low
   iv. *Locations:* nursing homes, retirement communities

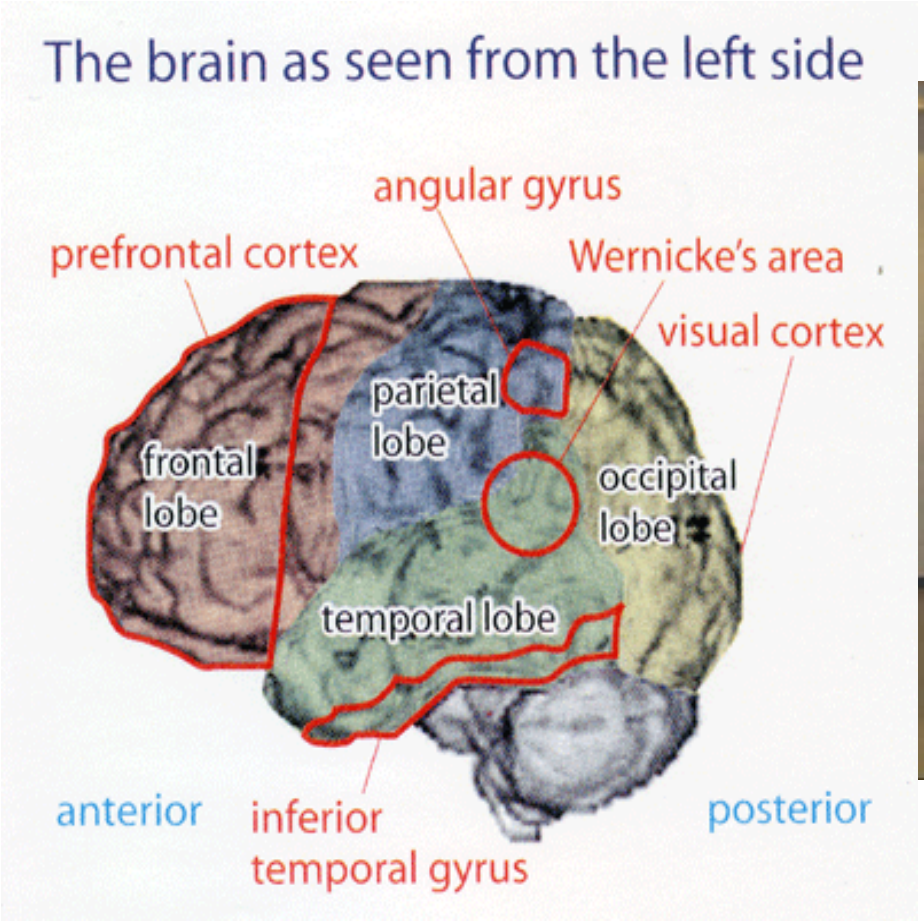
2. Dementia Prevention
   i. *Purpose:* to maintain prefrontal cortex functions
   ii. *Target:* people without dementia
   iii. *Cognitive level of materials:* Middle
   iv. *Locations:* senior centers, welfare centers, primary schools

# What are the differences between Learning Therapy and other approaches?

1. Direct activation of prefrontal cortex functions
2. Scientifically-proven, evidence-based
3. No use of drugs or pills
4. No need for IT devices such as personal computer
5. Social interaction-oriented
6. Supporters as well as learners benefit
7. Easy, fun, and inexpensive

# Selecting effective tasks to activate PFC

- Research on cortical activity by functional brain imaging studies

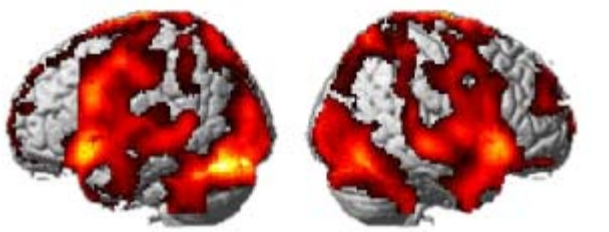



Functional MRI at IDAC

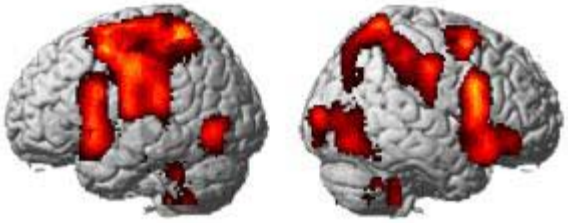
# Select Effective Tasks for Activating PFC
# Research Result

The tasks must

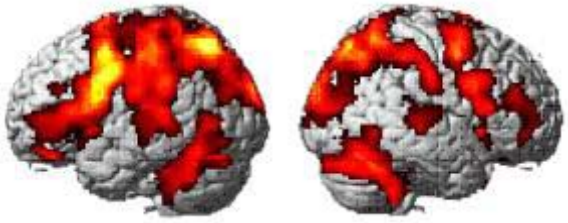
1. activate bilateral PFC
2. be simple and easy



Reading aloud



Hand writing



Simple arithmetic

**Materials design basis for Learning Therapy**

Randomized controlled trial of cognitive intervention in senile dementia Alzheimer type (SDAT)
（Eiju-en, Fukuoka Project
n = 32, mean age 85.7）

Kawashima et al. *J Gerontology Series A, Biological Sciences and Medical Sciences*, 2005

RCT-SDAT

# Examples of learning materials

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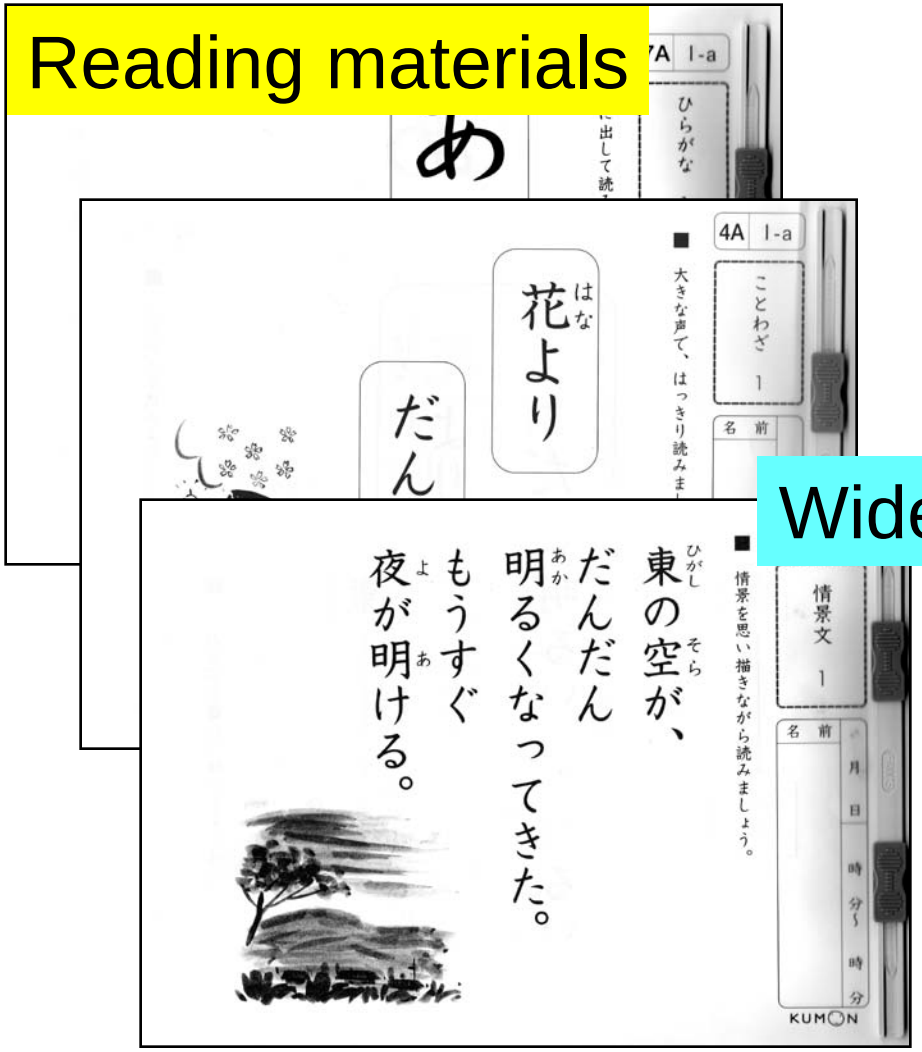
Reading materials




Wide Range

Arithmetic materials


Difficulty level: from 4 y. children to 2nd G elementary school

# Learning Therapy

- Wide range of materials
  - 10 ~ 15 min a day, 3 ~ 6 days a week

| | |
|---|---|
| Language Problems | Lowest level: read and write single syllables<br>Highest level: read aloud fairy tales. |
| Arithmetic Problems | Lowest level: counting practice<br>Highest level : three-digit division. |

- Assessment of Subjects

Diagnostic test → Appropriate degree of difficulty and workload

Subjects could continue to perform the tasks with ease

# RCT-SDAT

Case 1（76 year old Female: vascular dementia）
Showed major improvements after 4-year intervention


May 2004
Hard to talk and dysphonic
FAB：3　MMSE：20


November 2008
Learning actively
FAB：13　MMSE：29

# Effects of Learning Therapy

# RCT-SDAT

Case 2（85 years old Female: SDAT）
Showed major improvements after three-month intervention

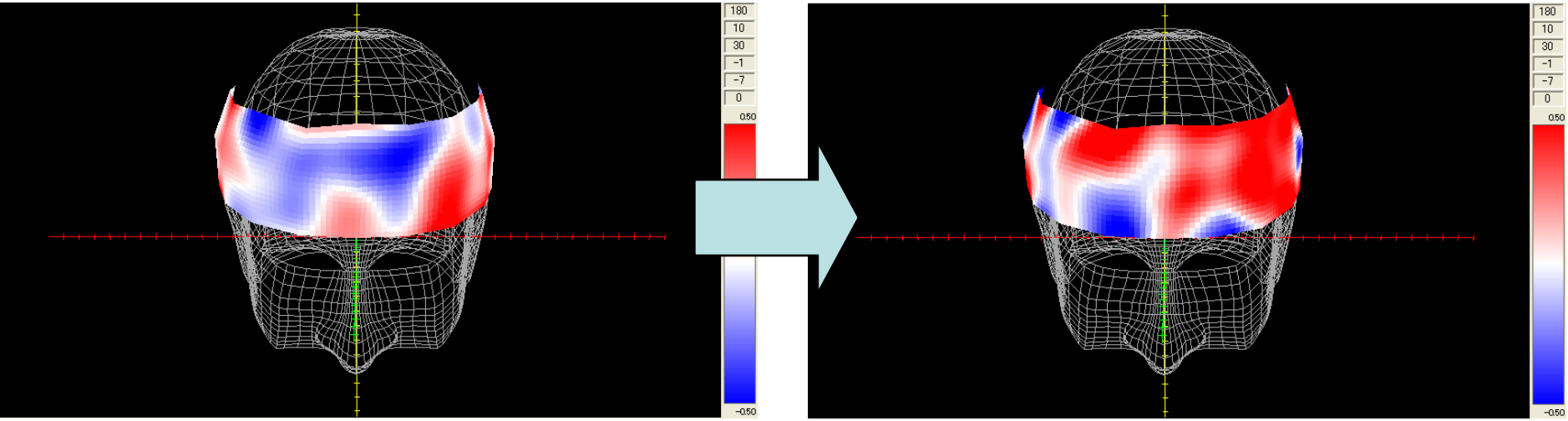
Jan. 2005
Bedridden more than three years

Mar. 2005
Learning in a wheelchair

# Changes in NIRs* measurements

Prefrontal cortex is much activated one-month after intervention

82 years old, Female, SDAT,
MMSE 15, FAB 7




Prior to Intervention

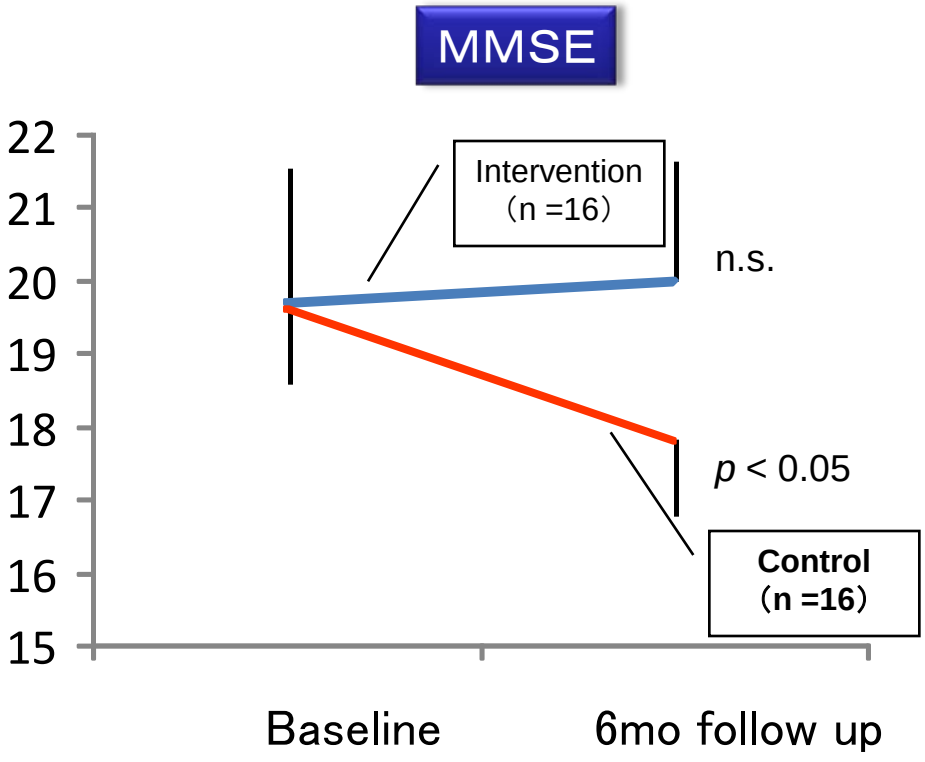
One month after intervention

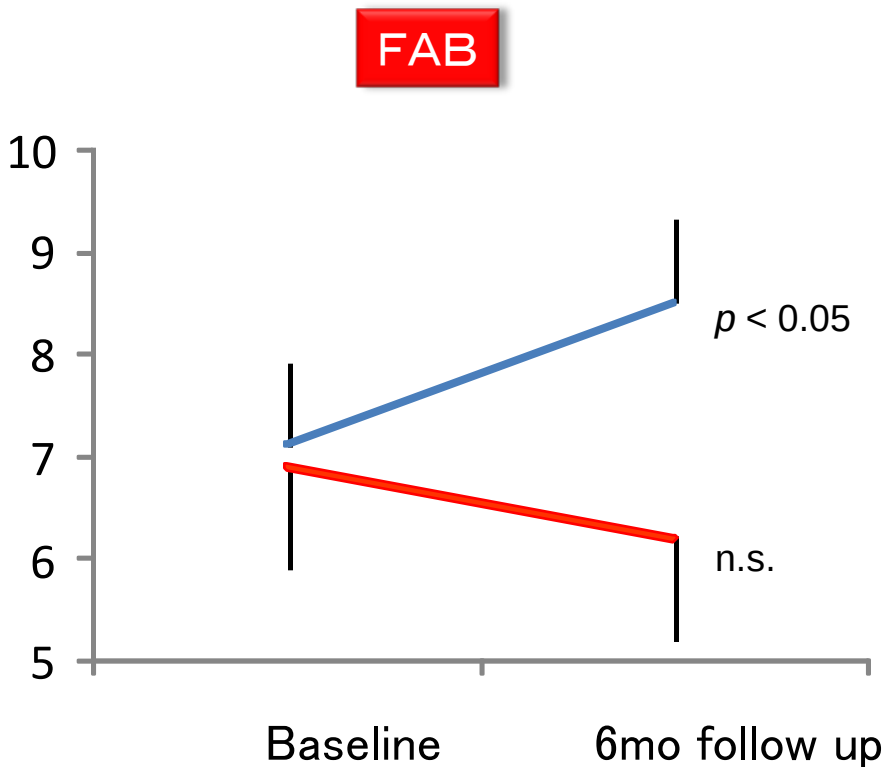


NIRs*: Near Infra-Red Spectroscopy

# Changes in Neuropsychological Characteristics

Much improvement for the intervention group
compared to the control group on standard mental assessments




Error bars indicate SEM

*MMSE: Mini-Mental State Examination
**FAB: Frontal Assessment Battery at Bedside



Source: *J Gerontology Series A, Biological Sciences and Medical Sciences*, 2005

# RCT-healthy seniors

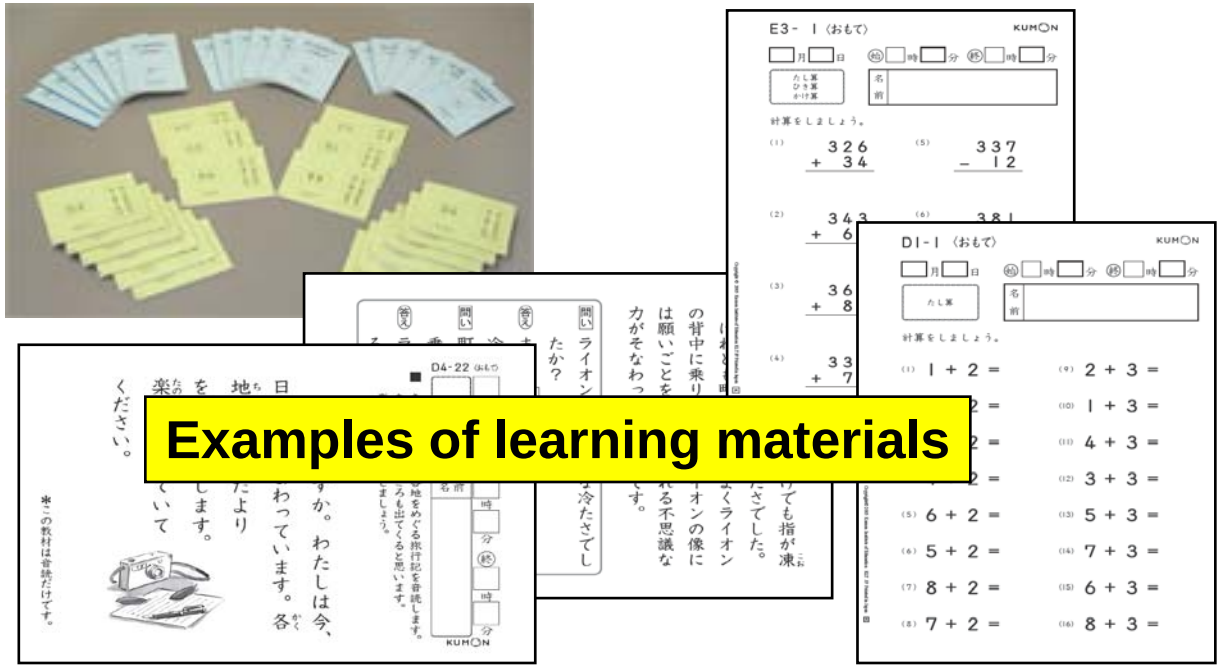
Single blind, randomized controlled trial
of cognitive intervention
in community dwelling seniors

（n = 98, mean age 75.4, 70 to 86 years old）

# Trial Structure

1. For daily cognitive intervention, participants were asked to solve basic problems in reading and arithmetic.

2. Participants participate one day at class and six days at home each week for six months.




Source: Kawashima et al. *J Gerontology Series A, Biological Sciences and Medical Sciences*, 2005

# Classroom Activity (once a week)

1. Participants in the experimental group were asked to come to class once a week at two elementary schools near their residence.

2. Daily learning time for the two tasks was approximately 15 minutes.

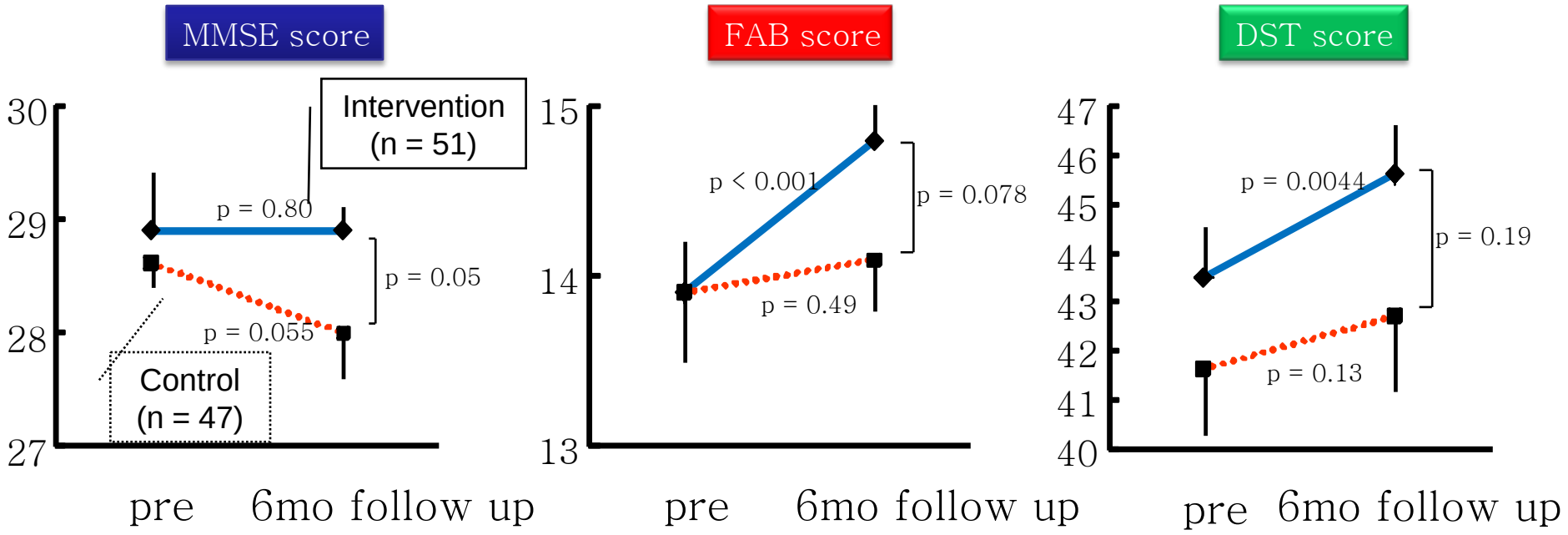
Tsurugaya Primary School, Sendai

Tsurugaya East Primary School

# Cognitive Intervention

# RCT-healthy seniors

## Changes in Neuropsychological Characteristics (Sendai Tsurugaya Project)




Cognitive measures:

- Mini-Mental State Examination (MMSE)
- Frontal Assessment Battery at Bedside (FAB)
- Digit Symbol Substitution Test of WAIR-R (DST)



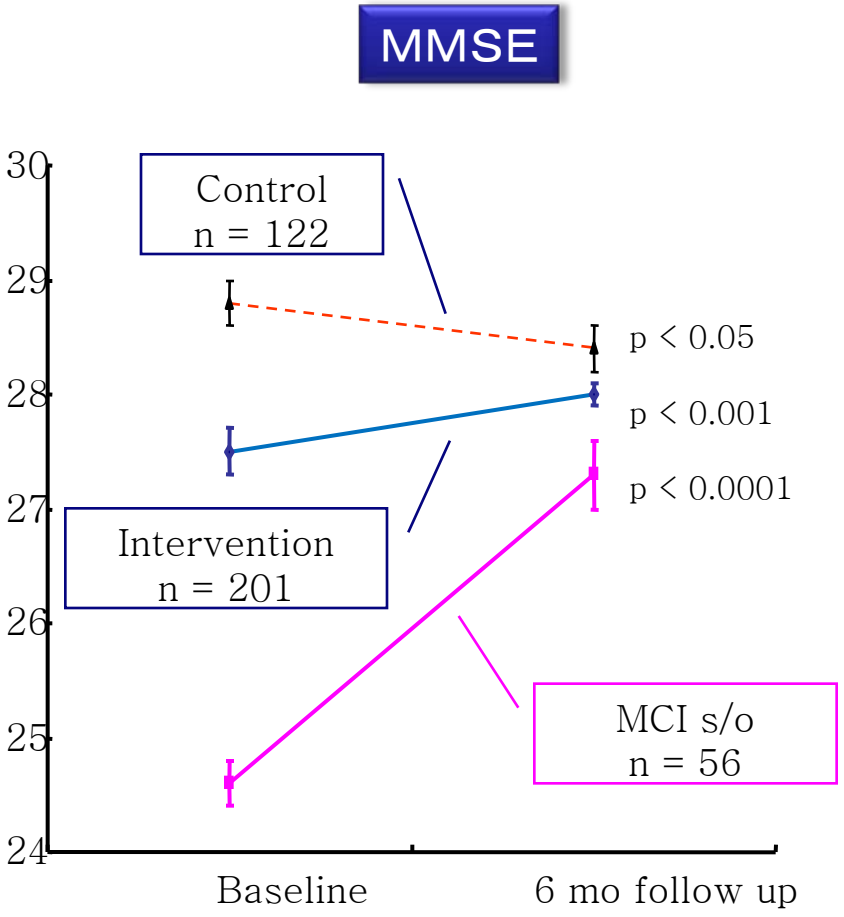
Uchida & Kawashima, *Age*, 2008

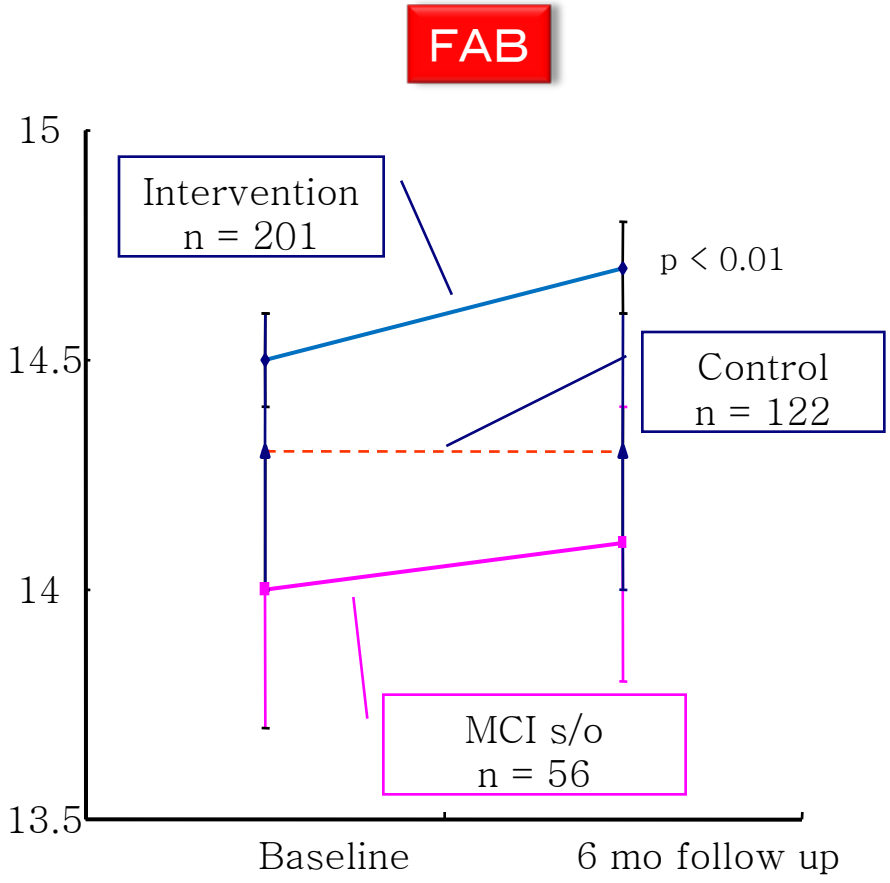
# Active Cohort

Large scale cohort study of people with normal cognitive function or mild cognitive impairment
（n = 323, n = 56）

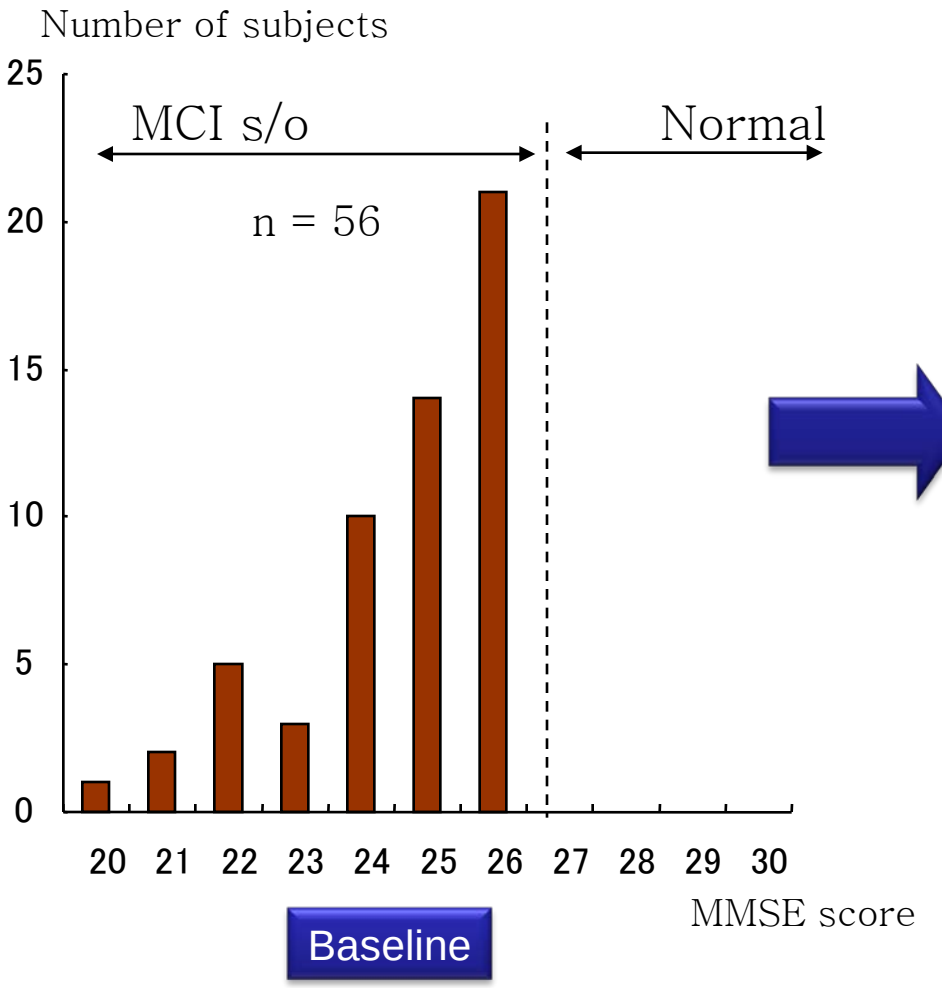
# Active Cohort

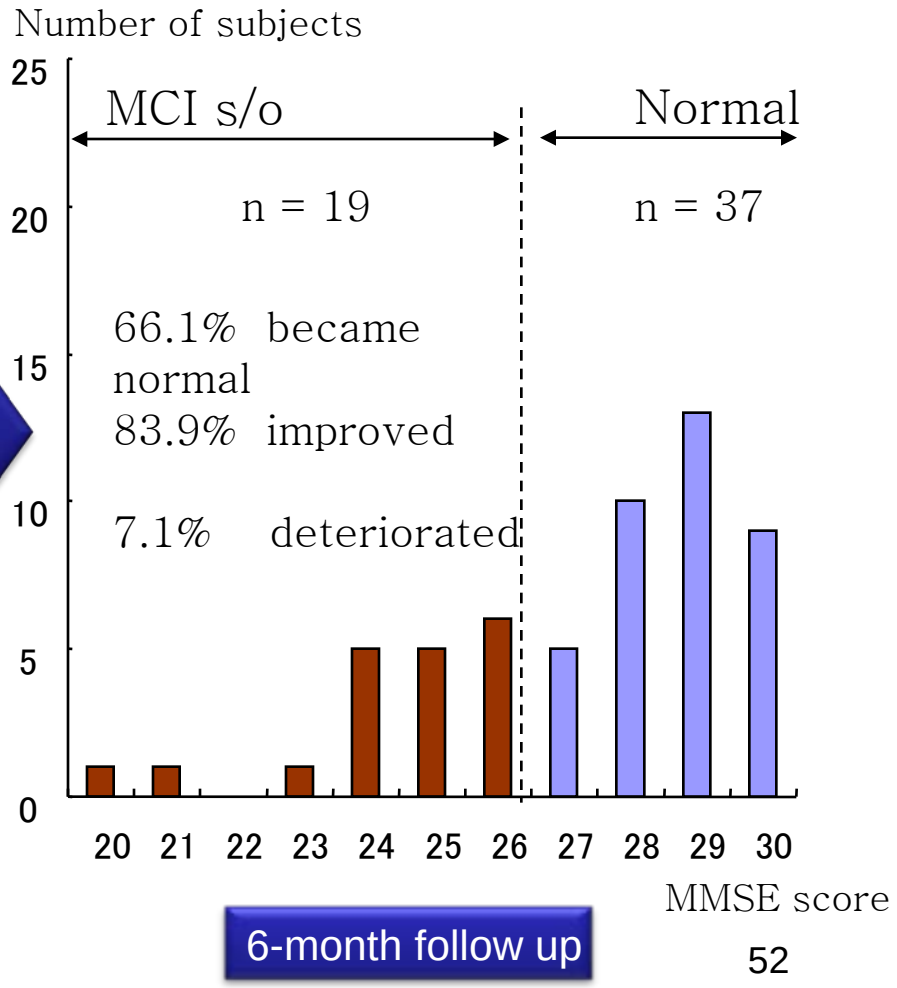
## Changes in Neuropsychological Characteristics in large scale cohort study



# Changes in Neuropsychological Characteristics of Mild Cognitive Impairment (MCI) subjects (Oogaki, Gifu Project)



# How is your life changed after joining the class?

Participants said their quality of lives were improved

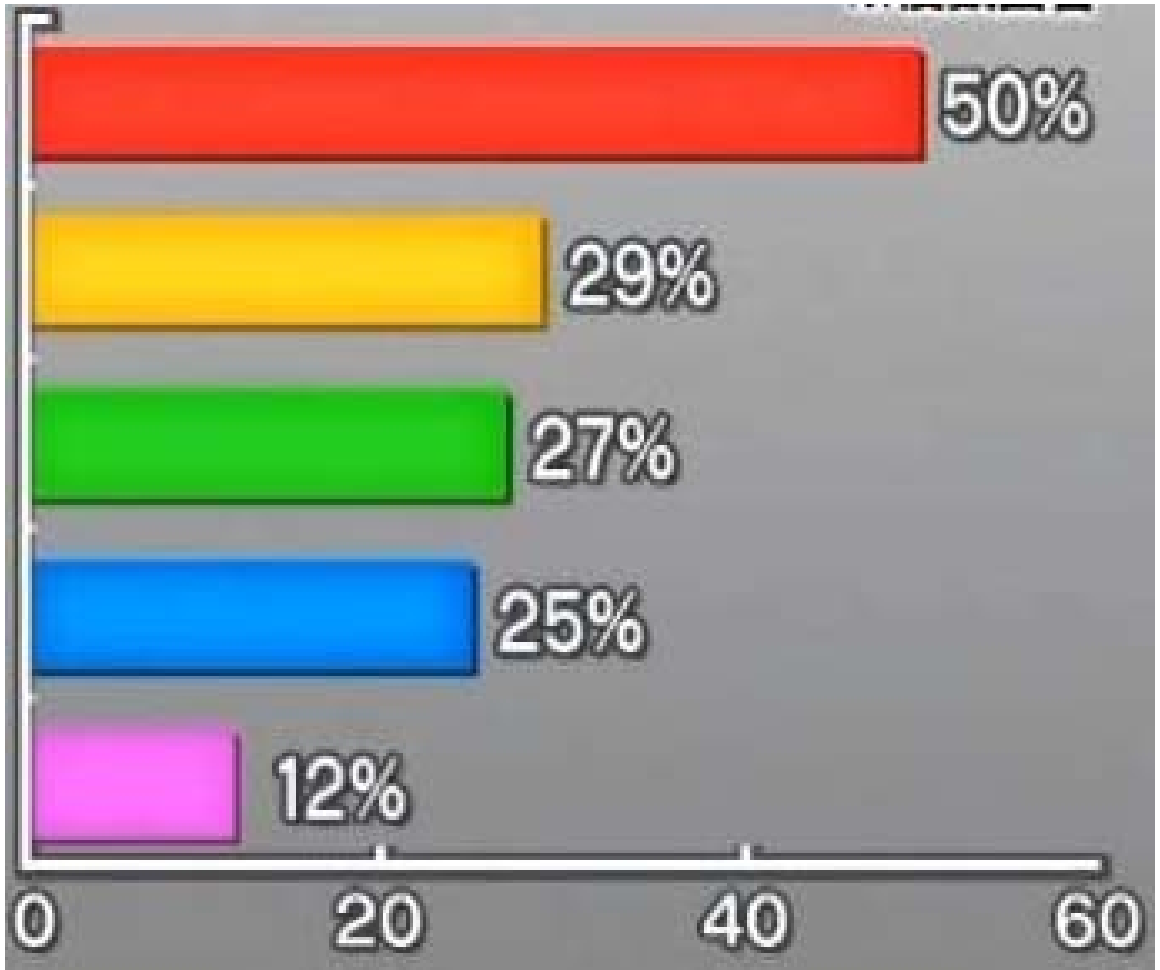
Became more vital

Became more motivated

Became more optimistic

Made new friends

Became less forgetful



# Person-to-person communication is the key to success for brain training

1. The “Class for Healthy Brain” serves as a place where learners and supporters can communicate with each other through learning.

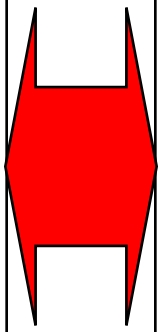
2. Learners not only practice at home but learn through communication with peers and supporters.

3. Learners enjoy Learning Therapy, which gives rise to new meaning in their lives.

# Difference 1:
# Direct activation of prefrontal cortex functions

## Traditional rehabilitation

- When a part of the brain is damaged, another part of brain can begin functioning instead of the damaged part in patients participating in a focused training program.



## Learning Therapy

- Various abilities of patients are improved by activating the prefrontal cortex.
- Functions of the prefrontal cortex are improved by training, rather than compensation by other parts of the brain upon the loss of pre-cortical functions.

# Difference 2:
# Scientifically-proven, evidence-based

There are many types of so-called “Therapy” such as

- Music Therapy
- Animal Therapy
- Forest Therapy
- Gardening Therapy
- Aroma Therapy……etc.

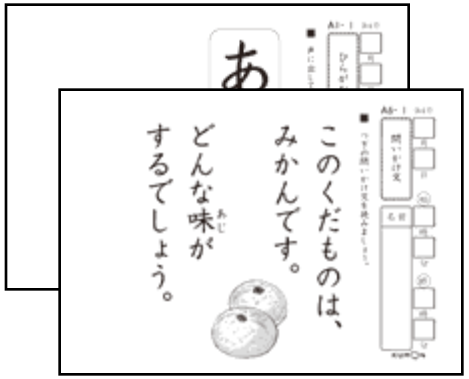
….However, most of them are not scientifically proven and lack of evidence

Learning Therapy is
scientifically proven therapy

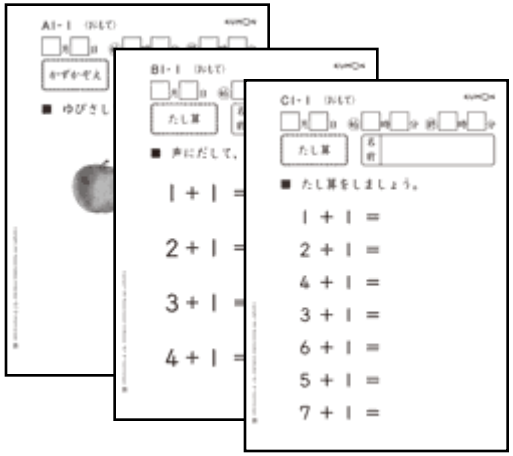
# Difference 3:
# No use of drugs or pills

# Difference 4:
# No need for IT devices such as personal computer

Reading and Writing




Arithmetic




Dementia Care

# Difference 5:
# Social interaction-oriented


The “Class for Healthy Brains” is a program to prevent dementia and maintain a healthy brain among normally functioning elderly people by incorporating reading, writing, and arithmetic calculations in their daily lives.

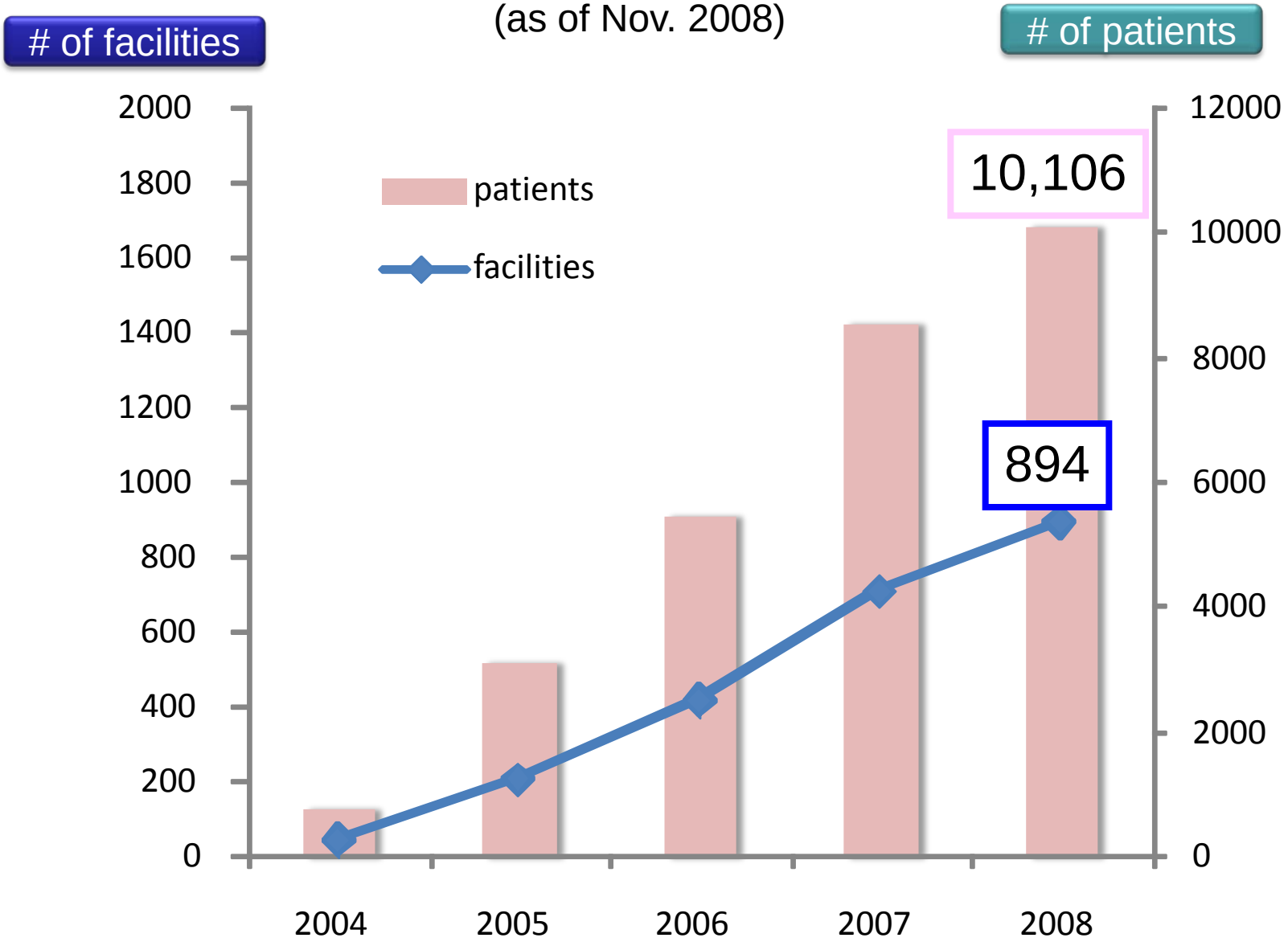
# Difference 6:
# Supporters as well as learners benefit from the program

| Before Program Participation | After Program Participation |
| --- | --- |
| 1. Negative view of caring for elders / aging is seen as “loss” | 1. Positive view of caring for elders / aging is seen as “gain” |
| 2. No sense of reward / endless work without clear goal | 2. Much sense of reward / opportunity to discover potential of elders |
| 3. Staff looks tired | 3. Staff looks motivated |

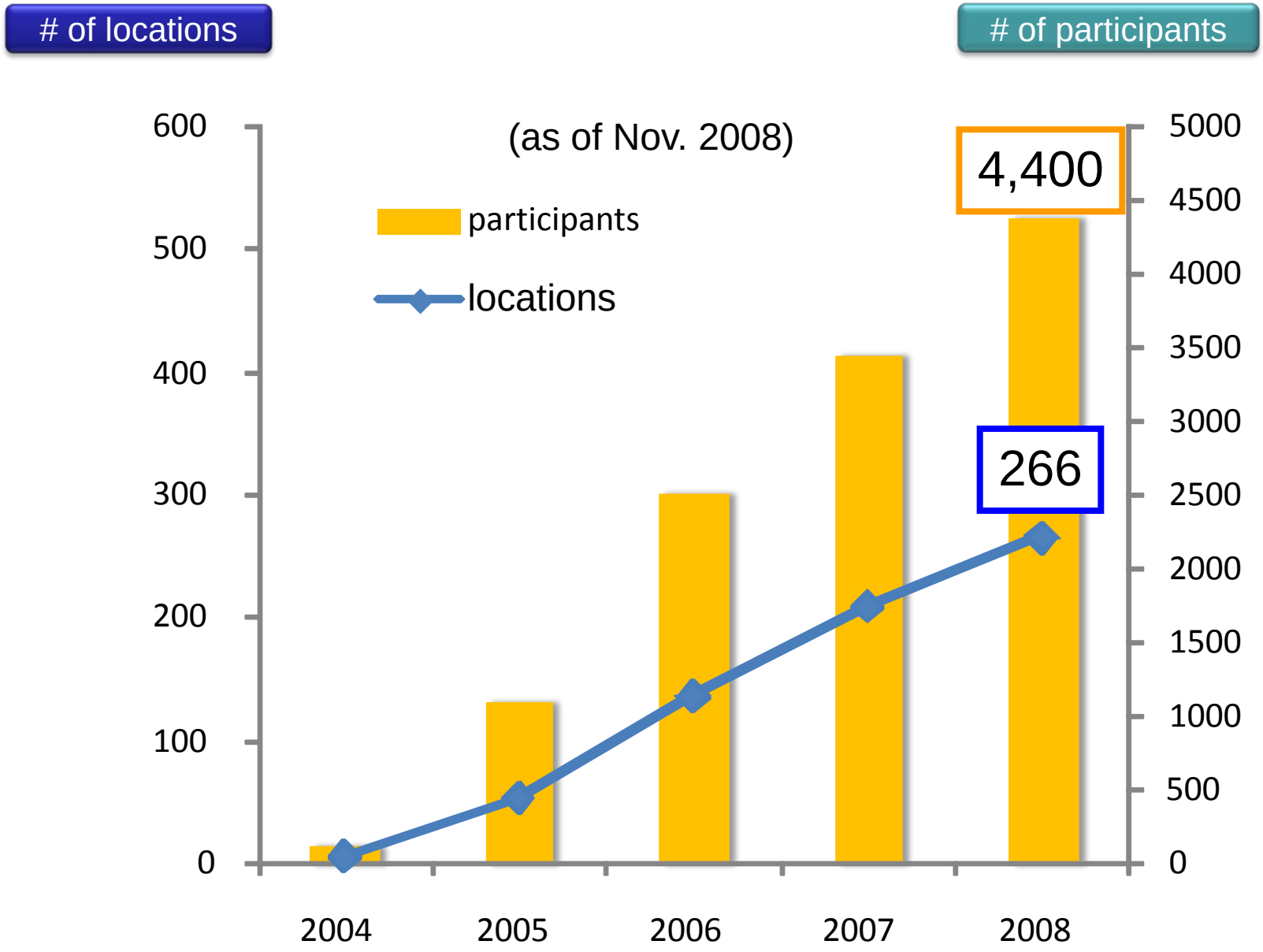
How has Learning Therapy been accepted in Japan?

# Learning Therapy for Dementia Care

(as of Nov. 2008)



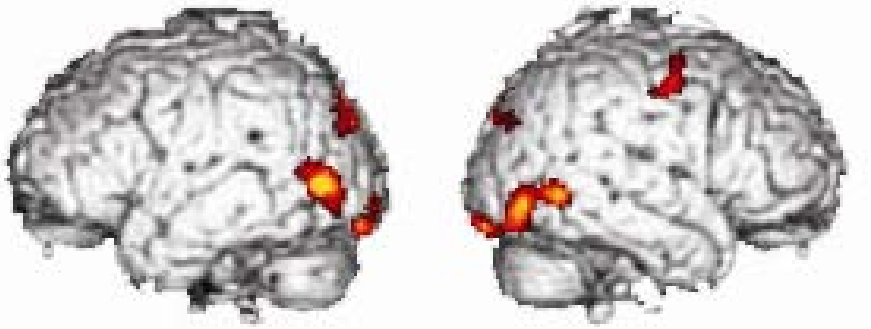
# Learning Therapy for Dementia Prevention (Class for Healthy Brains)



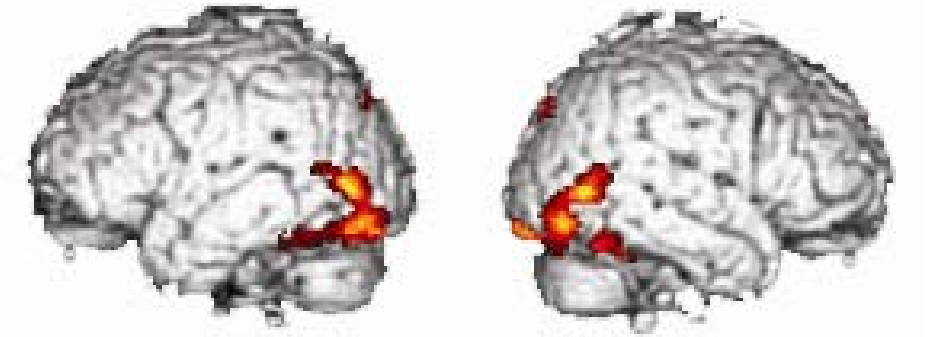
# Examples of Industry-University Joint Research

*-R&D of Games and TV Programs-*

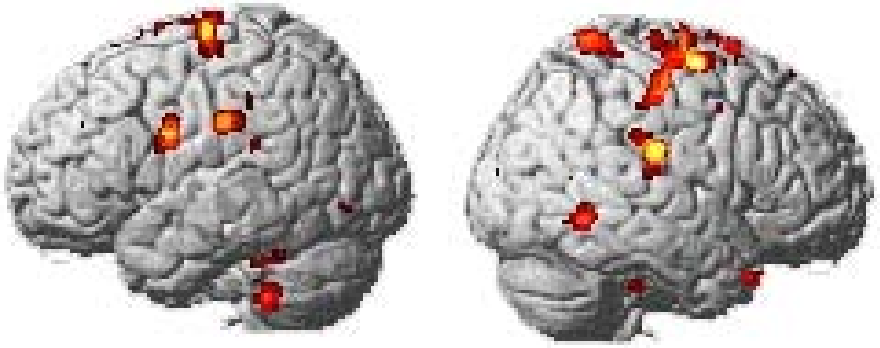
# Brain activity during playing video games



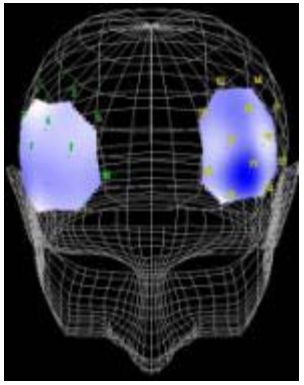
Fighting game（fMRI）



Shooting game（fMRI）



Puzzle game（fMRI）

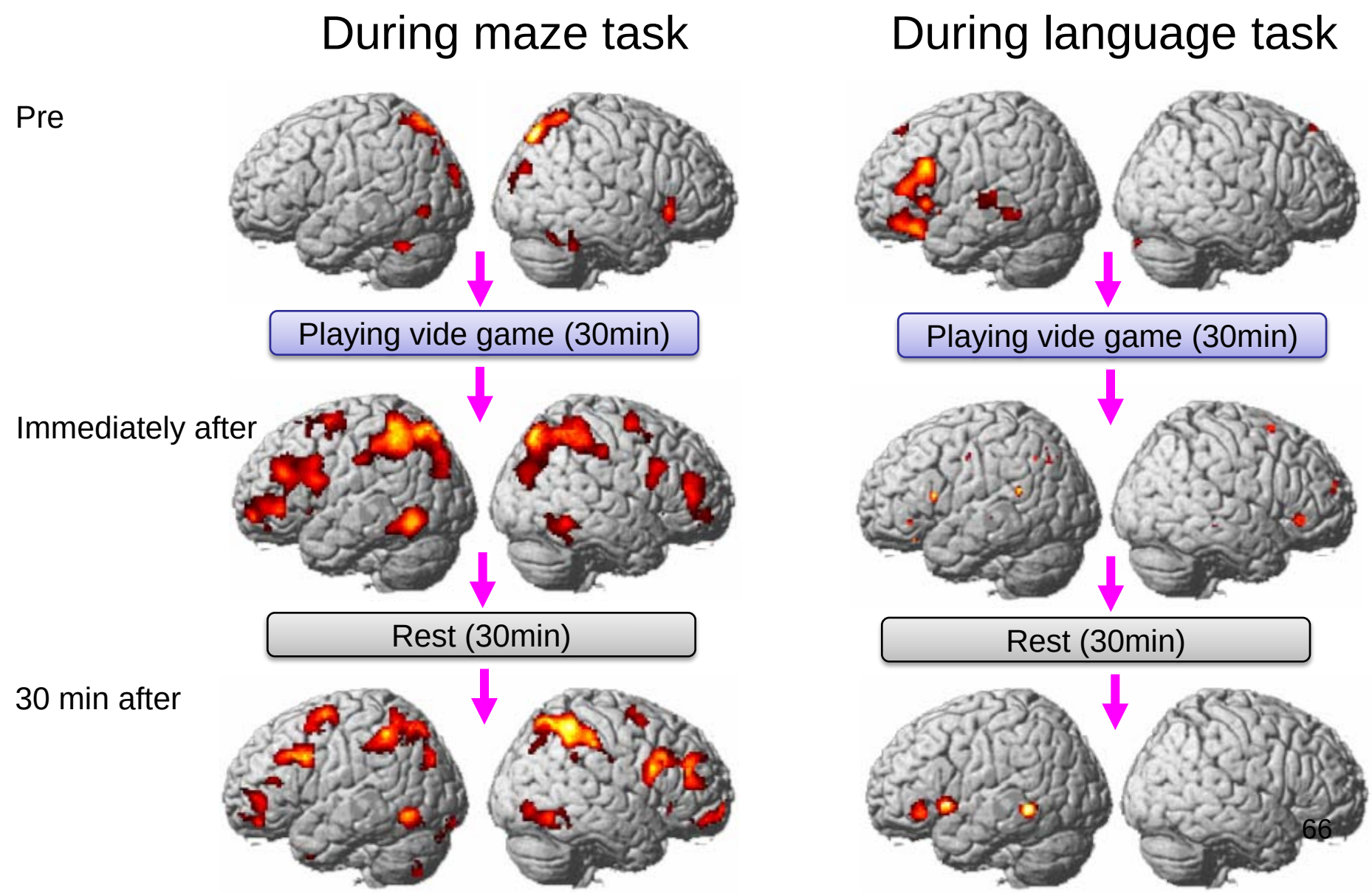


Puzzle game（NIRs）

The most videogames do not activate the prefrontal cortex.

In addition, they often ***deactivate*** the prefrontal cortex.

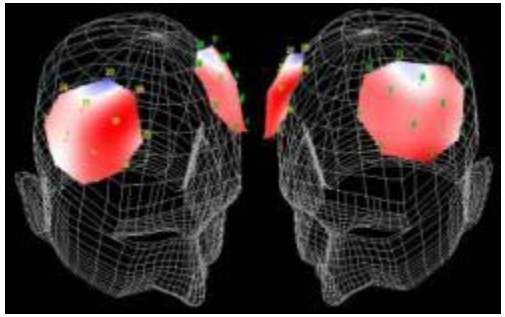
# Playing video game affects activity of the brain



# R&D of video game that can activate the prefrontal cortex

*Needs*
Company
(e.g. Nintendo)

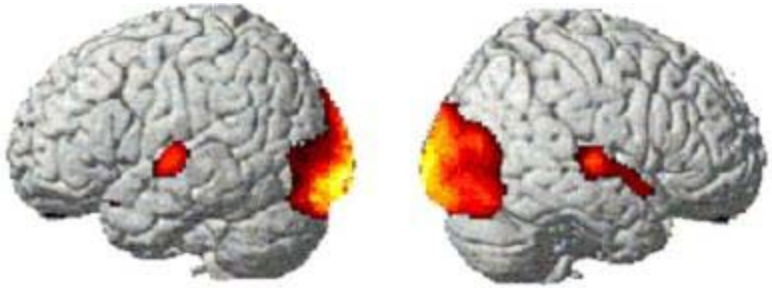
Game soft

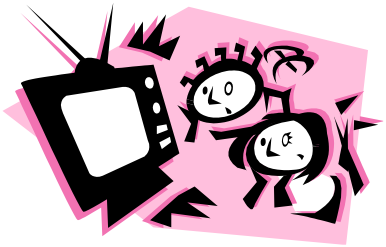



*Seeds*
Tohoku University
Measure brain activity

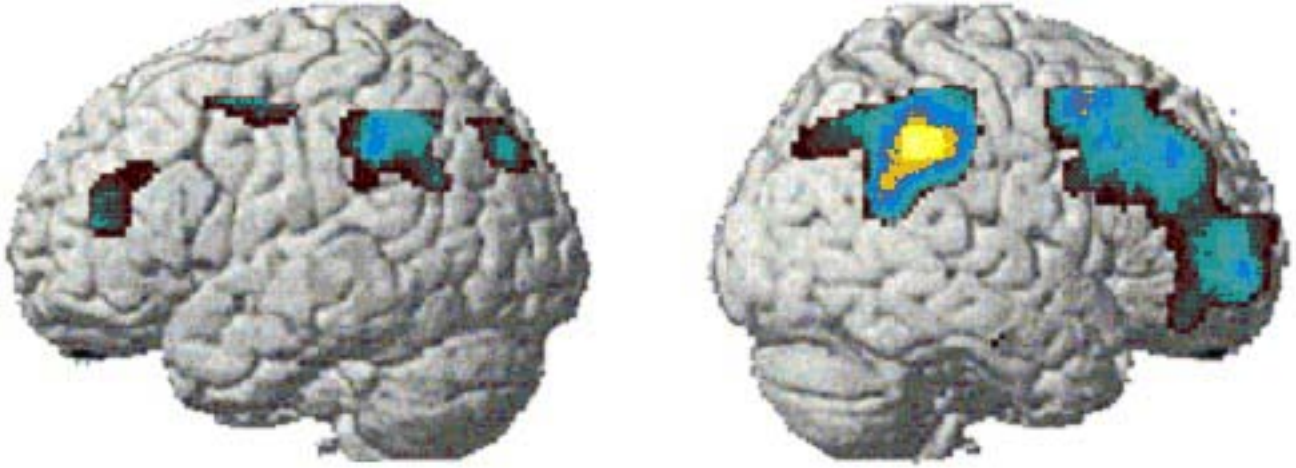
We evaluated and made suggestions how to activate the prefrontal cortex using brain imaging techniques.
This evaluation (scientific proof) added values to the game itself and made it mega-hit!

# Watching TV or Video





Brain activation during watching TV programs

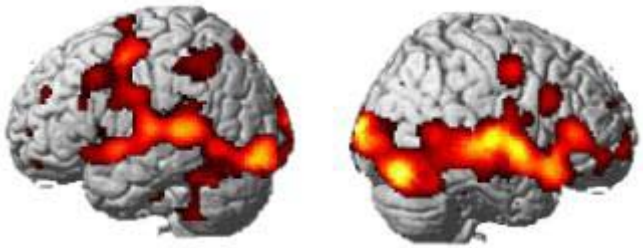


Brain *deactivation* during watching TV programs

# R&D of TV program that can activate the prefrontal cortex

*Needs*
Company
(e.g. TV station)

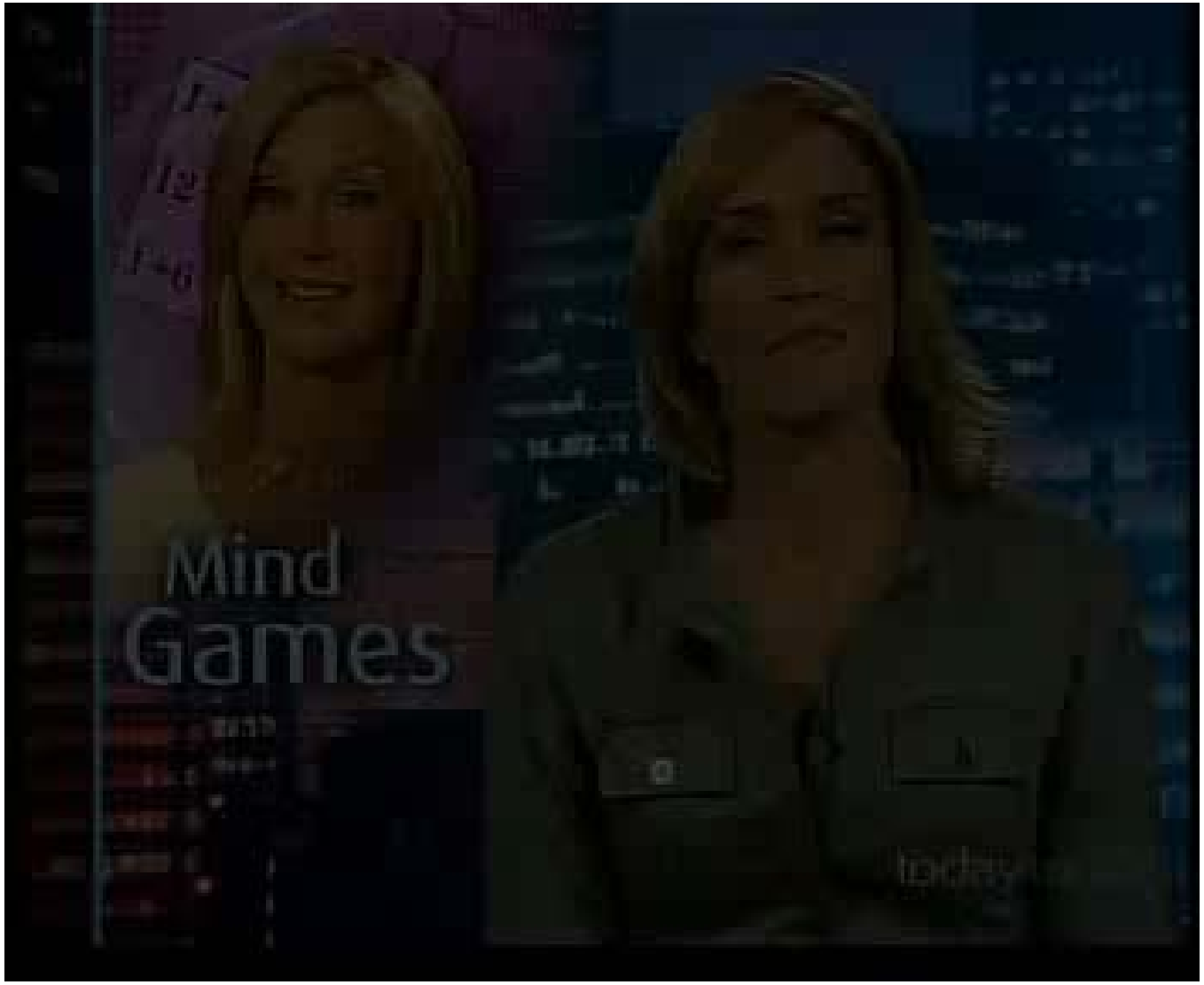
programs




*Seeds*
Tohoku University
Measure brain activity

We evaluated and made suggestions how to activate the prefrontal cortex by TV programs using brain imaging techniques.

# Beneficial Effects on Cognitive Functions by Nintendo DS Brain Training Games




“Today Tonight” 2008.06.24 Australia

TOHOKU

ブレインイメージング研究棟 竣工記念　平成20年4月28日