



Assessment of Higher Brain Functions in Everyday Life Using Virtual Reality Technology

Okahashi, Sayaka

(Degree)

博士 (学術)

(Date of Degree)

2014-09-25

(Date of Publication)

2015-09-01

(Resource Type)

doctoral thesis

(Report Number)

甲第6224号

(URL)

<https://hdl.handle.net/20.500.14094/D1006224>

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Doctoral Dissertation

**Assessment of Higher Brain Functions
in Everyday Life Using Virtual Reality Technology**

VR 技術を用いた日常生活における高次脳機能評価
に関する研究

July 2014

Department of Computational Science,
Graduate School of System Informatics, Kobe University

Sayaka Okahashi

Abstract

Recently, the percentage of elderly people with various physical and mental diseases has increased in many developed countries. Higher brain dysfunctions related to memory, attention, and language due to aging and brain damage lead to many difficulties in daily life. Such patients have difficulties not only in the basic activities such as clothing, bathing, but also other essential activities of daily living such as shopping, housework, medication management etc. It has been reported that the results of conventional assessment methods with a paper and pencil sometimes disagree with the actual cognitive level of individuals. Therefore, the development of more effective assessment methods is required to assist cognitive rehabilitation. For such kind of assessment, it is important to observe patients in an environment that is similar to their everyday life in order to understand the problems caused by their functional impairment.

Since 1990s, virtual reality (VR) techniques have been focused in the application of assessment of cognitive impairment. Previous studies have demonstrated that assessment of higher brain dysfunctions using VR technology has significant potential uses in clinical rehabilitation. However, there were various problems when we applied these systems for patients with brain damage in Japan. First of all, some systems required the use of joystick liked human interface, which was difficult to be operated by patients who were unfamiliar with a personal computer. In addition, the virtual environment and language used in these systems were foreign to Japanese patients. It was especially difficult for elderly people because they also needed to overcome a cultural gap to addition to understanding unfamiliar scenery. Finally, it seemed that the tasks were too complex. They required patients to buy several items and to respond to more than three targets in one test session.

In this dissertation, a new approach to evaluate patient's higher brain functions is proposed by using VR technology so as to overcome the limitations of conventional types of assessment in previous studies. A Virtual Shopping Test (VST), which introduces shopping tasks in a virtual shopping mall, is developed to assess comprehensive cognitive ability in routine daily tasks.

Higher brain dysfunctions and their assessment methods are explained briefly in Introduction. Then, a novel VST system is presented. In this program, the visual environment was made up of a Japanese shopping mall with 20 shops and a train station. An audio environment of the natural sounds in a shopping mall was also provided. Users could move in the virtual shopping mall freely, enter shops and buy items by touching a button or a picture on the screen. A log file was recorded automatically. In the VST, subjects were required to memorize specific items to buy, to look for the shops in the mall, choose the items in each shop, and to perform the whole task smoothly. The scores for evaluation included the number of items bought correctly, the number of times hints were used, the number of movements, and the total time spent to complete the task.

In this research, four evaluation experiments were performed on the clinical usefulness of VST. The objectives of the four experiments were to investigate 1) the effectiveness of VST by comparing with other conventional tests, 2) the applicability of VST in brain-damaged patients, 3) the performance of VST in relation to age differences, and 4) the reliability of two parallel forms of VST, respectively.

The participants included in these four experiments were ten patients with brain damage, ten age-matched healthy subjects as controls, ten elderly healthy subjects, and ten young healthy subjects. VST and neuropsychological tests/questionnaires about attention, memory and executive functions were conducted with the patients, and VST and the Mini-Mental State Examination (MMSE) were conducted with healthy subjects.

As a result, from the first experiment, some variables in the VST were found to correlate with the scores of conventional assessments about attention and everyday memory. In the second experiment, the mean number of times subjects referred to hints and the mean number of movements were significantly higher for the patients, and the mean total time was significantly longer for the patients than for the control subjects. For the aging related experiment three, the mean total time was significantly longer for elderly people than for young people, and in experiment four, it is clarified that there were no significant group differences in the basic variables between the two parallel tests. These results suggested that VST is able to evaluate attention and everyday memory capabilities in brain-damaged patients. The time taken in the VST increased with age. The two parallel tests were almost equal in difficulty level.

In cognitive rehabilitation, exercises with an appropriate difficulty level for each individual may increase their motivation and produce good results. Rehabilitation therapists clinically evaluate each patient's ability and try to provide them with a specific appropriate task. However, difficulties have been associated with establishing an appropriate task level because of a lack of evidence on their effectiveness. Although various VR techniques have been proposed for cognitive rehabilitation, the task difficulty level and related brain activation have not been sufficiently considered. In the following study, the VST was modified to a revised version (VST-R) that had three different task difficulty levels. The system could also output event signals that were synchronized with the user's inputs. These signals were used to assess event-related brain activation. The VST-R was used with functional near-infrared spectroscopy (fNIRS), a non-invasive and non-restrictive technique that allows blood oxygenation changes related to cerebral activation to be measured, to evaluate prefrontal cortex activity while subjects performed the test.

The VST-R system was refined and used in a clinical experiment in

convalescent brain-damaged patients. In the VST-R, test subjects were asked to buy two specific items in Task 1, four items in Task 2, and six items in Task 3 from a virtual mall. The tasks and questionnaires were undertaken by six healthy young adults and ten patients. Hemodynamic changes in the prefrontal cortex (PFC) during activation due to the tasks were examined using fNIRS. The results obtained showed that the mean total time was significantly longer for the patients than for the healthy subjects. PFC responses to the shopping and moving phase in Task 2 were greater in the patients than for the healthy subjects. Although task performance as well as PFC responses was not significantly changed in the healthy adults, they could subjectively evaluate differences between the three task levels, whereas the patients could not. These results suggested that the difficulty of the four-item shopping task may have been sufficient to cause brain activation in the brain-damaged patients.

As conclusions of this study, a VR system was developed for the realistic assessment of higher brain functions in brain-damaged patients in a virtual shopping situation. The results of the experiments showed the clinical usefulness of the VST in brain-damaged patients. It was pointed that, rehabilitation therapists should pay attention to not only the performance variables of the VST but also brain activation and psychological variables in assessing the progress of a patient's condition. Along with detailed assessment of each function by conventional methods, practical proposals are provided by the VST and VST-R to understand the patients' problems in everyday life related to various kinds of higher brain functions.

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List of Abbreviations

ADL: activities of daily living
BIT: Behavioural Inattention Test
CPT: Continuous Performance Test
CVA: cerebrovascular accident
DEX: Dysexecutive Questionnaire
EMC: Everyday Memory Checklist
FIM: Functional Independence Measure
fNIRS: functional near-infrared spectroscopy
IADL: instrumental activities of daily living
lPFC: the left lateral prefrontal cortex
MCI: mild cognitive impairment
MMSE: Mini-Mental State Examination
mPFC: the medial prefrontal cortex
OT: occupational therapist
PC: personal computer
PT: physical therapist
PFC: the prefrontal cortex
RBMT: Rivermead Behavioural Memory Test
rPFC: the right lateral prefrontal cortex
SD: standard deviation
SDMT: Symbol Digit Modalities Test
SLP: speech-language pathologist
SRT: Simple Reaction Time Task
TBI: traumatic brain injury
USN: unilateral spatial neglect
VR: virtual reality
VST: Virtual Shopping Test
VST-R: the revised version of Virtual Shopping Test

Chapter 1

Introduction

In this chapter we introduce medical, neurological, and social backgrounds of higher brain dysfunctions and their assessment methods.

1.1 Background on higher brain dysfunctions

Higher brain functions carry out important tasks in everyday life. That is clinically recognized to have several functions: verbal function, perception, attention, memory, executive functions and so on. Basically, attention is the most fundamental one, followed by consciousness. In such a way, these functions form a hierarchical structure to realize the human's cognitive function.

Higher brain functions make it possible for the people to recognize where, what, and how the object is, and to express or inform understanding of phenomena as well as thinking by using language function. In addition, memory function has an important role to acquire these abilities and use them from past to future efficiently. It is also higher level of cognitive function of us to organize various functions and perform something for the specific aim systematically. On the other hand, emotion influences on many domains of the functions. Sometimes, emotion expression and ability of auditory/optical reception are included in cognitive functions.

Therefore, higher brain dysfunctions caused by brain damage such as stroke

and traumatic brain injury seriously influence the independent life for patients. Patients demonstrate difficulties in activities of daily living (ADL, e.g. eating, bathing) and instrumental activities of daily living (IADL, e.g. cooking, shopping) (Chevignard et al., 2000; Fortin et al., 2003). In that case, it is important for cognitive rehabilitation to provide patients with abilities training of real life.

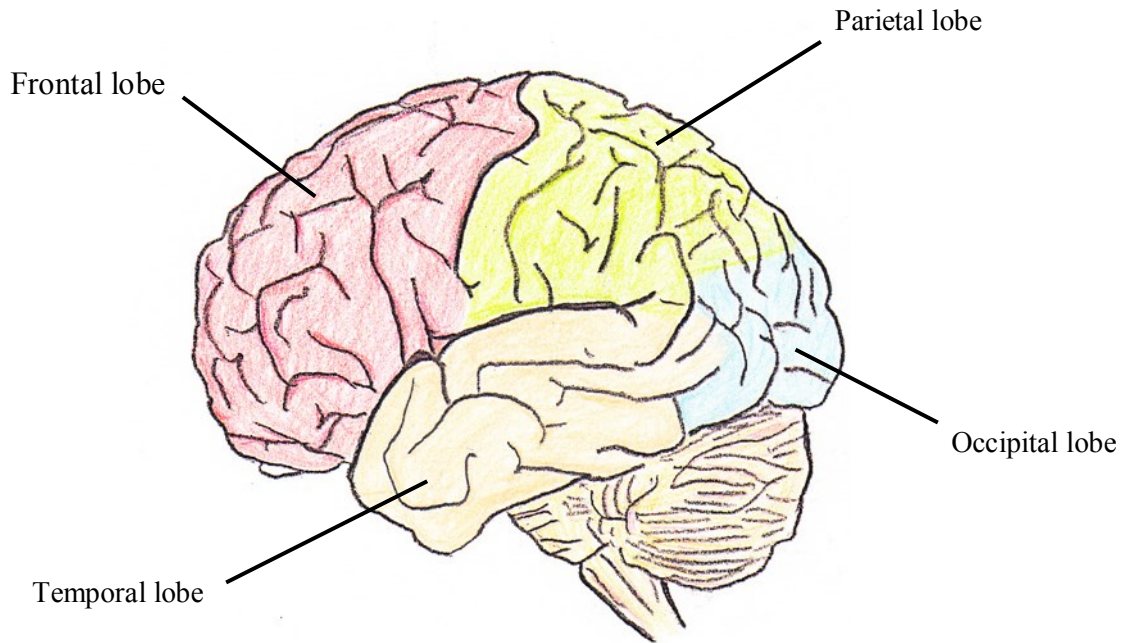
1.1.1 Medical background

Several types of organic brain disorder cause higher brain dysfunctions. There are the following primary diseases: a cerebrovascular accident (CVA) (e.g. cerebral hemorrhage, cerebral infarction, transient ischemic attack, subarachnoid hemorrhage etc.), traumatic brain injury (TBI) (e.g. cerebral contusion, traumatic intracranial hematoma, diffuse brain injury etc.), neurodegenerative diseases (e.g. Alzheimer's disease, frontotemporal lobar degeneration, diffuse Lewy body disease, multiple system atrophy etc.), encephalitis, and hypoxic encephalopathy caused by lack of oxygen in brain.

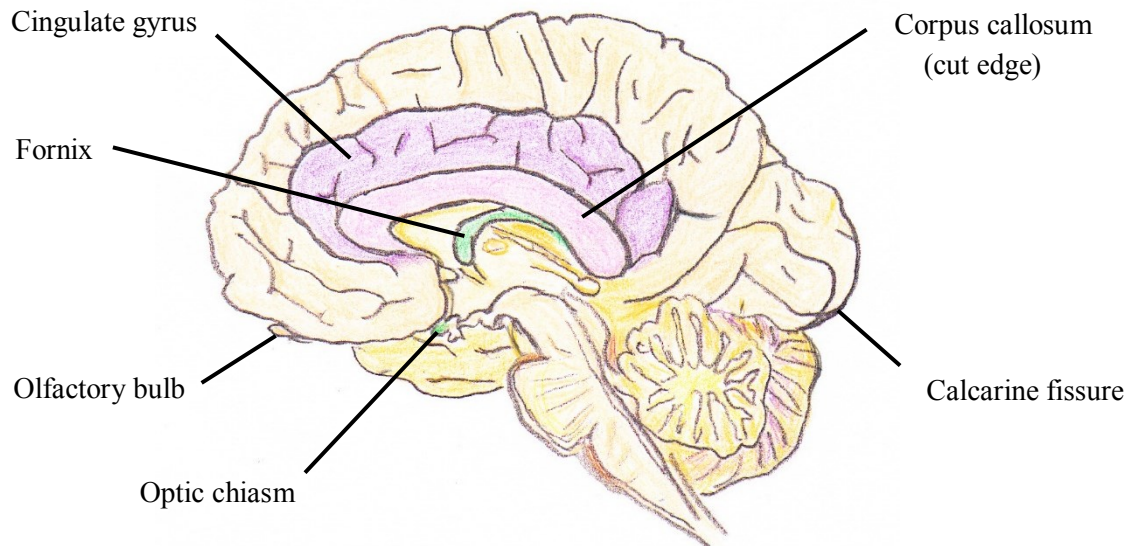
Regarding CVA, patients with cerebral hemorrhage have symptoms according to the cerebral region of infarction. The symptoms were often severe than that of a same size of cerebral infarction immediately after the onset, but it improve for a long time and the aftereffect was small. While, patients with cerebral infarction also have symptoms according to the damaged cerebral region. Each peripheral blood vessel provides almost fixed specific cerebral blood flow, so the damaged cerebral region caused by cerebral infarction is a fixed area. A specific brain artery lesion causes one symptom or mixed symptom composed of some fixed cognitive dysfunctions.

On the other hand, patients with TBI have rarely fixed symptoms according to a specific brain artery lesion. Cerebral contusion is crush injury, small hemorrhage, edema in cerebral parenchyma caused by external force like a traffic accident. The mechanism of injury is translational acceleration, and the brain regions frequently suffering from this are ventral frontal lobe, frontal pole, ventral temporal lobe and temporal pole (see Figure1-1). It often occurs in many places. The rate of deaths from this injury is high, about 50%. Cerebral contusion in frontal lobe sometimes causes executive dysfunction, character change, and behavior disorder.

Encephalitis is inflammation of cerebral parenchyma by pathogen, autoimmunity, and others. The region specificity by brain damaged is usually poor, and it often causes dementia with frontal lobe damaged symptom. Encephalitis in limbic system causes amnesia and emotional disturbance.



(a) A left exterior hemisphere



(b) A right interior hemisphere

Figure 1-1 A classification of cerebral lobe.

1.1.2 Definition of terms and neurological background

In this section, we describe definition of terms on higher brain functions and neurological background. Three important functions in daily life: attention, memory, and executive functions which are dealt with in the following experiments are mainly focused in this dissertation.

Usually, higher brain functions are represented in a hierarchal structure as shown in Figure 1-2, which is called “a neuropsychological pyramid”. This is used in Brain Injury Day Treatment Program as a clinical framework at Rusk institute in New York. Following this structure, attention is more fundamental one; memory and executive functions are more advanced.

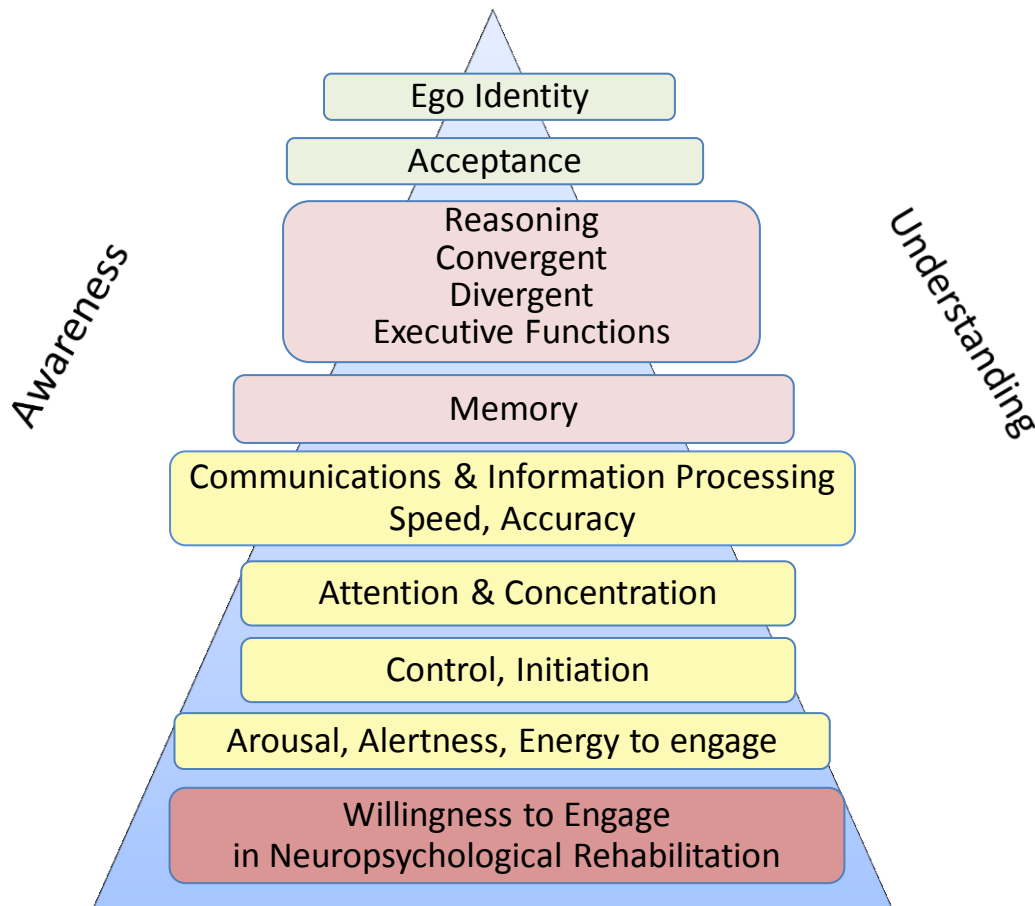


Figure 1-2 A hierarchical structure of higher brain functions.

1.1.2.1 Attention

Attention is a neural organization that is necessary for working each function (e.g. recognition, language, memory, and thinking) effectively. Definition of “attention” (by Mesulam) is as follows: When human is awake, they interact information outside world and phenomena such as memory retrieval and thinking, but it is limited the amount of information that he/she process in a fixed time period. Therefore, it is needed that a person concentrates the specific external/internal event. He/she selects the most appropriate event on the point of physical feature and the importance for the individual at that time. In addition, a person has to switch to the new target of the concentration in response to events that change with time reasonably and flexibly.

Attention has various aspects and it called by different names: alerting, orienting, and executive control.

Alerting. Alerting is attention function that maintains present state, alerts and responds something quickly. One side of this function is as same as conventional “sustained attention” or “vigilance”. The function avoids missing stimulations appear randomly without advance notice. It is called as “intrinsic alertness” and measured by a task that does not require quick response. On the other hand, “phasic alertness” such as quick response to external stimulation like an alert warning is measured by reaction time.

Orienting. Orienting is the directionality and selectivity in multiple environments. For this function, people can differentiate a partner’s voice from many voices in conversation and turn consciousness to a caution object in a specific direction and an

area in space. The spatial aspect on the latter corresponds to “spatial attention”.

Executive control. Executive control is the function selects a thing that required and executes something among response patterns that compete each other which are stimulus with multiple factor. The representation of this function is called “selective attention” and evaluated with Stroop task traditionally. In this test, words express color name (e.g. “red”, “blue”, “green” etc.) with another color differed from the mean of each word were presented. A subject is required the color of each word printed against the tendency of habitual response read the word itself.

Others. The function of process more than two tasks at the same time is sometimes called “divided attention”. This function is also expounded through a concept of “working memory” integrated temporary registration of information and executive function related to attention distribution.

Neural networks. Table 1-1 shows attention type and neural networks involved in each. Generally, the neural network consisting of anterior cingulate gyrus and the surrounding region—thalamus—midbrain involve Alerting and sustained attention. In addition, a specific brain region according to the stimulus sensory modality works.

Table 1-1 Attention type and related neural networks.

attention type	related neural networks
Visual Alerting	The frontal lobe in right cerebral hemisphere (anterior cingulate gyrus – dorsolateral cortex) – inferior parietal lobe – thalamus (pulvinar etc.) – brain stem (midbrain, pontine tegmentum etc.)
Auditory Alerting	The temporal lobe in addition to the neural network involved in Visual Alerting
Orienting	Neural networks involved in spatial attention (Mesulam, 1999) consisting of parietal lobe, frontal lobe, cingulate gyrus, thalamus, corpus striatum, superior colliculus etc. There is not always the predominance right cerebral hemisphere.
Executive control	<ul style="list-style-type: none"> • bilateral or right anterior ventral frontal lobe • anterior cingulate gyrus

1.1.2.2 Memory

Learning in the acquisition of new information; Memory is the retention of learned information. Memory is the whole functions including to encode, store, and retrieve the various things we have experienced on the processing them for brain. It is clinically difficult to determine which phase is affected in patients with memory deficit. Most of memory tests include Learning: process of through encoding phase and storing phase.

Memory can be classified into two types: Declarative memory and Non-declarative memory. Declarative memory is a kind of memory people express memory information consciously, while Non-declarative memory is contrasting one that

includes Procedural memory: a kind of memory on skill of action, performance, behavior (Squire, 2004).

Declarative memory is classified into several types as follows from the temporal view. As a clinical classification, there are immediate memory, recent memory, and remote memory. As a psychological classification, there are Short-term memory and Long-term memory. Declarative memory is also classified into two types as follows from the view of its content: Episodic memory and Semantic memory. Episodic memory is memory about the information of personal experiences in a specific time and place, while semantic memory is memory the whole knowledge about objects, facts, concepts etc.

In addition, memory contains not only past events, but also prospective things. People have to remember to carry out some action at a future time in their everyday lives. This type of memory is called 'Prospective memory'. It includes some parts of other functions such as attention, executive functions, working memory etc. Patients with TBI or mild cognitive impairment (MCI) often have prospective memory disorder. An fMRI study (Simons et al., 2006) reported the frontal cortex around Brodmann area 10 was related to prospective memory task performance.

Recently, 'Everyday memory' has been focused in assessment and rehabilitation. It is memory operations required in routine daily life and includes all memory aspects mentioned above. For example, remembering name and place, plan for tomorrow, and recent experienced events. It is the ability in not laboratory setting in real world.

Neural networks. Papez circuit is a closed circuit consisting of hippocampus—fornix—mamillary body—mamillary body thalamus road—thalamus pronucleus—thalamus cingulate gyrus projection—cingulate gyrus—cingulum—hippocampus. Papez reported it was the neural system of emotion, however it is regarded as an important neural system of memory nowadays.

1.1.2.3 Executive functions

Executive functions are intrinsic to the ability to respond in an adaptive manner to novel situations and are also the basis of many cognitive (e.g. language, recognition, and memory), emotional, and social skills. They can be conceptualized as having four components:

- Volition
- Planning and decision making
- Purposive action
- Effective performance

Each aspect involves a distinctive set of activity related behaviors. In everyday life, people plan something and do it effectively by working this function.

Neural networks. The neural network composed of the frontal lobes, nucleus basalis, and subcortical structure such as thalamus is responsible for this functions. Prefrontal cortex (PFC) area, especially dorsolateral PFC, superior medial PFC, ventromedial PFC, and ventrolateral PFC, plays an important part in this functioning.

1.1.3 Social background

As a medical term, “higher brain dysfunctions” means broadly the disorder of complex and abstract brain functions including memory, language, calculation, decision making, and execution caused by brain damage, while as an administrative term, the word means “the condition people have limitation in their daily life and/or social life because of cognitive dysfunction such as attention deficit, amnesia, executive dysfunction, social behavior disorder”. The purpose of the policy is that administration helps the patients with higher brain dysfunctions who could not be supported by conventional laws like Law for the Welfare of People with Physically Disabled. At the point of administration, the primary diseases caused by higher brain dysfunction are mainly CVA and TBI.

One survey (Hachisuka, 2011) reported that the crisis rate of new onset was 2.3 per 100,000 people in Fukuoka Prefecture. It could be estimated that the number of onset is about 2,884 in Japan one year. Based on this data, there would be about 70,000 patients with higher brain dysfunction in Japan. In addition, the population of people with dementia is reported about 4,600,000; the population of people with MCI is estimated 4,000,000 in 2012. Furthermore, the percentage of aged 65 or older is 25.0% in 2013 in Japan. It is expected 29.1% in 2020, 33.4% in 2035 by Ministry of Internal Affairs and Communications. Due to this change, the population of patients with higher cognitive dysfunction caused by various brain diseases including dementia would be increasing.

In Japan, Ministry of Health, Labour and Welfare started “model programs to support people with higher brain dysfunction” in 2001, and then changed over to

“project to support people with higher brain dysfunction” based on in the Act for Supporting the Independence of Persons with Disabilities (the Article 78 paragraph) in 2006. The law was revised in April 1, 2013, and also enforced as the Act for General Supporting the Persons with Disabilities.

1.2 Assessment of higher brain functions

There are some methods of assess higher brain functions clinically. In this section, we describe conventional assessment methods, and new assessment methods using virtual reality technology, separately.

1.2.1 Conventional methods

Traditionally, medical staff and therapists use neuropsychological tests with pencil and paper for objective assessment of higher cognitive functions. They usually use specific assessment for each cognitive function. For example, line cancellation test as shown (Albert, 1973) is used as a test for spatial attention, and the Rey-Osterrieth Complex Figure Test (Lezak, 2012) is used for visual memory. In addition, questionnaires are used for patients or their family/main caregivers are used to evaluate everyday disability as necessary.

Several popular tests and questionnaires are explained below about general cognitive function, attention, memory, and executive functions. The following tests and questionnaires were used in our experiments in Chapters 3, 4 and 5.

Assessment of general cognitive function.

- **Mini-Mental State Examination (MMSE):** The MMSE was a short screening test grouped into 7 categories: orientation, registration, attention and concentration, recall, language, repetition, and visual construction. It was scored out of a possible 30 points. A higher score meant a better cognitive function while a lower score (< 24) indicates cognitive impairments (Folstein et al., 1975).

Assessment of Attention.

- **Symbol Digit Modalities Test (SDMT):** The SDMT was a visual test of processing speed. Subjects held a sheet that contained the numbers and symbols to be processed. The top row of stimuli included nine symbols, each of which was paired with a single digit in the key. The remainder of the page had a randomized sequence of these symbols, and the participant's task was to respond orally with the digit associated with each of the symbols as quickly as possible. The SDMT lasted for 90 s and the completing rate was measured (Smith, 1982).
- **Simple Reaction Time Task (SRT):** The SRT was one of the tasks of Continuous Performance Test (CPT) using a PC. The participant was required to press a specially marked key on the keyboard whenever a number (e.g. 7) appeared on the screen. During the test, the number appeared at intervals varying between 1000 and 2000 milliseconds and remained on the screen either until a response occurred or 1000 milliseconds had elapsed. The total trial lasted approximately 3.3 min and consisted of 80 presentations of the target stimulus (Beck et al., 1956). The correct

rate and average reaction time were measured.

- **Star Cancellation Task:** The Star Cancellation task from the Behavioural Inattention Test (BIT) consisted of 56 smaller stars interspersed with distractors: words, letters, stars. An A4 sized task sheet divided 27 right-sided and 27 left-sided stars on each half of the array. Two stars on this vertical line were not included in the analysis (Ishiai, 1999; Wilson et al., 1987).
- **Letter Cancellation Task:** The Letter Cancellation Task from BIT consisted of 40 target letters arranged with other letter distractors. Japanese hiragana letters were printed in five lines of 34 items each, distributed equally on either side of the array on an A4 sized sheet. The patients' task was to mark all of target letters (Ishiai, 1999; Wilson et al., 1987).

Assessment of Memory.

- **Rivermead Behavioural Memory Test (RBMT):** The RBMT was an ecologically valid, broad measure of impairment in everyday memory functioning. It was composed of 12 subtests which required the patient to remember a name and a last name, a short newspaper article, and a route. It also required the patient to recognize objects and faces; to remember to request a hidden belonging; to ask a question when an alarm rings; and to answer questions about temporal and spatial orientation. The standard profile score was the sum of all the subtest scores, which ranged from 0 to 24 (Wilson et al., 1985; Wilson et al., 1989).
- **Everyday Memory Checklist (EMC):** The EMC consisted of 13 questions concerning memory problems in daily life (Kazui et al., 2006). Each answer was

rated on a four-point scale (1-4), and the total score ranged from 13 to 52. Higher scores indicated more severe memory impairments.

Assessment of Executive functions.

- **Zoo Map Test:** The Zoo Map Test from the Behavioural Assessment of the Dysexecutive Syndrome (BADS) was designed to assess the subjects' ability to formulate and implement a plan. Subjects were required to show how they would visit a series of designated locations on two drawn zoo maps without breaking a set of rules. In the first trial, they had to formulate the route (high-demand condition). In the second trial, they were simply required to follow written instructions (low-demand condition) (Evans et al., 1997; Wilson et al., 1996).
- **Dysexecutive Questionnaire (DEX):** The DEX scale consisted of 20 questions concerning executive function problems in daily life including difficulties with attention, memory, information processing, behavioural control, emotion regulation and awareness. Each answer was rated on a five-point scale (0-4), and the total score ranged from 0 to 80. Higher scores indicated more severe impairments of executive function (Evans et al., 1997; Wilson et al., 1996).

1.2.2 New methods using virtual reality (VR) technology

Conventional assessment methods mentioned above are effective for each higher brain function precisely. However, it is reported that results of neuropsychological tests sometimes disagree with the cognitive function level in real life of the patients (Alderman et al., 2003; Chaytor et al., 2006; Ord et al., 2010). It is difficult to evaluate the daily cognitive ability of people with cognitive dysfunction by only conventional neuropsychological tests. Therefore, in cognitive rehabilitation, before planning the detailed training program, it is important to understand that we should not only evaluate each cognitive function using pencil and paper tests, but also clarify the problems for the patients in their real life.

VR technology provides one of the most advanced interaction between human and computers. This approach has the advantage of providing realistic scenario repeatedly, cost-effectively and safely for patients (Morganti et al., 2007; Vincelli et al., 2001). By now, there are already some reports proposing to use VR for the assessment of higher brain functions (Kang et al., 2008; Knight et al., 2006; Knight et al., 2008; Titov et al., 2000; Titov et al., 2005; Zhang et al., 2003). We review two studies related to this dissertation.

- **A virtual kitchen:** Zhang et al. used a virtual kitchen for assessment of executive function in meal preparation task (e.g. a cup of soup and a sandwich) (Zhang et al., 2003). In this task, subjects operate personal computers (PC) by using a mouse and wearing head-mounted display. They investigated the correlation among VR performance, actual kitchen performance, occupational therapy evaluation, and neuropsychological evaluation of people with brain injury. The VR system showed adequate reliability and validity as a method of assessment.

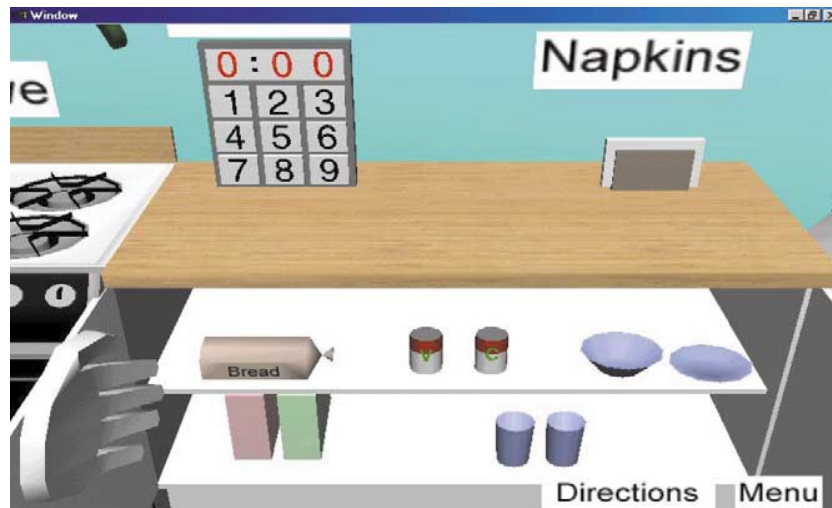


Figure 1-3 The virtual kitchen. (Zhang et al., 2003)

- **A virtual street:** Titov and Knight et al. reported a virtual street for assessment of deficits in prospective memory following chronic traumatic brain injuries. The virtual street was created by taking a series of 1500 photographs every few meters inside and outside of shops in the downtown shopping precinct of a real city in New Zealand. Subjects could move along the street by pressing buttons on the PC screen and complete ongoing and prospective memory tasks while walking along the

virtual street under conditions of high and low distraction. They were required to do ten errands with a checklist and respond to three targets that appeared repeatedly. Patients performed both tasks poorly compared with the controls as well as more affected by distractions (Titov et al., 2000; Titov et al., 2005; Knight et al., 2006).

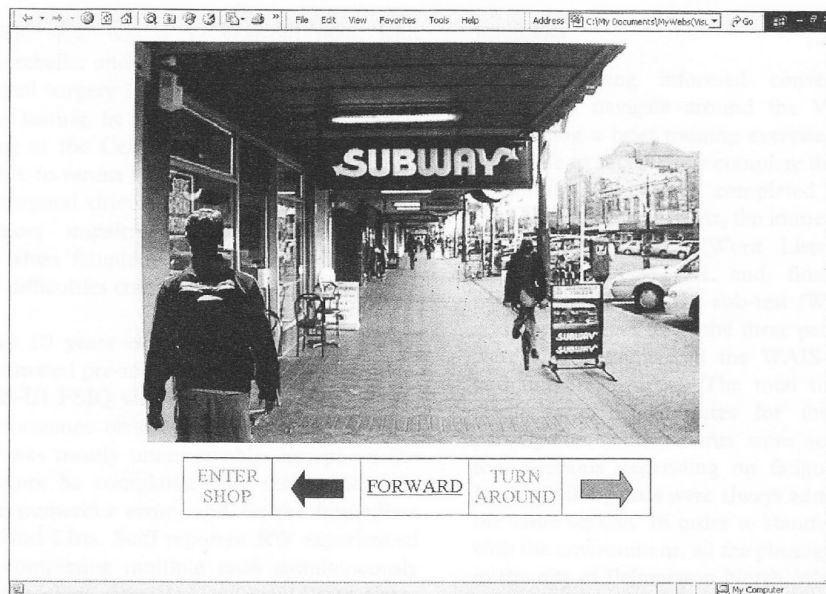


Figure 1-4 The virtual street. (Titov et al., 2005)

Limitations of the previous studies. These studies show assessment of realistic cognitive function using VR technology has significant possibility in future clinical rehabilitation. However, there were various problems when we applied these systems for patient with cognitive dysfunction in Japan. 1) Some systems required the use a joystick which was difficult to operate for people who were unfamiliar with using a personal computer (Kang et al., 2008). 2) The virtual environment and language used in these systems were foreign to the Japanese subjects. It was especially difficult for the elderly as they also needed to overcome a cultural gap in addition to understanding

unfamiliar scenery. 3) It seems that the tasks were too complex. They required the subject to buy several items and to respond to three targets in one test session (Knight et al., 2006; Knight et al., 2008).

In our project, we tried to overcome the limitation of conventional assessment methods and previous VR-based methods and propose an original approach to evaluate realistic higher brain function of various kinds of brain-damaged patients using VR technology.

1.3 Objectives of the dissertation

In order to establish a VR system to assess higher brain dysfunction in everyday life, a virtual shopping test using VR technology is developed in this research and evaluation experiments are performed in brain-damaged patients and elderly people with control subjects. The objectives of this dissertation are:

- develop an easy-operating VR-based realistic cognitive assessment system
- investigate clinical usefulness of the system in several kinds of brain-damaged patients and elderly people
- clarify the differences of the task performance, brain activation, and subjective assessments in relation to task difficulty levels in brain-damaged patients

Figure 1-5 shows concept to assess higher brain functions. Although conventional methods assessed human higher brain functions (e.g. attention, memory, executive functions) individually, the new VR system aims to understand the realization of these important sides of higher brain functions from the viewpoint of everyday life comprehensively.

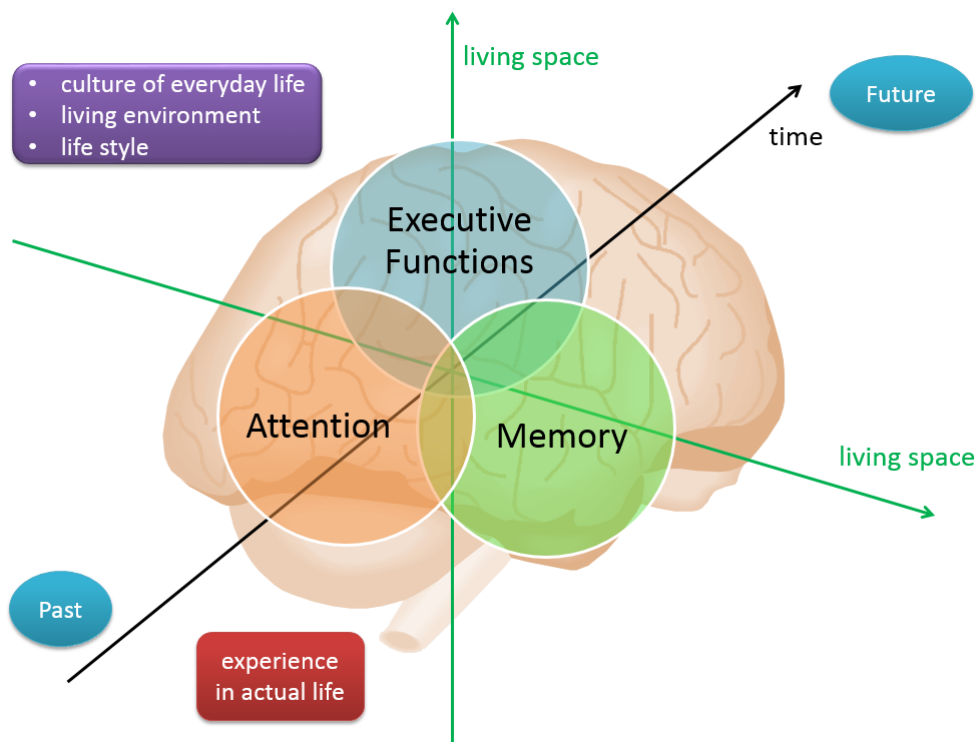


Figure 1-5 Concept to assess higher brain functions.

In addition, the system provides subjects with virtual everyday environment, in which 'time' and 'life space' are considered. They perform the test based on their past experience in actual life. Similar activities would be needed in their future daily life. Regarding life space, Japanese culture of everyday life, living environment, and life style are taken into consideration.

A project team was organized with members from both areas of engineering and clinical rehabilitation for the VR system development. In this project, each clinical member has individual study theme and different role. Sakai et al. studied on the test performances in healthy people with different age generation (age range: 20-79). She investigated age-related performance decline in this test. It was clarified that the test scores of people over 50 were decreased gradually. There was a relation between the VST test scores and a conventional cognitive screening test (Sakai et al., 2010). On the other hand, Kojima et al. developed an easy version of VR system for aphasic patients. From her experiments of the patients, it was understood that the easy version test might be useful in assessing attention and executive function of hemisphere-damaged aphasic patients, although there was some influence of linguistic function (Kojima et al., 2012). Endo et al. studied the task difficulties related VST performances while measuring brain activities by using fNIRS. They considered two difficulty levels of the VST tasks and compared the difference between high cognition group ($MMSE \geq 24$) and low cognition group ($MMSE < 24$) in elderly people. The study showed the possibility to use VST for their cognitive rehabilitation (Endo et al., 2012).

1.4 Dissertation overview

The dissertation is organized as follows: In Chapter 1, we outline the research area of higher brain dysfunctions assessment and look at the previous research in this area. In Chapter 2, we introduce our developed Virtual Shopping Test (VST) system including its program and task setting concretely. In Chapters 3 and 4, we describe two kinds of evaluation experiments on VST in chronic patients with brain damage and elderly subjects. Specifically, in Chapters 3, we clarify the significance of VST by comparing VST with other conventional tests/questionnaire and the applicability of VST to the patients, while in Chapter 4, we clarify the performance of VST in relation to age differences and the parallel form reliability of VST. To handle the application of VST in further rehabilitation, the proper level of task difficult is very important. Therefore, VST was modified to the revised version (VST-R) that had three different task difficulty levels and output event signals. In Chapter 5, we give a detailed description of VST-R system and show a clinical study in convalescent brain-damaged patients. This chapter investigates differences in task performance, brain activation, and subjective assessments in relation to the difficulty levels of the tasks. Finally, in Chapter 6, we provide conclusions and future works on cognitive rehabilitation using VR technology.

Chapter 2

Development of Virtual Shopping Test

In this chapter, we introduce our Virtual Shopping Test (VST) using VR technology to realistic higher brain functions of brain-damaged patients in laboratory environment.

2.1 Background

We have developed a new VR system to assess human cognitive function in everyday situation: the Virtual Shopping Test (VST). We emphasized the following three points during the system design: 1) the system should be easy for the beginners to operate, 2) it should represent everyday living environment in Japan, 3) the task levels should be appropriate for patients with cognitive dysfunction. With respect to the point 1), we used a touch screen as the interface instead of joystick. For point 2), we presented a virtual Japanese style shopping mall on the screen. In Japanese local shopping malls, there are shops on both sides of road, whose width is about five meters. The construction is relatively simple, which differs from Western style complex malls or hypermarkets. Most of shops are under small management, and a shop building is like a small house. They put up a signboard written in Japanese characters including Kanji. Usually, a shopping mall has from ten to thirty shops within walking distance. They are often located in front of a train station. Such kinds of shopping mall was much familiar by the Japanese elderly especially those who do not have foreign educations. For point

3), we arranged shopping tasks with four specific items and allowed users to refer to hints (e.g. a shopping list and a view of the shopping bag) in case when they needed help.

The reason to introduce a shopping task in a virtual shopping mall is because we aimed to assess the cognitive ability in daily routine. In VST, subjects were required to memorize items to buy, to look for specific shops on a street, to choose the items in a shop and perform the whole tasks smoothly. We assumed that subjects used ‘selective attention’ when they choose the target shop on a street and the correct item in a shop, and ‘sustained attention’ when they complete the shopping task. They were required to use ‘memory’ when they memorize the four specific items on the shopping list and recall them at the appropriate time. The test also required the use of ‘executive function’ when the subjects completed the tasks quickly and efficiently by using the shortest way from start to goal.

Another feature of our VST is that, a log file is recorded automatically. This file contains the important data during performing the tests (e.g. correct action and the time required to perform the test). We also prepared the instruction manual for a tester. Therefore, the examiner or clinician do not need specific skills to use VST, they can concentrate on the observation of the subjects’ behavior during the tests.

2.2 Virtual Shopping Test (VST)

2.2.1 Construction of the system

Experimental apparatus. The hardware system included a personal computer and a touch screen (1928L 19” LCD Desktop Touch monitor 5000series, Tyco Electronics, DE,

USA). The virtual environment was developed with Metasequoia and Open GL. Figure 2-1 shows the overall setup of the experimental device. Figure 2-2 shows the scene of the experiment.

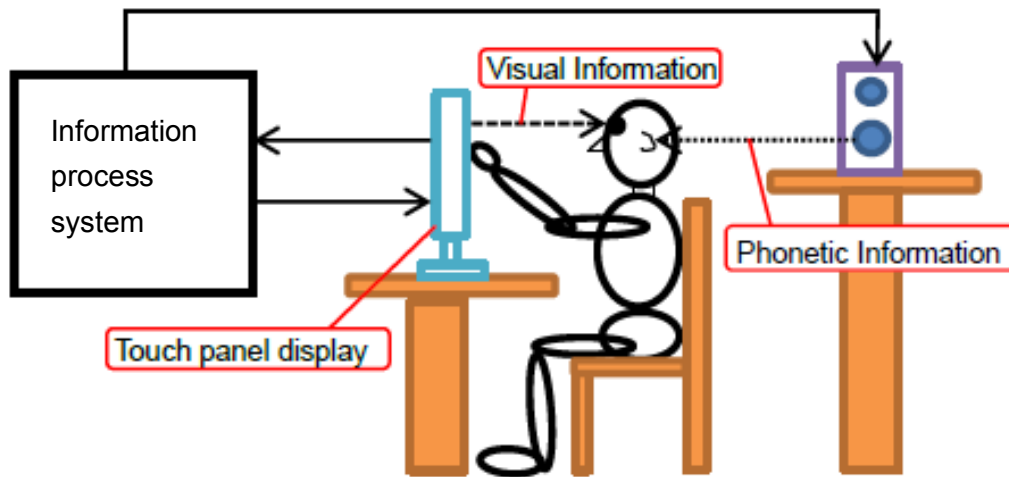


Figure 2-1 Composition of the experimental device.



Figure 2-2 Scene of the experiment.

In this program, visual environment was made up of a Japanese shopping mall with twenty shops and a train station. The width of the virtual mall was about five meters and the depth was about one hundred meters. An audio environment of natural sound of the shopping mall is also provided. As shown in Figure 2-3, there are main four buttons on bottom of the screen. By touching each button, users could move in the virtual shopping mall, entering a shop, and buying an item.

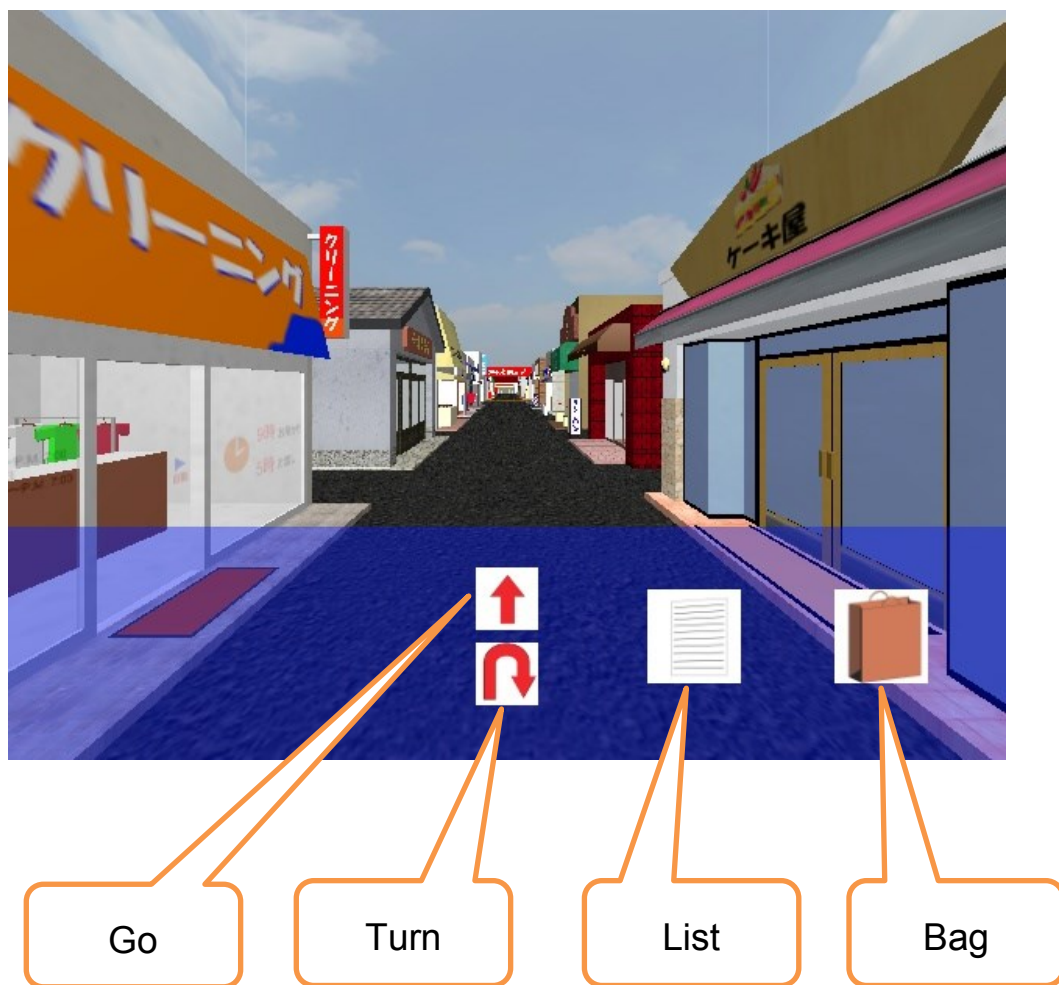


Figure 2-3 An example of a basic screen in VST.

2.2.2 Basic program and operation procedure

This system has three modes, namely BASIC MODE, SHOP MODE, and LIST/BAG MODE.

2.2.2.1 BASIC MODE

A flow chart of the data processing in BASIC MODE is show in Figure 2-4, that is a fundamental mode of VST. In this mode, users could move in virtual shopping mall by touching the upper and lower arrow button. Users could transfer LIST/BAG MODE and SHOP MODE from this mode.

In BASIC MODE, there were four buttons on the bottom of the screen (see Figure 2-3). Two arrow buttons were provided to allow users to move and perform direction changes freely. By touching the upper arrow button ('Go'), users can move forward to the next shop. By touching the lower button ('Turn'), users can turn 180 degrees at that point. In addition, two hint buttons (e.g. 'List' and 'Bag') were provided to allow users to view some hints during the shopping task.

End of a shopping task. When users finished all the shopping, they went for a station as a goal. A message 'Finish? / Yes or No' was appeared after going through a wicket over the yellow line by touching an upper arrow (Figure 2-5). They finish a task by touching 'Yes' button, while they return the mall and continue their shopping by touching 'No' button.

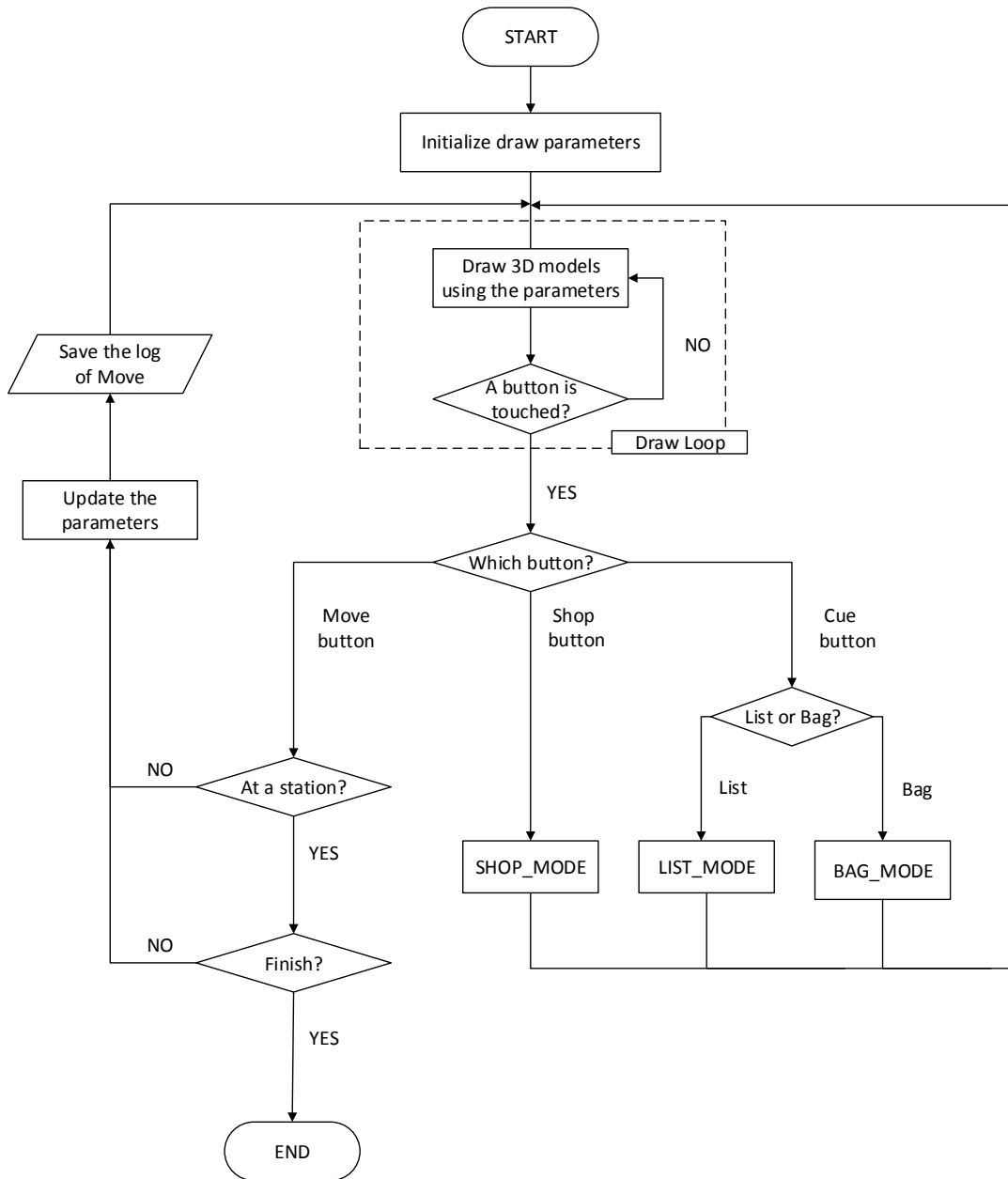


Figure 2-4 A BASIC MODE flow chart.



Figure 2-5 End of the shopping task.

2.2.2.2 SHOP MODE

A flow chart of the data processing in SHOP MODE is shown in Figure 2-6. In this mode, users could enter a shop, select a shopping item and buy it. After finishing shopping, they would be transferred to BASIC MODE.

We show the operation procedure of to buy something in Figure 2-7. This figure shows transfer from BASIC MODE to SHOP MODE on the screen. Firstly, a user have to go in front of a target shop to enter a shop. By touching a picture of the shop building, the screen was transferred to SHOP MODE and the full-screen picture of the shop was displayed (Figure 2-7b). By touching the shop picture again, users would be allowed to enter the shop. There were six shopping items displayed in every shop for sale (Figure 2-7c). By touching one of the six items on the screen, the picture of the chosen item was enlarged (Figure 2-7d). By touching the 'Buy' button on the bottom of the screen, the item was placed into the shopping bag and the user could then exit the shop.

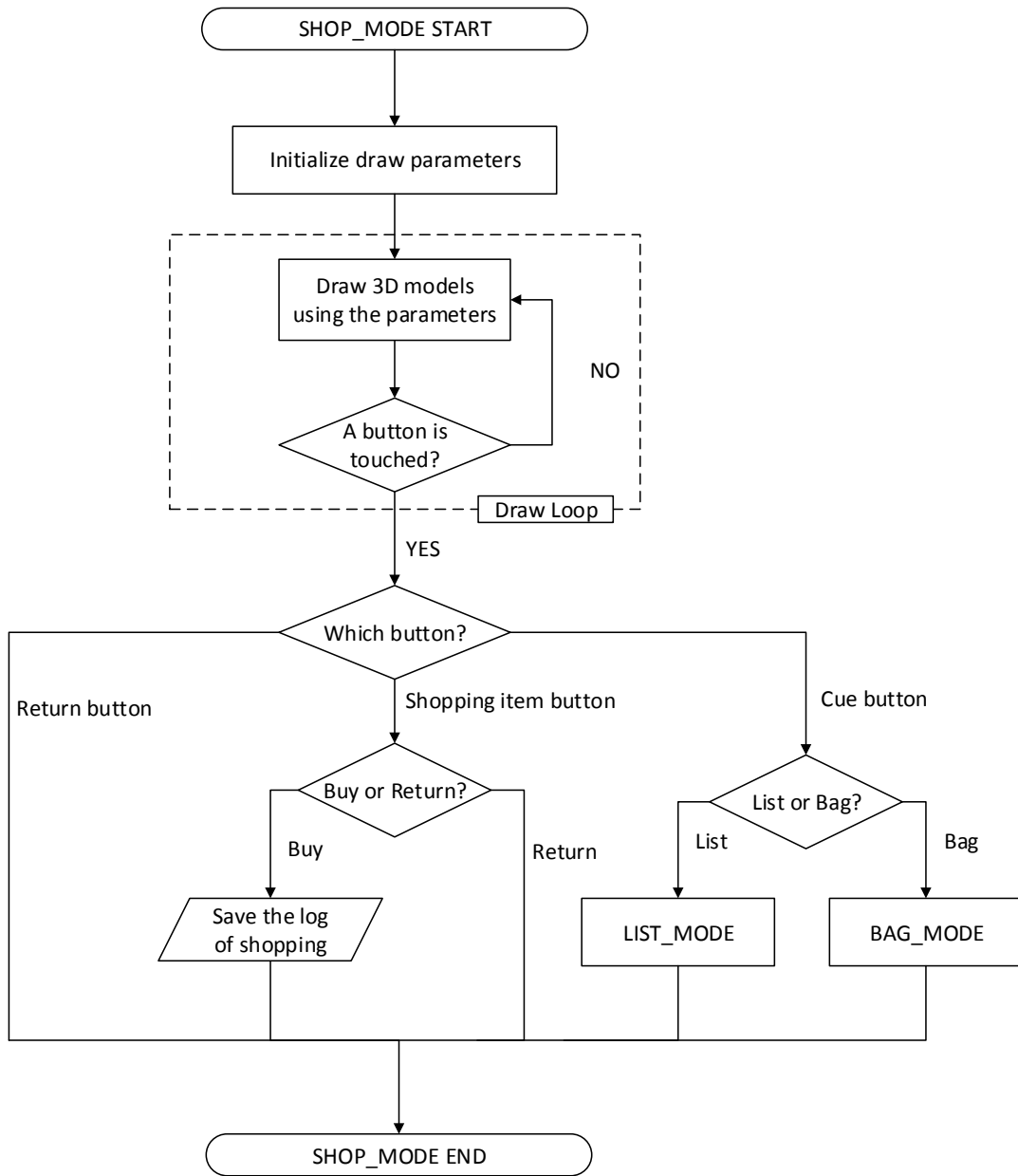
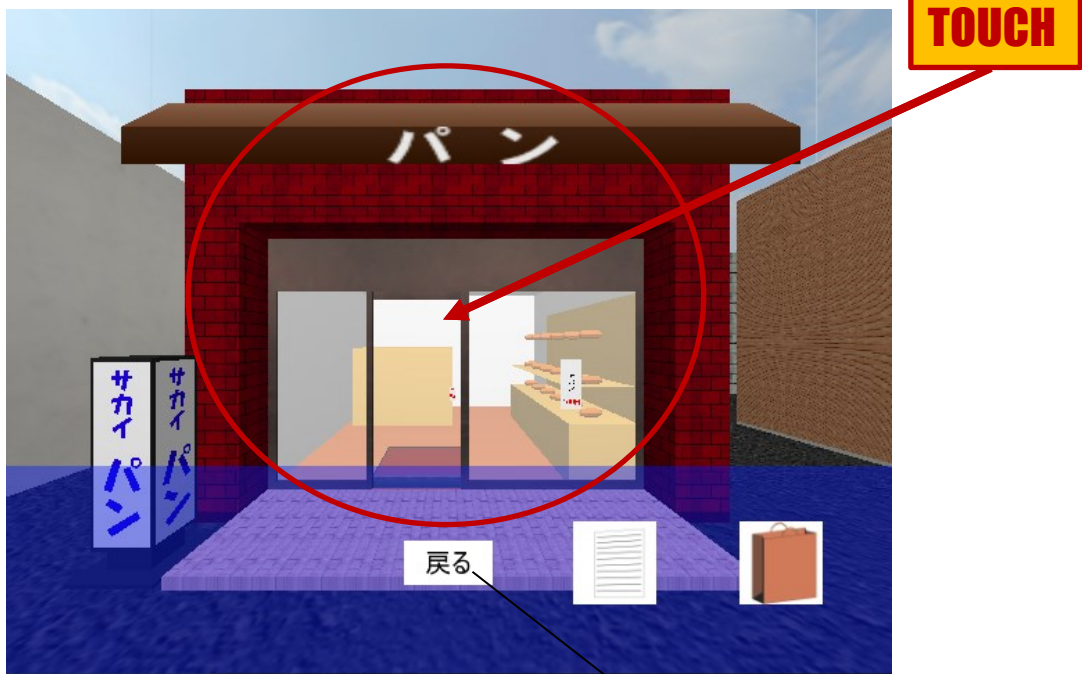


Figure 2-6 A SHOP MODE flow chart.



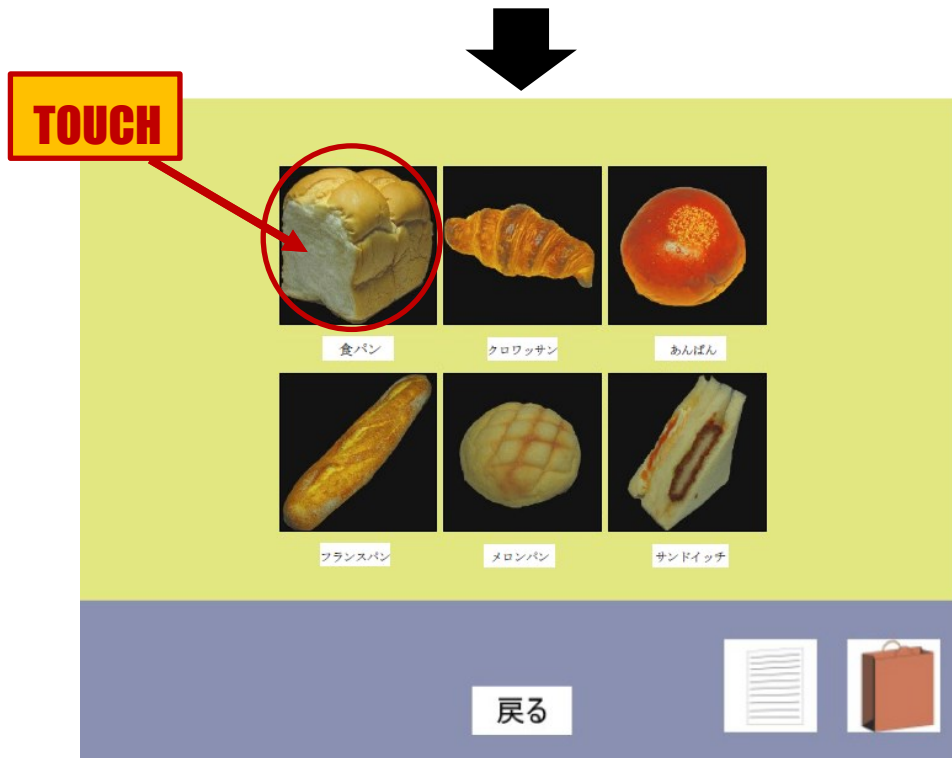
a) BASIC MODE



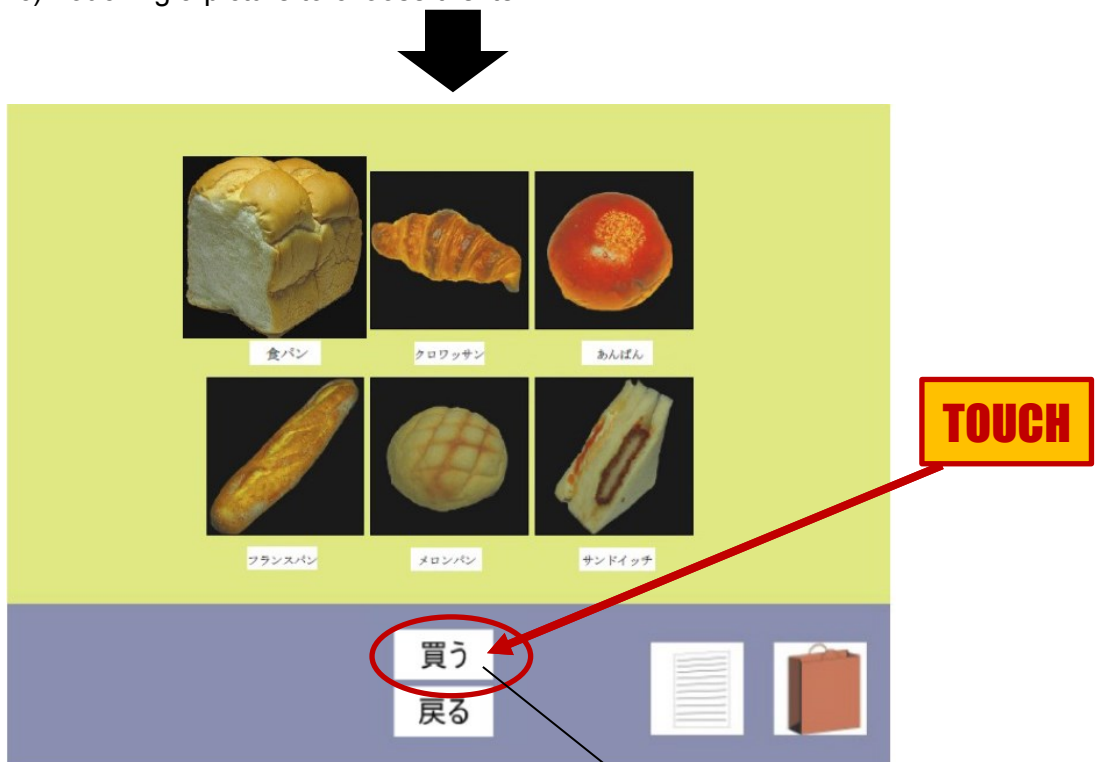
b) Touching a shop to enter the shop

'Return'





c) Touching a picture to choose the item



d) Touching 'Buy' button to buy the item

'Buy'

A user has bought a loaf of bread.

Figure 2-7 Operation procedure to buy an item.

If users enter any incorrect shop, there is no shopping item inside a shop and a message “regular holiday today” is displayed on the screen with buzzer sound (Figure 2-8).



Figure 2-8 A screenshot of an incorrect shop’s inside.

2.2.2.3 LIST/BAG MODE

A flow chart of the data processing in LIST/BAG MODE was shown in Figure 2-9. If users forgot items in the shopping list and items they bought already during VST performance, they could touch the list or bag button to transfer them to this mode.

By touching the List button in BASIC MODE, the screen transfers to LIST MODE and all shopping items on the shopping list are displayed (Figure 2-10). By touching the Bag button, the screen transfers to BAG MODE and displays all the pictures of the items that a user have already bought (Figure 2-11). Then, by touching a 'Return' button, the screen transfers to a previous mode.

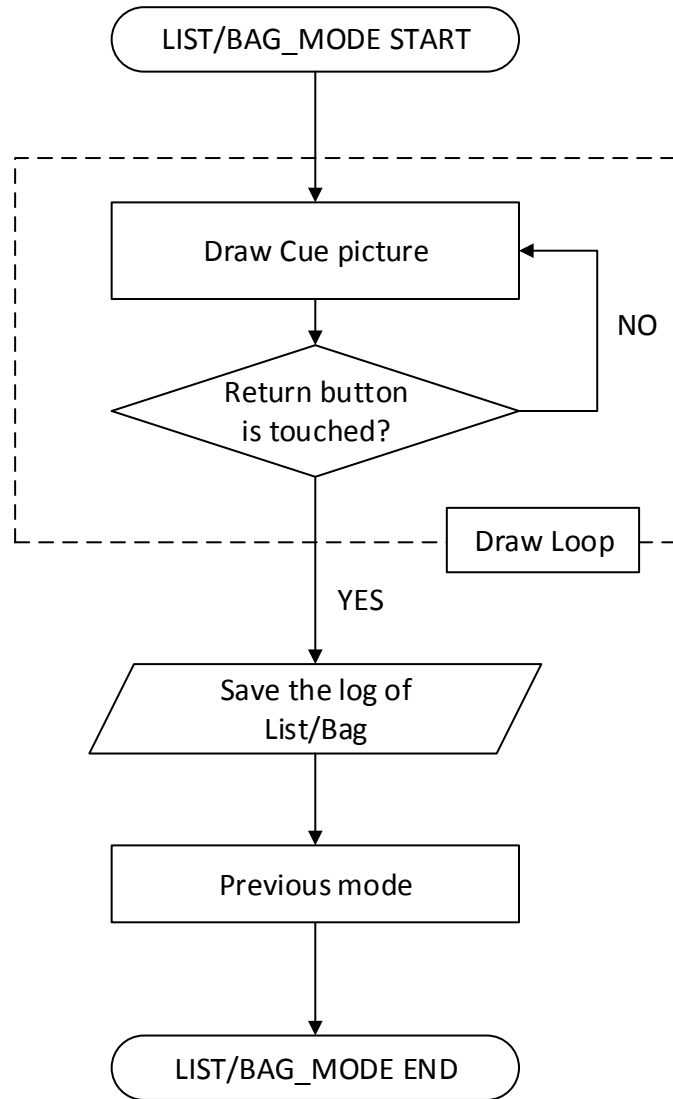


Figure 2-9 A LIST/BAG MODE flow chart.



Figure 2-10 Screen switching from BASIC MODE to LIST MODE.

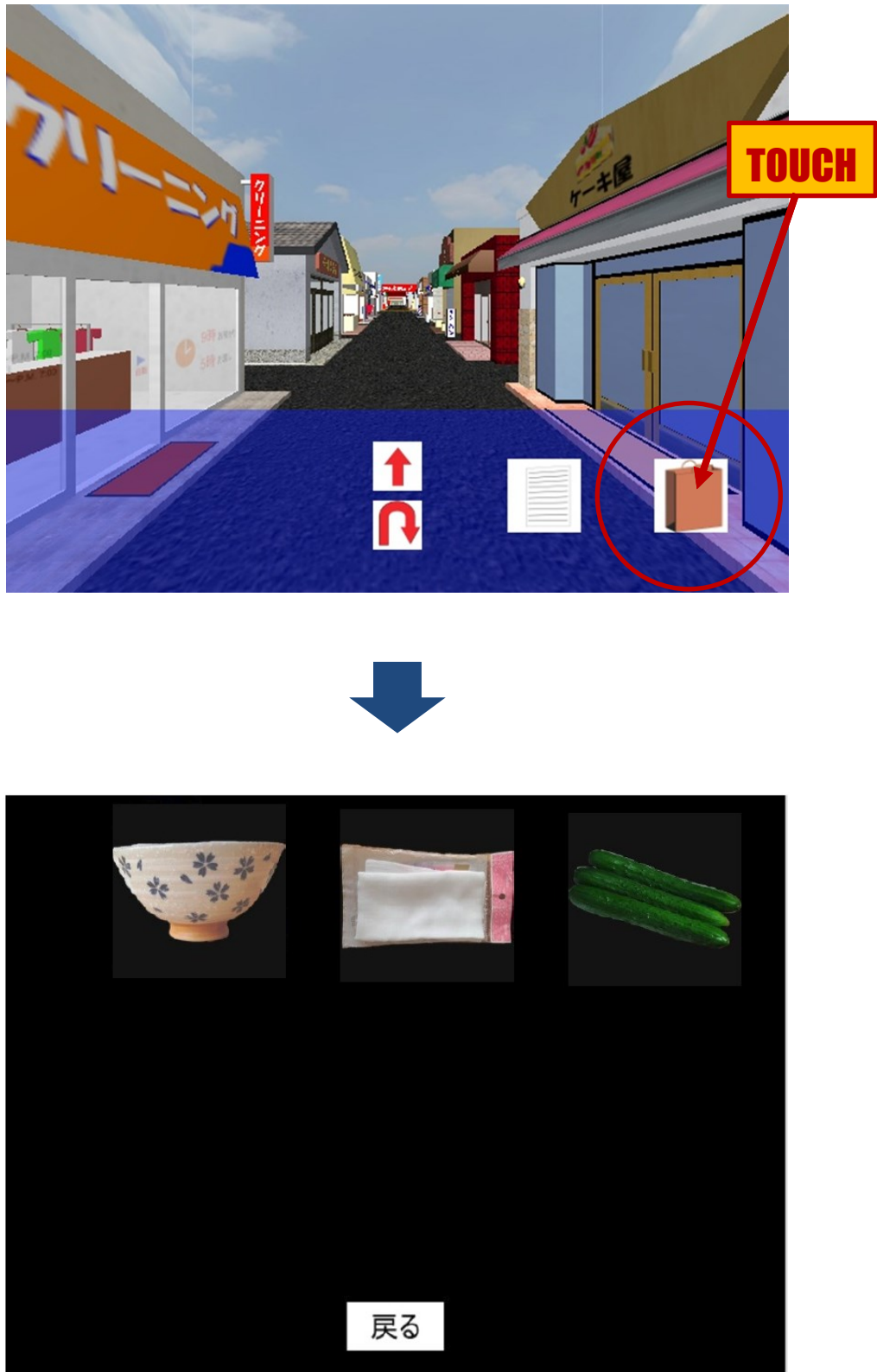


Figure 2-11 Screen switching from BASIC MODE to BAG MODE.

2.2.2.4 Other functions

VST has other convenient equipped function. Figure 2-12 shows a function selection screen. Before starting of VST, a tester could choose ‘On or Off’ about the following functions: 1) log recordings, 2) a timer function, that if a user does not operate for over 120 seconds, a mark is appeared on a corner of a screen, and 3) background music (BGM). In addition, there were three buttons on the bottom of the screen: VST-1, VST-2, and a practice task. A tester could choose one of three tasks.



Figure 2-12 A function selection screen.

2.2.3 Task setting

We set three tasks: a practice task and two parallel forms (e.g. VST-1, VST-2). We arranged VST-1 and VST-2 as same difficulty level because we would conduct the other to a same subject as a retest without leaning effect repeatedly.

Each shopping mall consisted of twenty shops and a train station. There was a characteristic red arcade at the midpoint of the mall (see Figure 2-13). The maps and shopping lists used in each task are shown in Figure 2-14, Figure 2-15, and Figure 2-16, respectively. We show another maps with model red routes in the figures. The red route showed efficient shopping order. The bottom of a map is a start point, and a top is a goal. An A4 sized sheet printed a blank map is provided to participants during VST performance.



Figure 2-13 A screenshot with an arcade.



■ 買い物もの Shopping list

- ・ 食パン a loaf of bread
- ・ ぬいぐるみ a stuffed toy

戻る



The red route showed efficient shopping order.

Figure 2-14 The map and shopping list used in a practice task.



■ 買いもの Shopping list

▪ 鉛筆	a pencil
▪ 茶碗	a rice bowl
▪ ガーゼ	a piece of gauze
▪ きゅうり	a cucumber

戻る



The red route showed efficient shopping order.

Figure 2-15 The map and shopping list used in VST-1.



買いもの Shopping list

- 長靴 a pair of boots
- 線香 incense sticks
- ボール a ball
- かなづち a hammer

戻る



The red route showed efficient shopping order.

Figure 2-16 The map and shopping list used in VST-2.

Shopping tasks. We set a shopping task which asks user to buy four specific items on VST-1 and VST-2. Participants have to search the shops that sell specific items and select the target item out of six items inside a shop. The four shopping items were “a pencil, a rice bowl, a piece of gauze, and a cucumber” for VST-1, and “a pair of boots, incense sticks, a ball, a hammer” for VST-2. These items were selected from Japanese words with high imageability (above 5.6) based on the NTT Psycholinguistic Databases “Lexical properties of Japanese” (Amano, 2000). Imageability in word recognition is a semantic property that is defined as the ease and speed with which a target word evokes a corresponding mental image (Clark et al., 2004). The words were also chosen from different word categories. The four shops that sold items were arranged such that two shops are located on each side of the street (i.e. a stationary shop, a chinaware shop, a pharmacy, and a fruit and vegetable shop for VST-1, and a shoe store, a Buddhist alter fittings store, a sporting goods shop, and a hardware store for VST-2) as shown in Figure 2-15 and Figure 2-16.

Goods arrangement. We arranged six shopping items in each shop with the following rule so that we could identify the reason for error when users made mistakes. In a shop, there were five specific false items and a correct item. The five false items were either similar or associate with the correct item in some way. One false item was usually used with the correct item (*Set*). Another false item had the same usage as the correct item (*Use*). The 3rd false item had the same initial sound in Japanese as the correct item (*Phoneme*). The 4th item had the same color as the correct item (*Color*). The 5th false item had the same shape as the correct item (*Shape*).

Figure 2-17 shows product cluster on four shops; Figure 2-18 shows the screen images of shop façade and the inside in VST-1. The six items were arranged in a table of 2 lines by 3 columns on a screen, and the place of correct item was set randomly. Appendix A provides the additional images in all tasks.


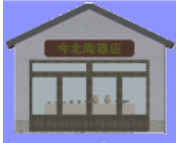
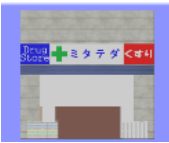

























Shop				
Rule	stationary shop	chinaware shop	pharmacy	fruit and vegetable shop
Task (Correct item)	 pencil	 rice bowl	 gauze	 cucumbers
Set	 eraser	 chopsticks	 disinfectant	 tomatoes
Use	 fountain pen	 teacup	 adhesive plaster	 eggplants
Phone	 paints	 tea strainer	 cold tablets	 kiwi fruits
Color	 tape	 bud vase	 bandage	 green peppers
Shape	 seal	 ashtray	 mask	 bananas

Figure 2-17 Product cluster on four shops in VST-1.

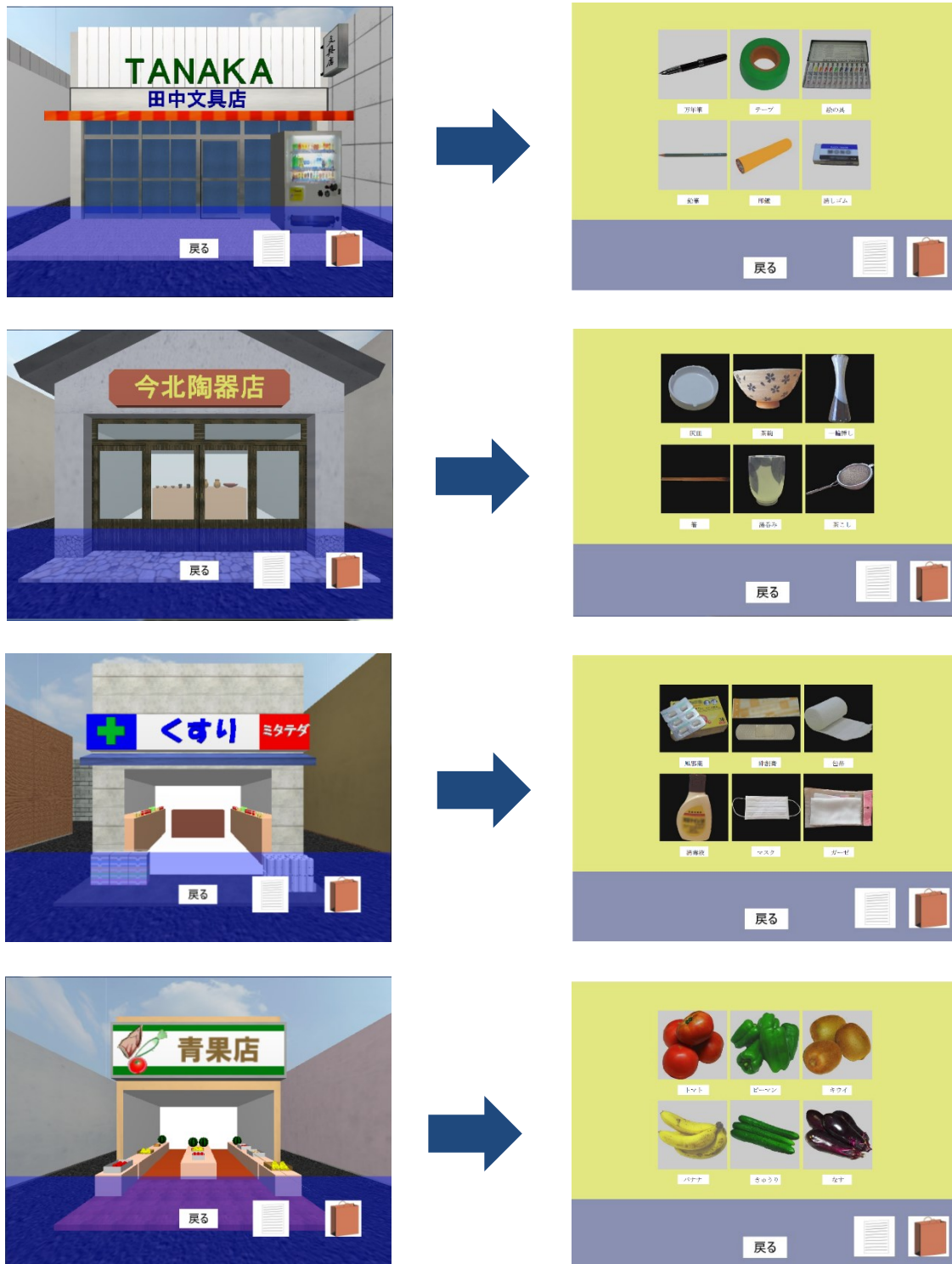


Figure 2-18 Screen images of shop facade and the inside in VST-1.

2.2.4 Experimental procedure

Before the test session using VST-1 or VST-2, the subjects were given a demonstration of the VR screen and were conducted a practice task. The demonstration of PC screen operation and instruction were provided to the subjects according to a standardized instruction manual (see Appendix B).

In the actual VST, the subjects were first asked to memorize four shopping items and were allowed to look at the shopping list for ten seconds. If they failed the first recall test, they were allowed to memorize the items again in the same way. Secondly, subjects were allowed to plan their shopping routes that they thought would be the most efficient by filling in a blank map sheet with a pencil. They were then asked to finish buying the four specific items as quickly and efficiently as possible, while minimizing the use of hints as much as possible. Subjects were allowed to refer to their planning using the blank map on the table during the VST at any time. It took about thirty minutes including the demonstration for one session of VST.

2.2.5 Data recording

Evaluation items. VST had ten evaluation items: Bag use, List use, Cue use, Forward movement, Reverse movement, Correct purchases, Total time, Time in the shops, Time on the road, and Mean time per shop. They could be calculated from the recording data.

Bag use, List use, Cue use, Forward movement and Reverse movement represent the number of times the subjects touched each button. For example, Bag use represents the number of times the subjects checked the items in the bag. List use represents the number of times the subjects referred to the shopping list. Cue use

represents the total number of times the subjects checked the shopping list and bag. Forward movement represents the number of times that the subjects pressed upper arrow. Reverse movement represents the number of times the subjects pressed lower arrow. If subjects did not check the items in the bag or refer to the shopping list or reverse direction, then Bag use, List use, Cue use, Reverse movement would have a value of 0, which would represent the most efficient performance. If subjects completed the task by moving from start to goal with the shortest path (see the red route as shown in Figure 2-14, 2-15, and 2-16), then Forward movement would have a value of 12, which would be the most efficient performance.

Correct purchases represents the number of items bought correctly. In VST, subjects were required to buy 4 specific items, and 4 would be the best score. The item ranged from 0 to 4.

Total time, Time in the shops, Time on the road, and Mean time per shop represent the time required in each place. For example, Total time represents the total time spent to complete the whole shopping task. Time in the shops represents the total time spent in each shop. Time on the road represents the total time spent on road. Mean time per shop represents the average time spent in one shop. Regarding these items, smaller number would represent higher performance.

Table 2-1 shows the hypothesis on the relationship between VST evaluation items and higher brain functions such as attention, executive functions, and memory. It is considered that Bag/List use and correct purchase would have relation to memory, and Movement button use would have relation to executive functions strongly. It is estimated that Time in the shop would have relation to selective attention, and Time on

the road would have relation to executive functions strongly.

Table 2-1 A hypothesis on the relationship between VST and higher brain functions.

VST Evaluation items	Attention	Executive functions	Memory
<i>Button use frequency</i>			
Bag use	+	+	++
List use	+	+	++
Forward movement	++	++	+
Reverse movement	++	++	+
Correct purchases	+	+	++
<i>Time required</i>			
Total time	++	++	++
Time in the shops	++	+	++
Time on the road	+	++	++
Mean time per shop	++	+	++

+: having relationship, ++: having relationship strongly

Data output. The operation of buttons during VST was recorded automatically, and outputted as a log file after finishing the test. There were two types of log file; the Hyper Text Markup Language (HTML) form for reading (see Figure 2-19a, b, c) and the Comma Separated Value (CSV) form for data analysis (see Figure 2-19d). Figure 2-19a shows a time series data and Figure 2-19b shows an integrated data as the total. If a user bought a false item, the *type* of error was recorded with the picture in the HTML form in a log file as shown in Figure 2-19c.

BGM: 有
本番: 1

00:00 START_INSTRUCTION

00:32 [in->]LIST_MODE
00:46 [-out]LIST_MODE(00:14)

01:17 [in->]LIST_MODE
09:16 [-out]LIST_MODE(07:59)

09:32 END_INSTRUCTION

00:00 START
00:00 Forward

00:08 [in->]CHINA_SHOP:3



00:19 Select-->item 課題

00:21 buy 課題

00:21 [-out]CHINA_SHOP:3(00:13)

00:32 Forward
00:43 Forward

(a) HTML: a time series data

RESULT

Bag	0
List	2
Cue	2
Go	12
Turn	0
Stop	0
Correct(Task)	4
Distracter(Set)	0
Distracter(Use)	0
Distracter(Phoneme)	0
Distracter(Color)	0
Distracter(Shape)	0
Time:All	264
Time:Shop	79
Time:Road	185
Ave Shop	00:19

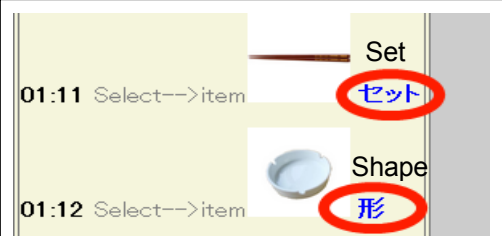
(b) HTML: an integrated data

01:11 Select-->item

Set
セット

Shape
形

01:12 Select-->item



(c) The type of error recorded in a log file

	A	B	C	D	E
1	Bag	List	Cue	Move	Turn
2		3		1	4
3					12
4					
5					
6					

(d) CSV

Figure 2-19 Log files.

2.3 Summary

In this chapter, we introduced our developed VST using VR technology to assess realistic higher brain functions of brain-damaged patients in laboratory environment. We constructed a Japanese virtual mall in virtual space. Subjects moved in the mall freely and executed four-items shopping tasks by touch screen operations. In the test session, they were asked to finish the task as quickly and efficiently as possible, while minimizing the use of hints as much as possible. The number of times they touched each hint/movement button, the number of items bought correctly, and the time required were recorded as evaluation items. The advantages of this system were:

- Virtual environmental condition which is similar to the real daily environment in Japan
- Interaction between a user and the virtual shopping mall environment
- Human interface device operated intuitively
- Automatic recording of various behavioral data
- Dealing with predictable human errors

In Chapter 3, we describe evaluation experiments on the clinical usefulness of VST in brain-damaged patients. In Chapter 4, we describe evaluation experiments in elderly people.

Chapter 3

VST Evaluation Experiments in Brain-damaged Patients

In this chapter, we describe two clinical evaluation experiments on VST in brain-damaged patients. The objectives were to find out 1) the significance of VST by comparing VST performance with conventional assessments, 2) the difference of VST performance between healthy subjects and brain-damaged patients. Ten age-matched control subjects and ten patients participated in the experiments.

3.1 Study 1: Relationships between VST and conventional cognitive assessment

The objective for this study was to evaluate the significance of VST by comparing VST performance with conventional tests. Participants came from patients with brain damage.

3.1.1 Methods

Participants. Ten patients with cognitive function disorder (6 males, 4 females, mean age 43.5 ± 16.0 years, mean years of education 13.2 ± 1.7) participated in this study. The participation criteria were as follows: 1) more than one year since brain damage onset, 2) between 20 and 69 years old, 3) cognitive ability to understand how to operate

a touch screen, and 4) physical ability to reach and touch the screen by their uninvolved upper limbs. Demonstration to operate the screen were given to the participants and then they were given a practice session of operating the touch screen. The participants were then given a practice test to ensure that they had a good understanding to operate the VR system. If they failed the first test, demonstration and practice time would be provided to them again. They were given a maximum of 3 tries. The study exclusion criteria were as follows: i) severe aphasia, and ii) severe unilateral spatial neglect (USN).

The patients' characteristics was presented in Table 3-1. The patients included some forms of brain damage; five of them had cerebrovascular disease and another five had traumatic brain injury. They all had difficulties in their instrumental activity of daily living. The cognitive dysfunction was related to more than one aspects of ability (e.g. attention, memory, and executive function). They either lived at home with their family or received residential rehabilitation services at a prefectural rehabilitation center. The average time since onset was 52.3 ± 50.9 months, and the average Functional Independence Measure (FIM) score (Kidd et al., 1995) was 112 ± 10.3 .

Table 3-1 Patient characteristics.

Patient ID	1	2	3	4	5	6	7	8	9	10
Age	32	36	61	51	57	62	59	28	22	27
Gender	M	M	M	M	M	F	F	M	F	F
Diagnosis	TBI	TBI	TBI	CVA	CVA	CVA	CVA	CVA	TBI	TBI
Site of paralysis	right	left	none	none	left	left	left	left	bilateral	bilateral
Disease duration (months)	143	144	21	45	25	16	23	17	18	71
MMSE /30	27	22	26	30	29	20	28	30	26	25

M: male, F: female, TBI: traumatic brain injury, CVA: cerebrovascular accident
MMSE: Mini-Mental State Examination

All participants received written and verbal information about the study and gave written informed consent. The protocol of the study was approved by the Kobe University Medical Ethic Committee.

Procedure. Participants were administered VST, seven conventional neuropsychological tests and two questionnaires. They did a practice task of VST, and then performed a real task: VST-1.

Attention was evaluated by symbol Digit Modalities Test (SDMT) (Smith, 1982) and Simple Reaction Time Task (SRT) (Beck et al., 1956). Regarding visual inattention, the presence of USN was assessed by Star and Letter Cancellation Task (Ishiai, 1999; Wilson et al., 1987). Everyday memory was assessed by Rivermead Behavioural Memory Test (RBMT) (Wilson et al., 1985; Wilson et al., 1989) and Everyday Memory Checklist (EMC) (Kazui et al., 2006). Executive functions was evaluated by Zoo Map Test and the Dysexecutive Questionnaire (DEX) (Evans et al., 1997; Wilson et al., 1996). In this study, the raw-score of each trial was adopted on Zoo Map Test. The whole assessments were conducted on three separate date. All tests were finished within one month before and after VST execution. The total time was about five hours for one patient.

Statistical analysis. Speaman's correlations were performed to determine the association between conventional cognitive assessments and VST in the patient group. Beforehand, Speaman's correlations were performed not only between each outcome variable in VST but also between each outcome variable in neuropsychological tests. If

a highly significant statistical correlation in the specific variable group was observed, one variable of the group was adopted as a typical variable. Differences were reported as significant if $p < 0.05$.

3.1.2 Results

Table 3-2 presents the patients' cognitive assessment data. Table 3-3 presents the correlation between VST and conventional cognitive assessments in the patients. In this table, we inserted the neuropsychological tests and questionnaires in which scores were correlated significantly with VST variables.

Table 3-2 Cognitive assessment data.

Patient ID	1	2	3	4	5	6	7	8	9	10
Attention										
SDMT /100	18	4	36	28	19	13	22	45	19	30
SRT: completing rate /100	96.3	—	97.5	98.8	100	87.5	92.5	100	97.5	98.8
SRT: correct time [s]	96.3	—	97.5	98.8	100	89.7	93.7	100	97.5	98.8
Star cancellation task /54	54	54	52	54	54	54	48	54	54	54
Letter cancellation task /40	37	37	40	40	36	39	36	36	39	39
Memory										
RBMT: standard profile score /24	8	9	17	21	12	5	15	20	18	22
EMC /52	50	35	40	22	13	31	25	24	22	23
Executive function										
Zoo Map Test: the 1 st trial /8	-6	—	1	1	2	5	3	3	1	2
Zoo Map Test: the 2 nd trial /8	7	—	8	8	5	8	8	8	8	8
DEX /80	63	40	51	16	5	21	17	32	18	30

SDMT: Symbol Digit Modalities Test; SRT: Simple Reaction Time Task; RBMT: Rivermead Behavioural Memory Test; EMC: Everyday Memory Checklist; DEX: Dysexecutive Questionnaire

Table 3-3 Correlation between VST and conventional cognitive assessments.

	Orientation	Attention		Memory					
	MMSE	SDMT	SRT	RBMT					EMC
		completion rate	correct rate	SPS	Belonging	Appointment	Pictures	Date	
Bag use	0.06	-0.29	-0.28	-0.41	0.31	-0.5	-0.65*	0.11	0.52
List use	-0.69*	-0.5	-0.63	-0.71*	-0.67*	-0.73*	-0.34	-0.59	0.76*
Forward movement	-0.31	-0.43	-0.62	-0.34	0.09	-0.56	-0.53	-0.3	0.01
Correct purchases	0.18	0.39	0.05	0.48	0.47	0.09	0.16	0.67*	0.26
Total Time	-0.6	-0.80**	-0.89**	-0.71*	-0.37	-0.88**	-0.45	-0.52	0.52

MMSE: Mini-Mental State Examination; SDMT: Symbol Digit Modalities Test; SRT: Simple Reaction Time Task; RBMT: Rivermead Behavioural Memory Test; EMC: Everyday Memory Checklist; SPS: standard profile score

‘Belonging’, ‘Appointment’, ‘Pictures’, and ‘Date’ are subtests of RBMT.

Speaman’s correlation: * $p < 0.05$, ** $p < 0.01$

As shown in Table 3-3, regarding general cognitive ability, the times of List use was correlated significantly with the MMSE score on VST ($r = -0.69$). The significant negative correlation indicated that if the number of references to the shopping list on VST was high, then the performance of MMSE was also low. Regarding attention, the Total time spent to complete the whole shopping task on VST were correlated significantly with the each score on two tests (the completing rate in SDMT, the correct rate in SRT) ($r = -0.80$ and -0.89 , respectively). The significant negative correlations indicated that longer time spent to complete the whole shopping task on VST related to a poorer performance on SDMT and SRT.

With regard to memory, there were significant negative correlations between the times of List use on VST and the RBMT standard profile score and the two subtests:

‘Belonging’, ‘Appointment’ ($r = -0.71, -0.67$ and -0.73 , respectively). There was also positive correlation between the times of List use on VST and the EMC score ($r = 0.76$). The significant negative/positive correlations indicated that higher number of times that the patients referred to the shopping list on VST related to a poorer performance on RBMT and severer memory impairments on EMC. There were significant negative correlations between the times of Bag use on VST and the one subtest in RBMT: ‘Pictures’ ($r = -0.65$). The significant negative correlation indicated that higher number of times that the patients check the items in the bag on VST related to a poorer performance on the picture remembering task in RBMT.

There were significant negative correlations between the Total time spent to complete the whole shopping task on VST and the RBMT standard profile score and one subtest: ‘Appointment’ ($r = -0.71$ and -0.88 , respectively). The significant negative correlation indicated that longer time was spent to complete the whole shopping task on VST related to a poorer performance on the prospective remembering task in RBMT.

There were significant positive correlations between the number of Correct purchases on VST and one subtest of the RBMT: ‘Date’ ($r = 0.67$). The significant positive correlation indicated that less correct items purchased on VST related to a lower orientation score in RBMT.

On the other hand, there was no significant correlation between VST variables and some conventional cognitive assessments (including Star and Letter Cancellation Task, Zoo Map Test, and DEX).

3.1.3 Discussion

We discuss the validity of VST to assess cognitive functions of brain-damaged patients, in detail, their attention, visual perception, memory, executive function, the overall cognitive function, respectively as following.

Regarding attention, the scores on the two tests (the completing rate in SDMT, the correct rate in SRT) were correlated significantly with the Total time spent to complete the whole shopping task on VST. SDMT is closely related to divided attention, switching attention, and attention capacity (Ponsford et al., 1992; Smith, 1982). It is also connected with the central executive system of working memory and visual sketch pad function from cognitive psychological point of view. Working memory is the function of keeping information temporarily, processing and operating it. It is also closely related with attention (Baddeley, 2000). SRT is a visual input task related to sustained attention (Beck et al., 1956). In this task, subjects were instructed to concentrate on a screen and they were asked to respond to the specific number as soon as possible for a specific period of time. SRT and VST both share common features to gauge attention based on visual input tasks. We considered that the function of working memory would be required when the subjects memorized the items on the shopping list while shopping.

Regarding visual perception, there was no statistically significant correlation between VST and the Star/Letter Cancellation Task. We considered that one of the reasons was the patient group did not include typical patients with USN. As shown in Table 1, the mean score of star cancellation task ranged from 48 to 54 out of 54, and the mean score of letter cancellation task ranged from 36 to 40 out of 40. These data

indicated a ceiling effect. Further studies will be needed to elaborate on these findings.

Regarding memory, there were significant negative/positive correlations between the number of times the shopping list were used on VST and the RBMT standard profile score and the two subsets: ‘Belonging’, ‘Appointment’ and the EMC score. There was significant negative correlation between the numbers of times the shopping bag were used on VST and the one subtests in RBMT: ‘Pictures’. Similarly, there was significant negative correlation between the Total time spent to complete the whole shopping task on VST and the one subset of RBMT standard profile score: ‘Appointment’. However, there was significant positive correlation between the number of Correct purchases on VST and the one subtest of the RBMT: ‘Date’.

RBMT has ecological validity as a set of tests for everyday memory (Wilson et al., 1985; Wilson et al., 1989). The two subtests: ‘Belonging’, ‘Appointment’ are related to prospective memory, which involves bringing a previously formed plan back to consciousness at the right time and place (Uttl, 2008). Prospective memory is a sort of recent memory and has two characterized functions; memorizing the content and reminding it at the appropriate time (Fish et al., 2010; Shum et al., 2011). ‘Picture’ is related to visual memory, while ‘Date’ is related to orientation. EMC is a questionnaire about everyday memory (Kazui et al., 2003).

These findings reflected the fact that participants were able to encode something and retrieve the information on demand during the VST, as all these measures were related to linguistic and visual memory. It also suggested that VST could be a useful battery for prospective memory because participants were asked to memorize four shopping items and to repeatedly remind them when they approached

each target shop during the performance. One of the reasons was because participants visually memorized the items already bought on VST. We considered that List use, Bag use and Total time on VST were related to everyday memory, especially prospective and visual memories.

Regarding executive function, there was no statistically significant correlation between VST and Zoo Map Test/DEX. We considered the reason was because Zoo Map Test (Wilson et al., 1996) had a more difficult task with a more complex map than VST; namely it asked subjects to go to six places in a zoo. In order to prove VST could be a new test for executive function, we needed to find out its significance by comparing VST with the real performance test such as Multiple Errands Test (Burgess et al., 2006). It is performed at a real shopping mall environment and involves the completion of various tasks, rules to adhere to and a specified time frame.

In Conclusion, these results suggested that the number of times to refer to the shopping list is related to everyday memory and the general cognitive ability. The total time spent to complete the whole shopping task was related to attention and everyday memory. VST could evaluate some aspects of higher brain functions on virtual shopping scene through one test session.

3.2 Study 2: Comparison of VST performance between control subjects and the patients

The objective of this study was to test the applicability of VST to brain-damaged patients with normal subjects. Patients were tested together with age-matched healthy subjects that were acted as control.

3.2.1 Methods

Participants. Ten age-matched healthy subjects (4 males, 6 females, mean age 47.1 ± 20.1 years, mean years of education 14.1 ± 2.0) and ten patients with cognitive function disorder (6 males, 4 females, mean age 43.5 ± 16.0 years, mean years of education 13.2 ± 1.7) participated in this study.

For healthy control subjects, the inclusion criteria were as follows: 1) no history of neurological or psychiatric disorders, 2) between 20 to 69 years old. The subjects who scored less than 24 (cutoff score) on MMSE (Folstein et al., 1975) were excluded. For the patients, the inclusion criteria were as same as Study 1. There was no significant difference in average age and average years of education between control subjects and the patients.

Procedure. All participants were administered VST and MMSE. They did a practice task of VST, and then performed a real task: VST-1. The tests were conducted on one date within one hour.

Statistical analysis. Comparison between control subjects and the patients was

performed with Mann-Whitney test for each outcome variable in VST. Differences were reported as significant if $p < 0.05$.

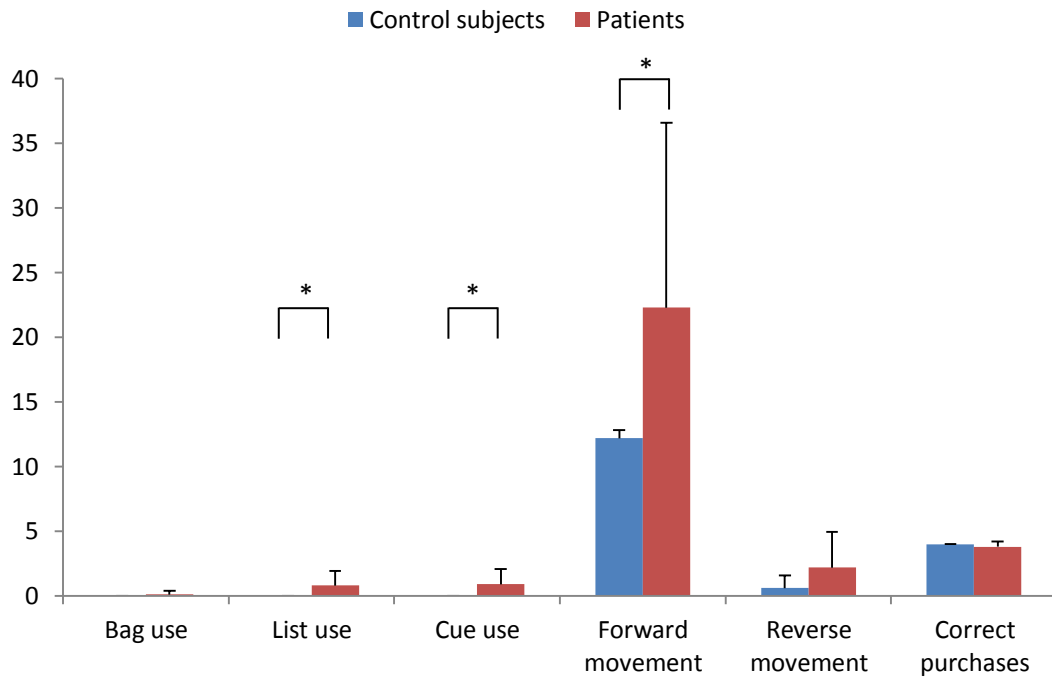
3.2.2 Results

Table 3-4 and Figure 3-1 present comparison of VST performance between control subjects and the patients. There were significant differences in seven out of ten VST variables (excluding Bag use, Reverse movement, and Correct purchases) with the patients performing worse than control subjects. For example, the patients bought correct items but they had to refer to the shopping list more often. They also moved erratically on the street while referring to the shopping list. They also needed more time to complete the whole shopping task.

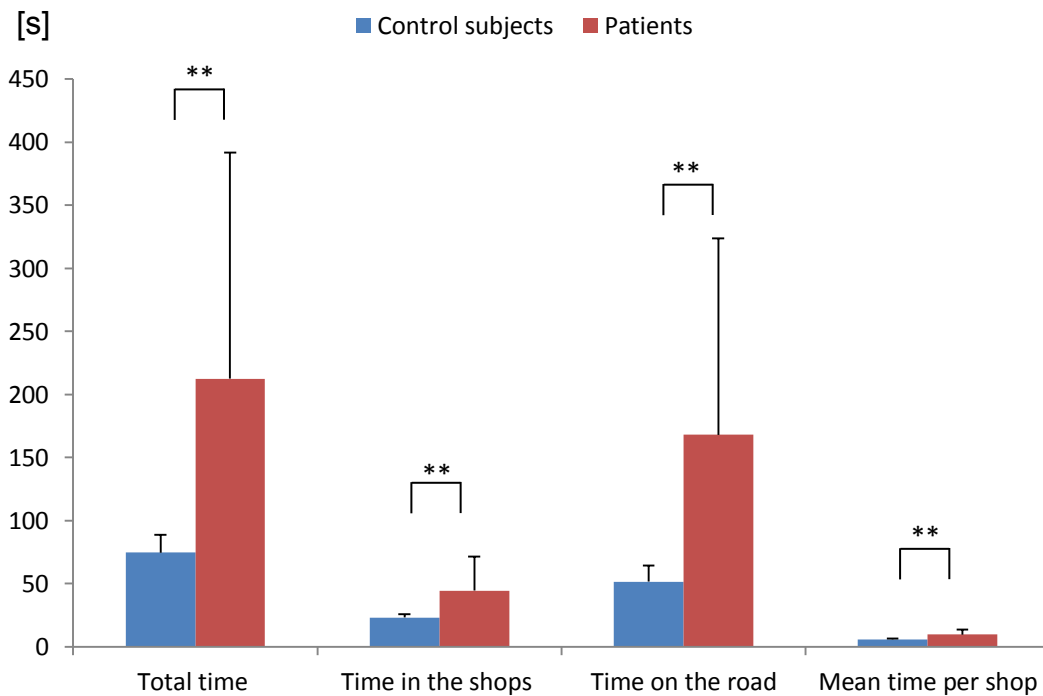
Table 3-4 Comparison of VST performance between control subjects and the patients.

VST evaluation items	Control subjects (n=10)			Patients (n=10)			p
	Mean	SD	(min - max)	Mean	SD	(min - max)	
Bag use, n	0.0	0.0	(0 - 0)	0.1	0.3	(0 - 1)	0.31
List use, n	0.0	0.0	(0 - 0)	0.8	1.1	(0 - 3)	*
Cue use, n	0.0	0.0	(0 - 0)	0.9	1.2	(0 - 3)	*
Forward movement, n	12.2	0.6	(12 - 14)	22.3	14.3	(12 - 47)	*
Reverse movement, n	0.6	1.0	(0 - 2)	2.2	2.7	(0 - 8)	0.17
Correct purchases, n	4.0	0.0	(4 - 4)	3.8	0.4	(3 - 4)	0.15
Total Time, sec	74.5	14.0	(59 - 107)	212.4	179.1	(77 - 605)	**
Time in the shops , sec	23.1	2.6	(21 - 27)	44.4	26.7	(22 - 102)	**
Time on the road, sec	51.4	12.7	(37 - 81)	168.0	155.7	(52 - 503)	**
Mean time per shop, sec	5.8	0.6	(5.3 - 6.8)	9.5	4.1	(6 - 19)	**

min: the minimum, max: the maximum. Mann-Whitney test: * $p < 0.05$, ** $p < 0.01$



(a) Button use frequency and correct purchases: * $p < 0.05$.



(b) Time required: ** $p < 0.01$.

Figure 3-1 Comparison of VST performance between control subjects and the patients.

3.2.3 Discussion

We discuss the difference between control subjects and the brain-damaged patients in VST performance. As shown in Table 3-4 and Figure 3-1, the patients performed significantly worse than control subjects on seven out of ten VST variables: List use, Cue use, Forward movement, Total Time, Time in the shops, Time on the road, and Mean time per shop. The significant difference between control subjects and the patients in time required to complete the task was consistent with the findings of previous study using Virtual Mall in patients with stroke (Rand et al., 2007). Similarly, the significant difference between the two groups in the scores related to event-based prospective memory was consistent with the findings of previous study using Virtual Library Task in patients with TBI (Renison et al., 2012).

We believe that VST is applicable to patients with cognitive dysfunction without severe aphasia and/or severe USN. We consider that not only the number of items bought correctly, but also the times to referring to hints, the times of movement, and the total time spent on road/shop are important points for cognitive assessment of the brain-damaged people using VST.

3.3 Summary

In this chapter, we described two evaluation experiments on the clinical usefulness of VST in brain-damaged patients. The objectives were to reveal 1) the significance of VST by comparing VST performance with conventional neuropsychological tests and questionnaires, 2) the difference of VST performance between control subjects and brain-damaged patients. Ten age-matched healthy control subjects and ten patients participated in the VST experiments.

As a result, some VST variables correlated with the scores of other cognitive assessments related to attention and everyday memory. The result demonstrated that VST could be used to evaluate the ability of attention and memory in patients with brain damage through one test session. In addition, the number of times referring to the shopping list, the number of movements, and the total time to complete the task were all significantly larger/longer for the patients than for control subjects. Therefore, we concluded that VST can be used as a cognitive assessment tool in rehabilitation for brain-damaged patients.

The VST performance in relation to age differences and the parallel form reliability remain unclear, then Chapter 4 describes another two evaluation experiments on VST in elderly people.

Chapter 4

VST Evaluation Experiments in Elderly People

In this chapter, we describe two clinical evaluation experiments of VST in elderly people. The objectives were to investigate 1) the age differences of VST performance between healthy young and old subjects, 2) the parallel form reliability between VST-1 and VST-2. Ten healthy young subjects and ten elderly subjects participated in the experiments.

4.1 Study 3: Comparison of VST performance between young and elderly subjects

The objective for this study was to investigate the performance of VST in relation to age differences. Young and old healthy subjects joined the experiment for the objective.

4.1.1 Methods

Participants. Ten young healthy subjects (5 males, 5 females, mean age 25.2 ± 3.0 years, mean years of education 14.9 ± 1.4) and ten old healthy subjects (1 males, 9 females, mean age 68.9 ± 3.9 years, mean years of education 13.0 ± 1.7) participated in this study. The inclusion criteria were as follows: 1) no history of neurological or psychiatric disorders, 2) between 20 and 29 years old for young group, between 60 and

79 years old for elderly group. The subjects who scored less than 24 points on MMSE were excluded. There was no significant difference in average years of education between the young and elderly healthy subjects.

Procedure. All participants were administered VST and MMSE. They did a practice task of VST, and then performed VST-1 as a real task.

Statistical analysis. Comparison between the two groups was performed with Mann-Whitney test for each outcome variable in VST. Differences were reported as significant if $p < 0.05$.

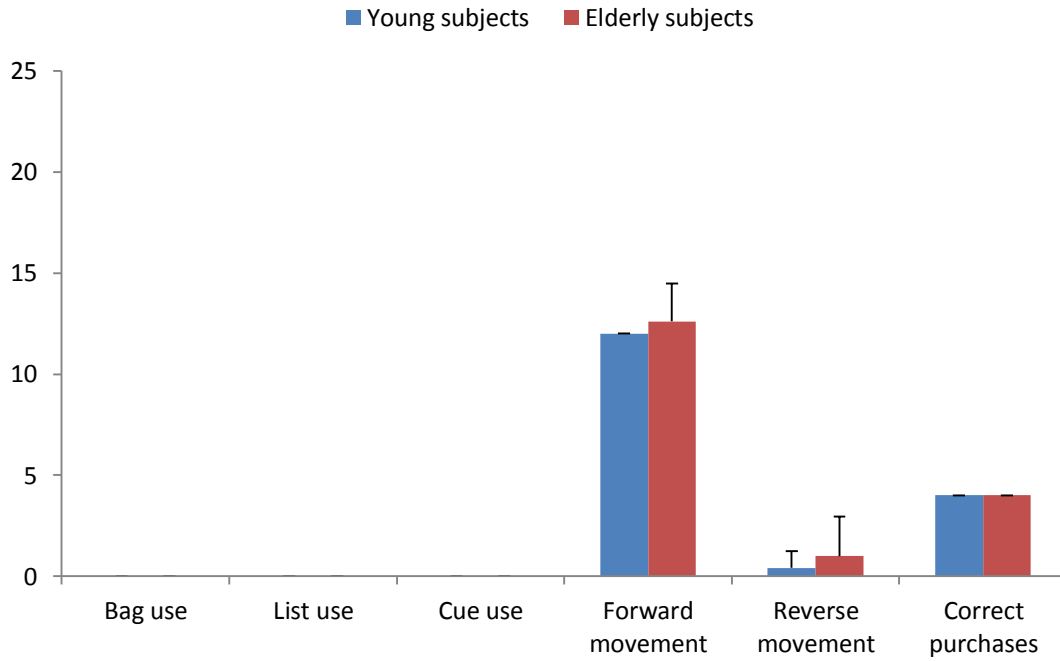
4.1.2 Results

Table 4-1 and Figure 4-1 present comparison of VST performance between young and elderly subjects. There were significant differences in four out of ten VST variables (Total time, Time in the shops, Time on the road, and Mean time per shop) between young and elderly subjects. The performance was worse in the elderly group than the young group. For example, although elderly subjects bought the same number of correct items without using hints such as referring to the shopping list or looking at the shopping bag, they needed more time to complete the whole shopping task than young subjects. There were no significant differences on Forward movement and Reverse movement between the two groups, although the ranges of these variables were wider in elderly subjects than young subjects.

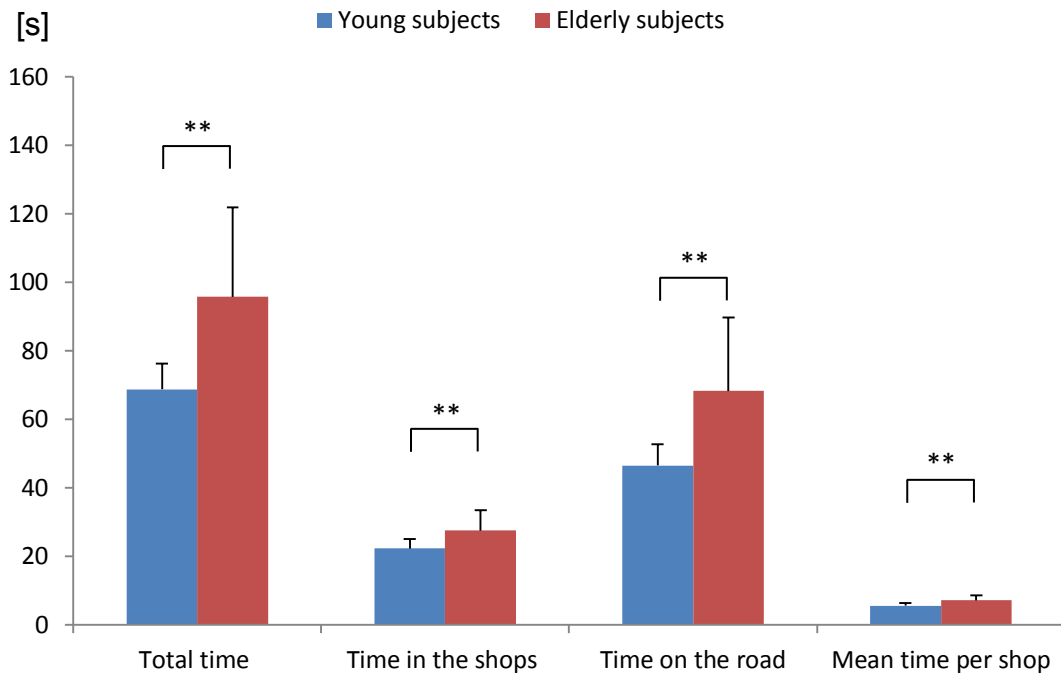
Table 4-1 Comparison of VST performance between young and elderly subjects.

VST evaluation items	Young subjects (n=10)			Elderly subjects (n=10)			p
	Mean	SD	(min - max)	Mean	SD	(min - max)	
Bag use, n	0.0	0.0	(0 - 0)	0.0	0.0	(0 - 0)	—
List use, n	0.0	0.0	(0 - 0)	0.0	0.0	(0 - 0)	—
Cue use, n	0.0	0.0	(0 - 0)	0.0	0.0	(0 - 0)	—
Forward movement, n	12.0	0.0	(12 - 12)	12.6	1.9	(12 - 18)	0.32
Reverse movement, n	0.4	0.8	(0 - 2)	1.0	1.9	(0 - 6)	0.55
Correct purchases, n	4.0	0.0	(4 - 4)	4.0	0.0	(4 - 4)	—
Total Time, sec	68.8	7.5	(59 - 83)	95.8	26.0	(68 - 144)	**
Time in the shops , sec	22.3	2.8	(20 - 30)	27.5	5.9	(22 - 42)	**
Time on the road, sec	46.5	6.2	(37 - 57)	68.3	21.5	(46 - 112)	**
Mean time per shop, sec	5.6	0.7	(5.3 - 7.5)	7.1	1.5	(6 - 11)	**

min: the minimum, max: the maximum. Mann-Whitney test: **p < 0.01



(a) Button use frequency and correct purchases



(b) Time required: ** $p < 0.01$.

Figure 4-1 Comparison of VST performance between young and elderly subjects.

4.1.3 Discussion

We discuss the basic age difference in VST performance. As shown in Table 4-1 and Figure 4-1, elderly subjects performed significantly worse than young subjects on four out of ten VST variables: Total Time, Time in the shops, Time on the road, and Mean time per shop. It was suggested that the longer time required in elderly subjects in VST was related to the decline in their cognitive process and their ability in physical movement. However, there was no statistical difference between the two groups on other variables; Bag use, List use, Cue use, Forward movement, Reverse movement, and Correct purchases.

The significant difference between young and elderly subjects not in behavioral variables such as the number of correct answer but in the total time spent to complete the task was contrary to the findings of previous study using CPT. In the study, it was suggested that increasing age was associated with increased numbers of commission and false alarm errors, while elderly subjects were not significantly slower at responding to stimuli than young subjects (Mani et al., 2005). We considered the reason was because the participants tried to complete the whole shopping tasks on VST correctly even if it took longer, which was similar to the way they behave in their daily life.

Therefore, we will need to take the age-related performance especially time required into consideration on VST. In order to standardize VST for a wide clinical application, we will need to collect data and establish the nominal value for each age bracket in VST. Results from VST in the clinic may also underestimate the practical cognitive problems experienced by elderly subjects with mild cognitive impairments.

4.2 Study 4: Comparison of VST performance between two parallel forms

The objective for this study was to validate two parallel forms of VST. Healthy elderly subjects joined the experiment for the objective.

4.2.1 Methods

Participants. Ten healthy elderly subjects (1 males, 9 females, mean age 68.9 ± 3.9 years, mean years of education 13.0 ± 1.7) participated in this study. The inclusion criteria were as same as that in Study 3.

Procedure. All participants were administered two parallel forms: VST-1, VST-2 after a practice task of VST. They completed the two tests in random order at two weeks intervals. MMSE was also conducted to them.

Statistical analysis. Comparison between the two forms was performed with Mann-Whitney test for each outcome variable in VST. Differences were reported as significant if $p < 0.05$.

4.2.2 Results

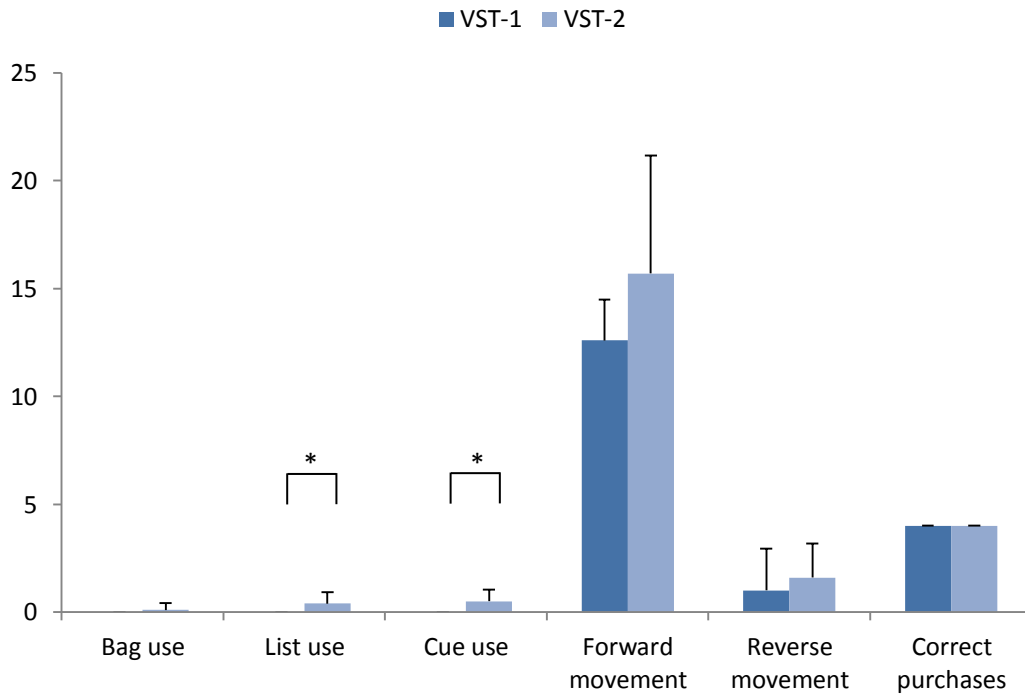
Table 4-2 and Figure 4-2 present comparison of VST performance between VST-1 and VST-2. There was no statistically significant difference in eight out of ten VST variables between the two parallel forms (Bag Use, Forward/Reverse movement, Correct Purchases, Total time, Time in the shops, Time on the road, and Mean time per

shop). The number of times of List use and Cue use were larger in VST-2 than in VST-1 significantly ($p = 0.03, 0.01$, respectively). Bag use, Forward/Reverse movement, Total time, and Time on the road tended to larger/longer in VST-2 than VST-1.

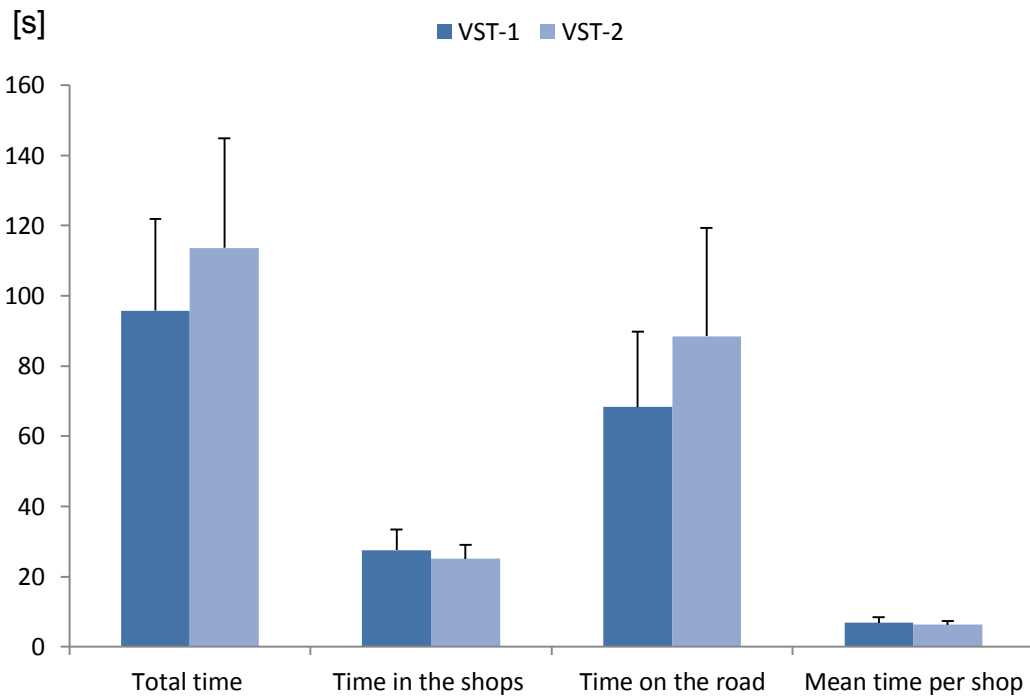
Table 4-2 Comparison of VST performance between VST-1 and VST-2.

VST evaluation items	VST-1			VST-2			p
	Mean	SD	(min - max)	Mean	SD	(min - max)	
Bag use, n	0.0	0.0	(0 - 0)	0.1	0.3	(0 - 1)	0.31
List use, n	0.0	0.0	(0 - 0)	0.4	0.5	(0 - 1)	0.03 *
Cue use, n	0.0	0.0	(0 - 0)	0.5	0.5	(0 - 1)	0.01 *
Forward movement, n	12.6	1.9	(12 - 18)	15.7	5.5	(12 - 28)	0.06
Reverse movement, n	1.0	1.9	(0 - 6)	1.6	1.6	(0 - 4)	0.24
Correct purchases, n	4.0	0.0	(4 - 4)	4.0	0.0	(4 - 4)	—
Total Time, sec	95.8	26.0	(68 - 144)	113.6	31.3	(68 - 178)	0.13
Time in the shops , sec	27.5	5.9	(22 - 42)	25.1	4.0	(20 - 32)	0.32
Time on the road, sec	68.3	21.5	(46 - 112)	88.5	30.8	(48 - 149)	0.11
Mean time per shop, sec	6.9	1.5	(6 - 11)	6.3	1.0	(5 - 8)	0.32

min: the minimum, max: the maximum. Mann-Whitney test: * $p < 0.05$



(a) Button use frequency and correct purchases: * $p < 0.05$.



(b) Time required

Figure 4-2 Comparison of VST performance between VST-1 and VST-2.

4.2.3 Discussion

There were no significant group differences on eight out of ten variables including all four temporal variables and the number of correct purchases. It was suggested that two parallel tests were almost equal difficult level from a point of view of the time required and correct purchases.

However, the mean number of times referring to the list and cue were significantly larger in VST-2 than in VST-1. As reason for that, we consider the items on the purchase list of VST-2 (e.g. a pencil, a rice bowl, a piece of gauze, and a cucumber) might be less familiar for the participants than that of VST-1 (e.g. a pair of boots, incense sticks, a ball, and a hammer), although we took condition of the word characteristics used in the shopping lists and the shop arrangement into consideration as mentioned in Section 2.2.3. In a future study, we need to modify these word lists for shopping tasks.

4.3 Summary

In this chapter, we described two evaluation experiments on the clinical usefulness of VST in elderly people. The objectives were to reveal 1) the age differences of VST performance between healthy young and elderly subjects, 2) the parallel form reliability between VST-1 and VST-2. Ten healthy young subjects and ten elderly subjects participated in the VST experiments.

As a result, the total time spent on VST was significantly longer for elderly subjects than for young subjects. There was no statistically significant difference between two parallel forms on the number of correct purchases and each temporal variable on VST. In conclusion, the total time spent on VST represented the basic difference of cognitive function between the age groups. The parallel forms of VST appeared to be equivalent measures of higher brain functions. Therefore, clinical testers should interpret VST performance taking ageing effects into consideration. The parallel forms could be used in clinical retest sessions on the same difficulty level with each other.

We adopted 4-item shopping tasks and conducted VST evaluation experiments in Chapters 3 and 4, but it is not still clear how the VST task difficulty level influences the performance, brain activation during the execution and subjective assessments of the tasks. In Chapter 5, we modify VST to have three task difficulty levels and reveal the above point in convalescent brain-damaged patients.

Chapter 5

VST considering Task Difficulties

In this chapter, we introduce a revised Virtual Shopping Test (VST-R) with three different task levels in order to assess daily cognitive function, and describe a clinical study using the system. The objective of this study was to investigate differences in task performance, brain activation, and subjective assessments in relation to the difficulty levels of the tasks. Six healthy young subjects and ten convalescent brain-damaged patients participated in this study.

5.1 Background

In cognitive rehabilitation, exercises with an appropriate difficulty level for each individual may increase the patient's motivation and produce good results. Rehabilitation therapists clinically evaluate each patient's ability and try to provide him/her with specific appropriate tasks. However, difficulties have been associated with establishing an appropriate task level because of the lack of evidence on its effectiveness (Cicerone et al., 2008). Although various VR techniques have been proposed for cognitive rehabilitation (Kang et al., 2008; Knight et al., 2006; Zhang et al., 2003), few studies including a virtual action planning supermarket considered the task difficulty level and/or related brain activation (Josman et al., 2009; Tarnanas et al., 2012).

We previously developed a Virtual Shopping Test (VST) for a realistic assessment of cognitive function using VR technology (Okahashi et al., 2013). In the present study, VST was modified to a revised version (VST-R) that had three different task difficulty levels. The system could also output event signals that were synchronized with the user's PC operation. We used these signals to assess event-related brain activation. In the present study, we used our VST-R with functional near-infrared spectroscopy (fNIRS) to evaluate prefrontal cortex activity while subjects performed the test.

fNIRS is a non-invasive and non-restrictive technique that allows blood oxygenation changes related to cerebral activation to be measured (Gagnon et al., 2012; Villringer et al., 1997). Unlike other modern neuroimaging techniques such as functional magnetic resonance imaging (fMRI) and positron emission tomography (PET), fNIRS is advantageous for daily clinical therapy situations and has recently been used to study the development and recovery of physical/cognitive function in healthy people and brain-damaged patients of various ages (Miyai et al., 2003; Moriguchi et al., 2013).

The objective of this study was to investigate differences in task performance, brain activation, and subjective assessments in relation to the task difficulty levels. Subjects were asked to buy 2, 4, and 6 specific items in a different virtual mall in each task. These tasks were conducted and questionnaires answered by convalescent brain-damaged patients and healthy young subjects. Hemodynamic changes in the prefrontal cortex (PFC) during activation due to the tasks were examined using fNIRS. A previous study reported that executive functions and attention were related to

activation of the PFC (Godefroy, 2003). We hypothesized that each task level would activate the brain differently and lead to more subjective assessments. In addition, differences were expected in the activation pattern between the two groups.

5.2 A revised version of Virtual Shopping Test (VST-R)

5.2.1 Construction of the system

The hardware system included a personal computer, touch screen (LCD-MF222FBR-T, I-O DATA), and 16-channel OEG-16 fNIRS system (Spectratech Co., Yokohama, Japan). Figure 5-1 shows the overall setup of the experimental device. Figure 5-2 shows the scene of the experiment.

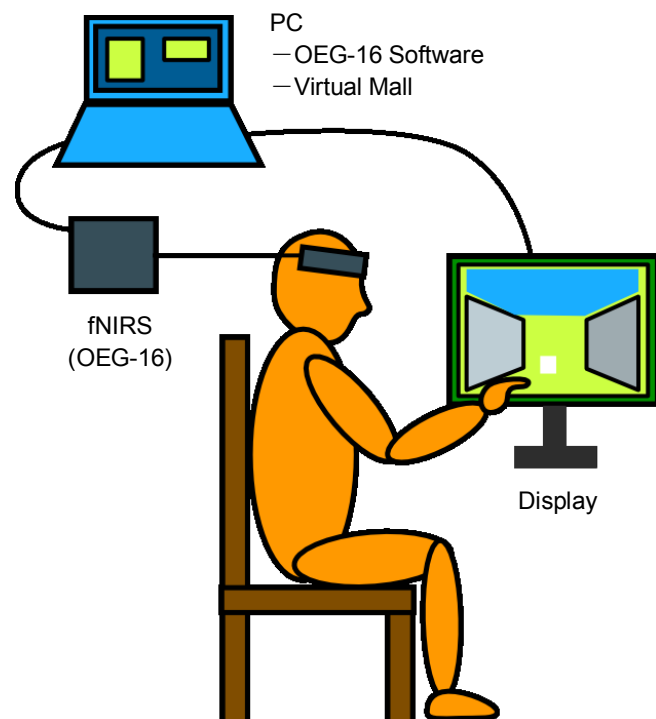


Figure 5-1 Composition of the experimental device.

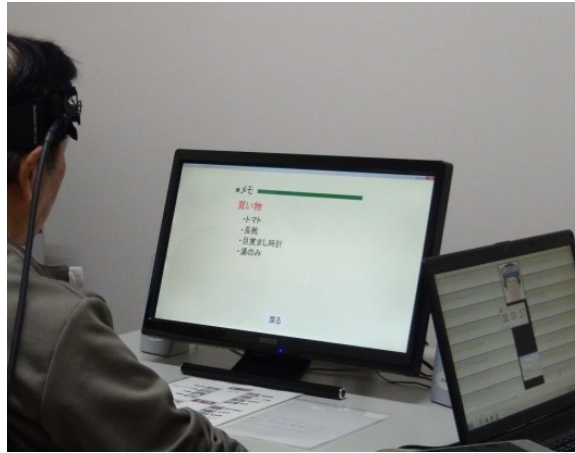


Figure 5-2 Scene of the experiment.

A virtual environment was developed with Metasequoia and Open GL. In this program, the visual environment consisted of a Japanese shopping mall with 20 shops and a train station. An audio environment of the natural sounds associated with a shopping mall was also provided. By touching the bottom of the screen, users could move forward and turn back in the virtual shopping mall, enter a shop, and buy an item. Two hint buttons (e.g. List and Bag) were provided to allow users to view some hints during the shopping task. The operation of buttons was recorded automatically, and outputted as a log file after finishing the test. In addition, this system output event signals when users entered/exited the shop, bought an item, and checked the purchase list. fNIRS data was also recorded with these signals. Figure 5-3 shows an example of waveforms with event signals. Vertical lines on the waveforms represent event signals.

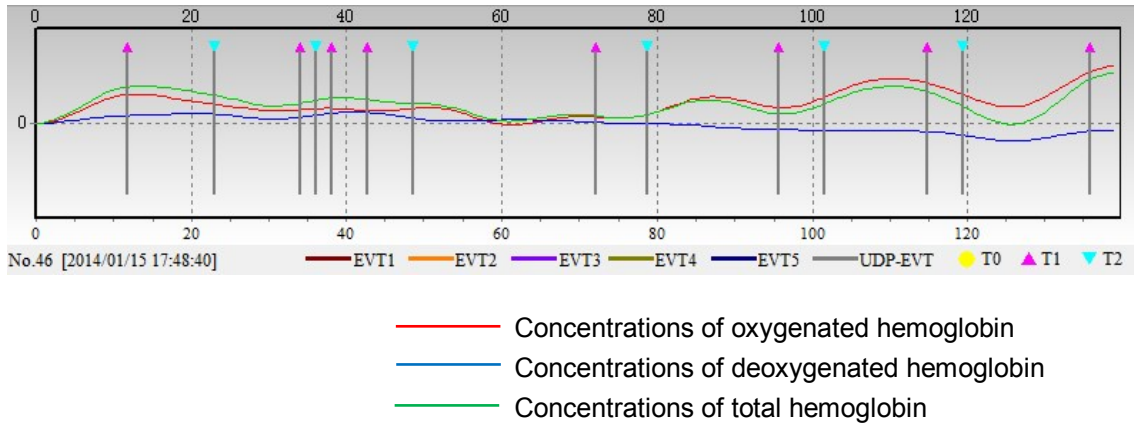


Figure 5-3 An example of waveforms with event signals on fNIRS data.

5.2.2 Task setting and procedure

Task Setting on VST-R. We constructed a virtual shopping mall in a virtual space, and set up three different tasks with different difficulties. Task 1 asked subjects to buy 2 specific items (a pudding and AAA-sized batteries), Task 2 asked them to buy 4 specific items (tomatoes, rubber boots, an alarm clock, and a teacup), and Task 3 asked them to buy 6 specific items (an eraser, plum liqueur, incense sticks, building blocks, a 80-yen stamp, and a baseball glove). The virtual shopping mall used in each task had twenty shops and a train station, whereas the arrangement of these shops in the mall differed between tasks. Subjects had to search the shops that sold specific items and select the target item from six items inside the shop. Figure 5-4 shows an example of a basic VST-R screen.

Figure 5-5 shows the virtual shopping mall map and the purchase list used in Task 1; Figure 5-6 shows that used in Task 2; and Figure 5-7 shows that used in Task 3.

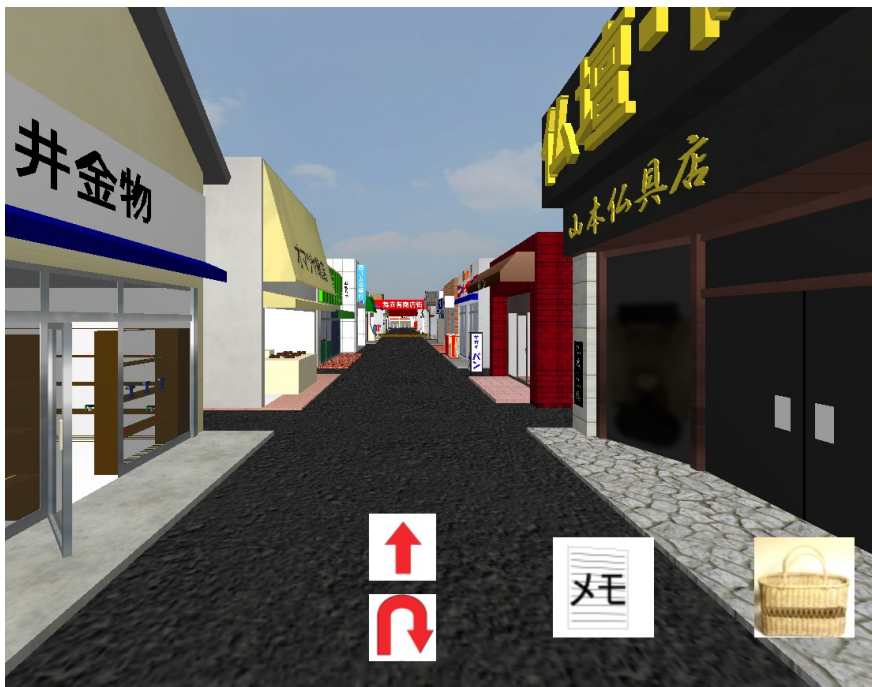


Figure 5-4 An example of a basic screen in VST-R.



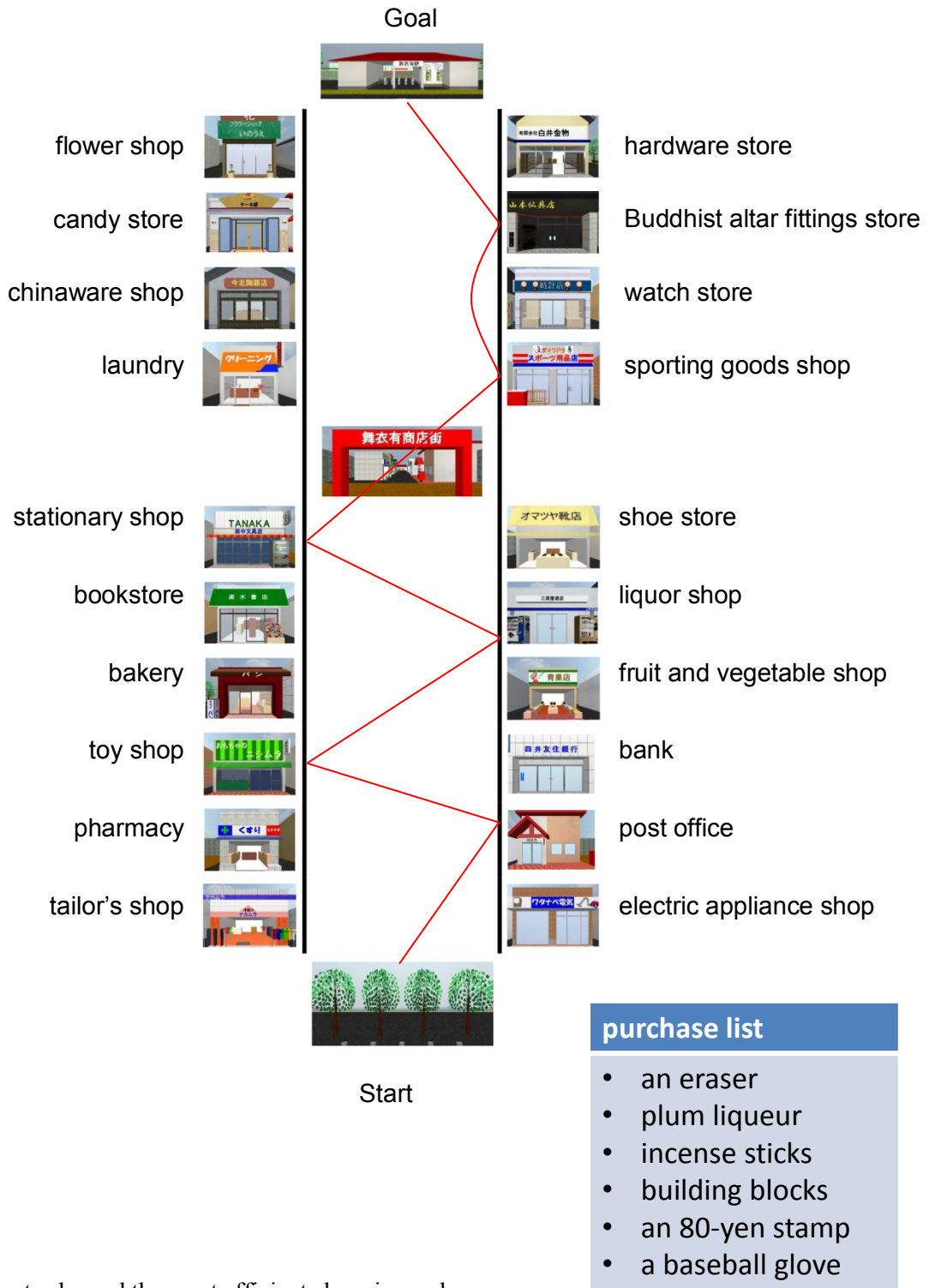
The red route showed the most efficient shopping order.

Figure 5-5 Map of the virtual shopping mall and the list used in Task 1.



The route showed the most efficient shopping order.

Figure 5-6 Map of the virtual shopping mall and the list used in Task 2.



The route showed the most efficient shopping order.

Figure 5-7 Map of the virtual shopping mall and the list used in Task 3.

Experimental procedure. The subjects were first asked to memorize the specific shopping items while looking at the shopping list for 10 seconds. They were then allowed to plan the shopping routes that they considered to be the most efficient by filling in a blank map sheet with a pencil. They were asked to buy the specific items as quickly and efficiently as possible, while minimizing the use of hints. They were allowed to refer to the blank map at any time during the VST-R.

Evaluation items. VST-R had eight basic evaluation items: the number of times subjects used each button (Bag use, List use, Forward movement, and Reverse movement), the number of items bought correctly (Correct purchases), Total time, Time in the shops, and Time on the road, and these could be calculated from the recording data.

In addition, the following three items were calculated for fair analysis between tasks and groups. The typical three VST evaluation items (e.g. Correct purchases, Total time, and Time in the shops) were corrected.

- Overs and shots of purchases:

The differences between Correct purchases and the optimal number in each task (2, 4, 6 for Task 1, 2, 3, respectively)

- Corrected Total time:

A number obtained by dividing Total time by a specific number based on migration length in each task (14.7, 17.7, 21.2 for Task 1, 2, 3, respectively)

- Corrected Time in the shops:

A number obtained by dividing Time in the shops by a number of Correct purchases

5.2.3 functional near-infrared spectroscopy (fNIRS)

A 16-channel OEG-16 fNIRS system was used at a sampling time of 0.65 seconds, the intensity of the light detected at two wavelengths, 770 and 840 nm, was measured, and changes in the optical density were calculated. The system then calculated changes in the concentrations of oxygenated hemoglobin [oxyHb], deoxygenated hemoglobin [deoxyHb], and total hemoglobin [totalHb] based on the Beer-Lambert approach. Emission and detection probes were bilaterally attached to the forehead of each subject. As shown in Figure 5-8, channels covered the left and right PFC. The detection probes were set at Fp1 and Fp2, which corresponded to the international 10-20 system (Figure 5-9) of electrode placement with emission probes.

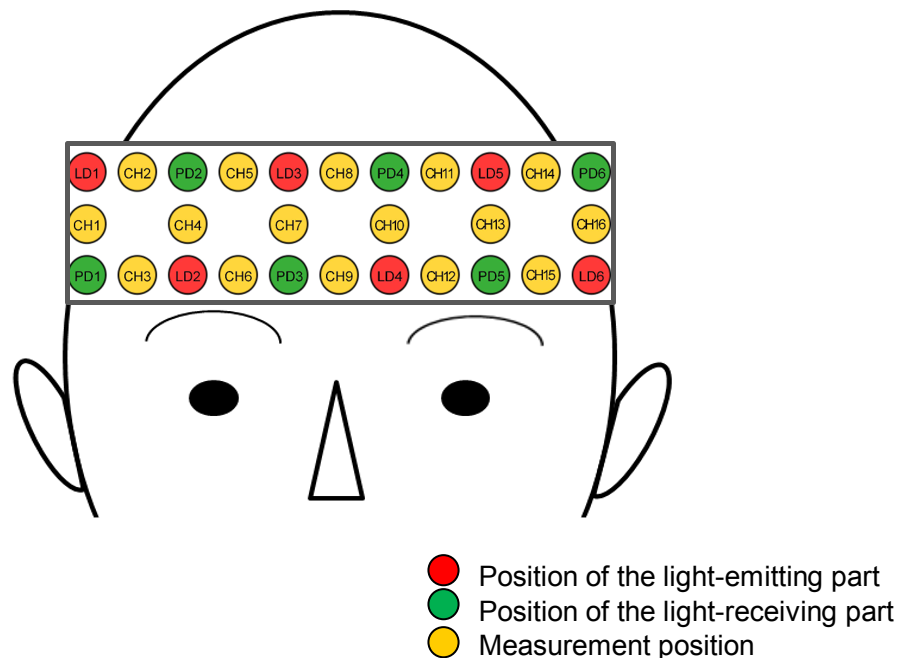


Figure 5-8 fNIRS channel arrangement on the forehead.

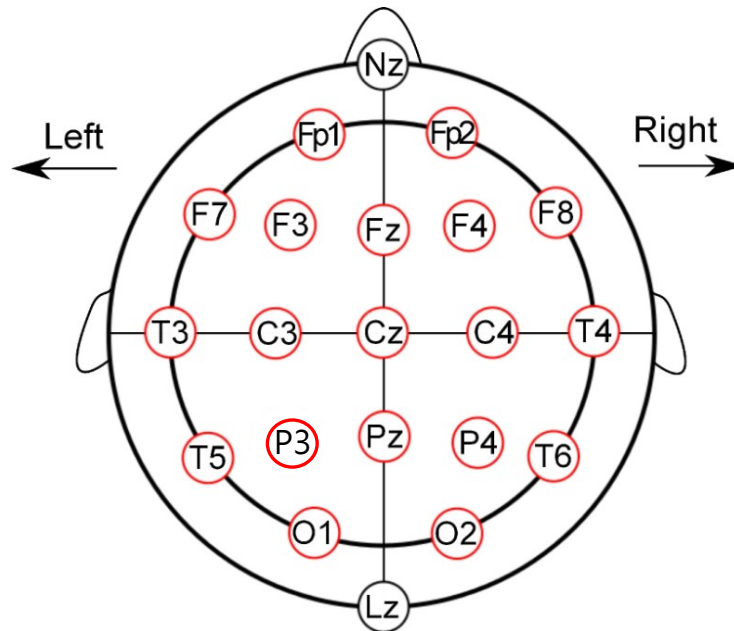


Figure 5-9 The international 10-20 system.

5.3 Study 5: A VST-R evaluation experiment in convalescent brain-damaged patients

5.3.1 Methods

Participants. six young healthy subjects (4 males, 2 females, mean age 23.2 ± 1.0 years) and ten brain-damaged inpatients with cognitive dysfunctions in the convalescence rehabilitation ward (5 males, 5 females, mean age 61.2 ± 16.2 years) participated in this study. The participation criteria for the patients were as follows: 1) cognitive ability to understand how to operate a touch screen and 2) physical ability to reach and touch the screen by their uninvolved upper limbs. The study exclusion criteria were as follows: i) severe aphasia, and ii) severe unilateral spatial neglect. All participants received written and verbal information about the study and gave written informed consent. The protocol of the study was approved by the Kobe University

Graduate School of System Informatics Ethic Committee, Nishi Memorial Port Island Rehabilitation Hospital Ethic Committee and Kyoto University Medical Ethic Committee.

Procedure. All participants were administered VST-R in the order of Tasks 1, 2, and 3 and questionnaires concerning subjective task difficulty after each task. The questionnaire consisted of three questions concerning the degree of task difficulty, the effort required, and psychological load. Each answer was rated on a five-point scale (1-5). Higher scores indicated a higher load task. Patients also performed seven conventional neuropsychological tests and answered two questionnaires. The general cognitive level was evaluated using MMSE. Attention was evaluated by SDMT (Smith, 1982) and SRT (Beck et al., 1956). Regarding visual inattention, the presence of USN was assessed by the Star and Letter Cancellation Task (Ishiai 1999; Wilson et al., 1987). Everyday memory was assessed using RBMT (Wilson et al., 1985; Wilson et al., 1989) and EMC (Kazui et al., 2006). Executive function was evaluated by the Zoo Map Test and DEX (Evans et al., 1997; Wilson et al., 1996). All tests were finished within one month before and after the execution of VST-R.

Data analysis. We reset the data at the two points when subjects start to memorize shopping items and perform VST-R for fNIRS data analysis. We used a low pass filter (cut-off frequency 0.05 Hz and attenuation slope 40dB/Oct). As shown in Figure 5-10 we used a Ch4-6 data as the right lateral prefrontal cortex (rPFC), Ch7-10 data as the medial prefrontal cortex (mPFC), and Ch11-13 data as the left lateral prefrontal cortex

(IPFC). The average change in [oxyHb] in each area was calculated for the memorizing phase: while subjects memorized the shopping items, shopping phase: while they were in a shop, and moving phase: while they were on the road. A task difficulty level (Task 1, Task 2, Task 3) \times Phase (memorizing, shopping, moving) \times Group (patient, healthy) analysis of variance (ANOVA) was conducted to evaluate changes in [oxyHb] in each area of PFC. A task difficulty level (Task 1, Task 2, Task 3) \times Group (patient, healthy) ANOVA was conducted for behavioral data and subjective assessment analysis. Descriptive statistics of performance in all evaluation items were also performed in this study.

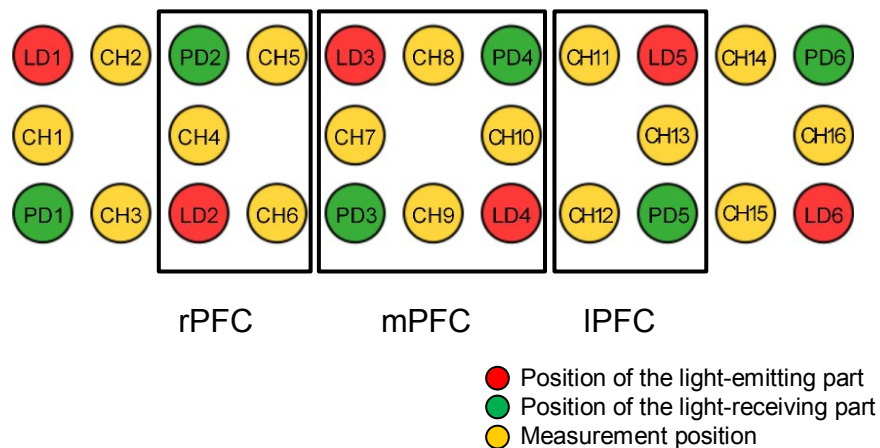


Figure 5-10 fNIRS channels for analysis.

5.3.2 Results

Characteristics in patient group. The characteristics and cognitive assessment data of the patients were presented in Table 5-1. Patients included some forms of brain damage that were within six months of their onset. Nine of the patients were over the age of fifty. They all had difficulties in their instrumental activity of daily living. Cognitive dysfunctions were related to more than one aspect of their ability: attention, memory, and executive functions.

Table 5-1 Patient characteristics and cognitive assessment data.**(a) Basic information**

Patient ID	1	2	3	4	5	6	7	8	9	10
Age	58	64	23	81	59	76	73	66	51	61
Gender	M	M	F	F	M	M	F	F	M	F
Diagnosis	E	CVA	E	TBI	CVA	CVA	TBI	CVA	CVA	CVA
Disease duration (days)	89	157	172	143	55	42	56	101	87	64
Duration of education (years)	16	15	16	13	16	16	12	12	12	12
FIM /126	126	86	114	111	103	109	120	96	109	125
MMSE /30	28	26	30	29	27	25	27	26	30	29

M: male, F: female, E: encephalitis, CVA: cerebrovascular accident, TBI: traumatic brain injury
MMSE: Mini-Mental State Examination, FIM: Functional Independence Measure

(b) Cognitive assessment

Patient ID	1	2	3	4	5	6	7	8	9	10
Attention										
SDMT (%)	42	30	33.6	17	25	30	25	21	35	31
SRT: correct rate (%)	100	93.8	68.8	93.8	100	88.8	76.3	62.5	100	96.3
Star cancellation task /54	54	52	54	51	64	54	54	54	54	54
Letter cancellation task /40	37	38	37	35	35	39	38	39	40	39
Memory										
RBMT: standard profile score /24	20	22	16	14	11	12	9	15	22	16
EMC /39	12	13	2	25	4	19	12	12	4	5
Executive function										
Zoo Map Test: the 1 st trial /8	8	6	5	0	5	8	4	7	8	1
Zoo Map Test: the 2 nd trial /8	8	8	5	4	8	8	4	8	8	8
DEX /80	4	19	41	1	34	1	8	17	5	17

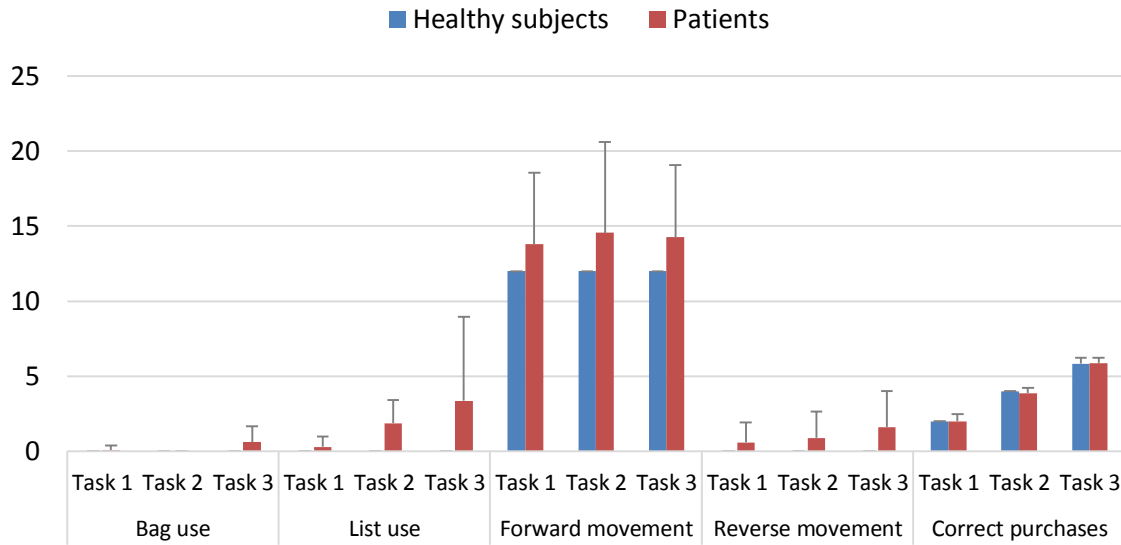
SDMT: Symbol Digit Modalities Test, SRT: Simple Reaction Time Task, RBMT: Rivermead Behavioural Memory Test, EMC: Everyday Memory Checklist, DEX: Dysexecutive Questionnaire

Behavioral data. A comparison of the VST-R performance on basic evaluation items between the two groups was presented in Table 5-2 and Figure 5-11. All ten patients accomplished Task 1, all patients, except for a patient (ID 5), could do Task 2, and all patients, except for two patients (ID 4 and 5) could do Task 3. The Patient (ID 4) who needed the longest time to complete Task 1 got lost in the mall and bought the same item twice. The Patient (ID 5) did not complete Task 2 using hints and the map efficiently and needed some assistance from a tester. The number of purchases in each task was not sufficient or excessive for some patients. The mean time required to complete the task was longer for the patients than for the healthy subjects in all tasks. The results of ANOVA showed a significant main effect of Task difficulty level ($p < 0.01$) and Group ($p < 0.01$) at the time required (e.g. Total time/Time on the road/Time in the shops), but no interactions, except for that of the Task difficulty level \times Group interaction with Time in the shops ($p < 0.05$). The Total time and Time on the road were longer in Task 3 than in Task 1 ($p < 0.01$). Time in the shops in Tasks 2 and 3 was longer in the patients than in the healthy subjects ($p < 0.01$). However, there was no main effect and no interaction for other variables.

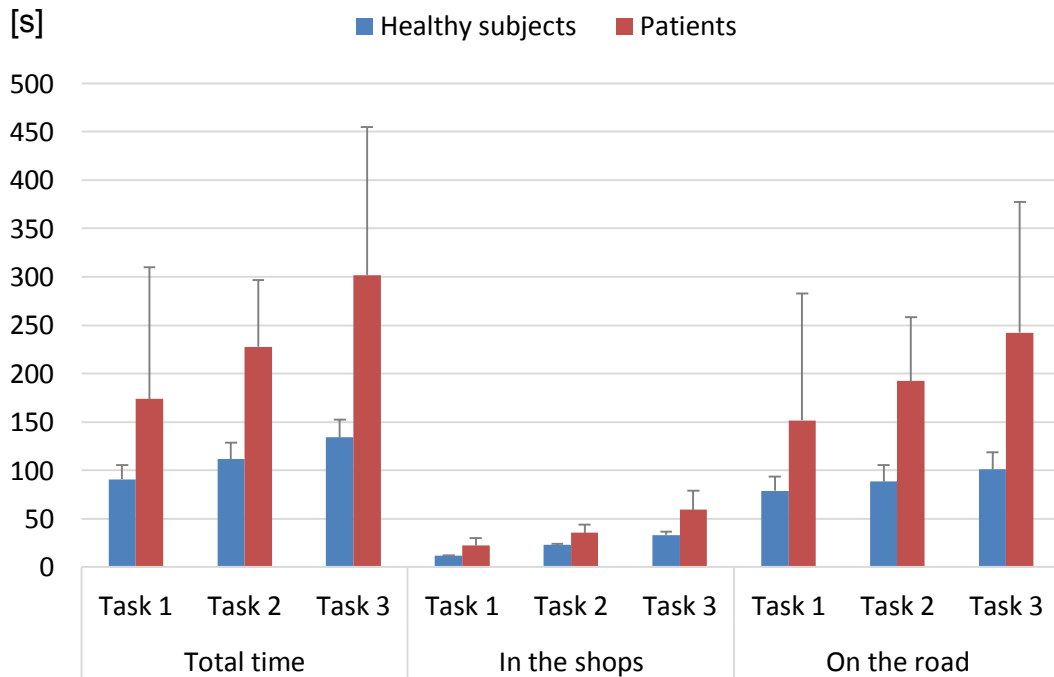
Table 5-2 Comparison of VST-R performance between healthy subjects and the patients (1).

VST evaluation items	Task 1		Task 2		Task 3	
	Healthy subjects (n=6)	Patients (n=10)	Healthy subjects (n=6)	Patients (n=9)	Healthy subjects (n=6)	Patients (n=8)
Bag use, n	0 ± 0 (0 - 0)	0.1 ± 0.3 (0 - 1)	0 ± 0 (0 - 0)	0 ± 0 (0 - 0)	0 ± 0 (0 - 0)	0.6 ± 1.1 (0 - 3)
List use, n	0 ± 0 (0 - 0)	0.3 ± 0.7 (0 - 2)	0 ± 0 (0 - 0)	1.9 ± 1.5 (0 - 4)	0 ± 0 (0 - 0)	3.4 ± 5.6 (0 - 17)
Forward movement, n	12 ± 0 (12 - 12)	13.8 ± 4.8 (12 - 26)	12 ± 0 (12 - 12)	14.6 ± 6.0 (12 - 30)	12 ± 0 (12 - 12)	14.3 ± 4.8 (12 - 26)
Reverse movement, n	0 ± 0 (0 - 0)	0.6 ± 1.3 (0 - 4)	0 ± 0 (0 - 0)	0.9 ± 1.8 (0 - 4)	0 ± 0 (0 - 0)	1.6 ± 2.4 (0 - 7)
Correct purchases, n	2 ± 0 (2 - 2)	2.0 ± 0.5 (1 - 3)	4 ± 0 (4 - 4)	3.9 ± 0.3 (3 - 4)	5.8 ± 0.4 (5 - 6)	5.9 ± 0.4 (5 - 6)
Total Time, sec	90.7 ± 15.0 (71 - 114)	173.7 ± 136.0 (84 - 552)	111.5 ± 17.1 (98 - 142)	227.8 ± 68.8 (109 - 328)	134.2 ± 18.2 (103 - 151)	301.8 ± 153.0 (136 - 647)
Time in the shops , sec	11.8 ± 0.4 (11 - 12)	22.1 ± 8.0 (14 - 38)	23.0 ± 1.3 (22 - 25)	35.6 ± 8.2 (25 - 48)	33.2 ± 3.7 (29 - 39)	59.4 ± 19.6 (36 - 101)
Time on the road, sec	78.8 ± 15.0 (69 - 102)	151.6 ± 131.4 (65 - 519)	88.5 ± 16.8 (73 - 118)	192.2 ± 66.0 (84 - 285)	101.0 ± 17.6 (74 - 117)	242.3 ± 134.9 (100 - 546)

Result shows mean ± SD (the minimum - the maximum).



(a) Button use frequency and correct purchases



(b) Time required

Figure 5-11 Comparison of VST-R performance between healthy subjects and the patients (1).

Next, a comparison of the VST-R performance on three corrected evaluation items between the two groups was presented in Table 5-3 and Figure 5-12. There was no difference between two groups on Overs and shots of purchases, while the values of both Corrected Total time and Corrected Time in the shops were larger in the patients than in healthy subjects in all tasks. The standard deviations (SD) on these items were also larger in in the patients than in healthy subjects.

Table 5-3 Comparison of VST-R performance between healthy subjects and the patients (2).

VST corrected items	Task 1		Task 2		Task 3	
	Healthy subjects (n=6)	Patients (n=10)	Healthy subjects (n=6)	Patients (n=9)	Healthy subjects (n=6)	Patients (n=8)
Overs and shorts of purchases	0 ± 0 (0 - 0)	-0.2 ± 0.4 (-1 - 0)	0 ± 0 (0 - 0)	-0.1 ± 0.3 (-1 - 0)	-0.2 ± 0.4 (-1 - 0)	-0.1 ± 0.4 (-1 - 0)
Corrected Total Time	6.2 ± 1.0 (4.8 - 7.8)	11.8 ± 9.2 (5.7 - 37.6)	6.3 ± 1.0 (5.5 - 8.0)	11.6 ± 5.5 (6.2 - 18.5)	6.3 ± 0.9 (4.9 - 7.1)	11.4 ± 8.7 (6.4 - 30.5)
Corrected Time in the shop	5.9 ± 0.2 (5.5 - 6.0)	11.6 ± 5.1 (7.0 - 22.0)	5.8 ± 0.3 (5.5 - 6.3)	9.3 ± 2.7 (6.3 - 14.3)	5.7 ± 0.7 (4.8 - 6.5)	10.1 ± 3.2 (6.0 - 16.8)

Result shows mean ± SD (the minimum - the maximum).

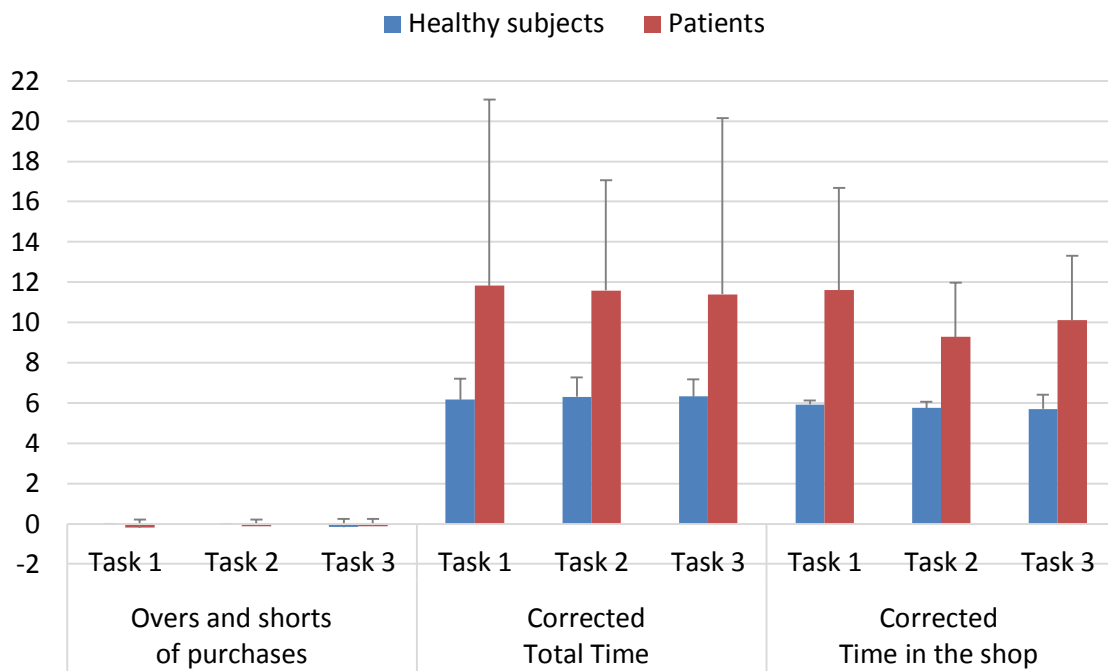


Figure 5-12 Comparison of VST-R performance between healthy subjects and the patients (2).

fNIRS data. Figure 5-13 shows mean changes in [oxyHb] ($\Delta[\text{oxyHb}]$) in the memorizing, shopping, and moving phases in healthy subjects (see the upper three charts) and the patients (see the lower three charts).

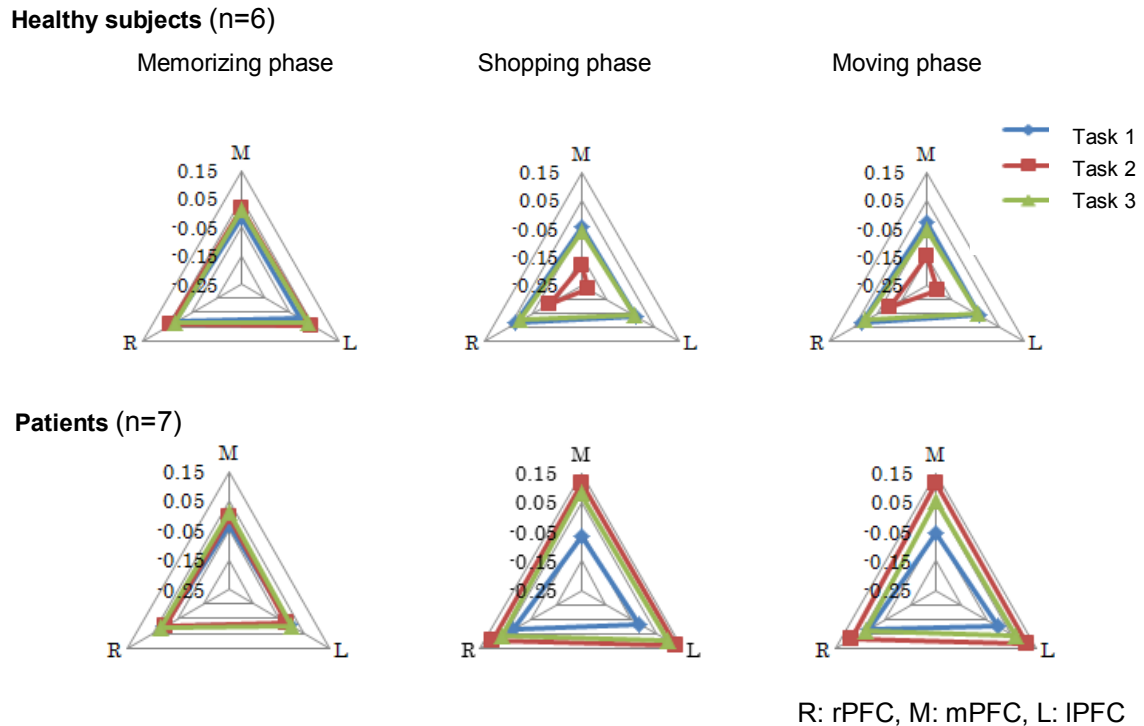


Figure 5-13 Mean changes in the concentration of oxygenated hemoglobin in each phase.

We analyzed data obtained in seven patients (except ID 3, 4, and 5) in consideration of small artifacts and an elderly age range. In the patients, $\Delta[\text{oxyHb}]$ decreased in Tasks 1 and 2, and increased in Task 3 in the memorizing phase, while $\Delta[\text{oxyHb}]$ decreased in Task 1 and increased in Tasks 2 and 3 in the shopping and moving phases. In the healthy subjects, $\Delta[\text{oxyHb}]$ decreased in Task 1 and increased in Tasks 2 and 3 in the memorizing phase, while it decreased in all tasks in the shopping and moving phases.

Statistical analyses on $\Delta[\text{oxyHb}]$ were separately conducted in each area of PFC. The results of ANOVA showed a significant Phase \times Group interaction ($p < 0.05$), Task difficulty level \times Group interaction ($p < 0.05$), and Task difficulty level \times Phase \times Group interaction ($p < 0.01$) in IPFC. $\Delta[\text{oxyHb}]$ in IPFC in the shopping and moving phases performed in Task 2 was significantly higher for the patients than for the healthy subjects ($p < 0.01$). A significant Task difficulty level \times Phase \times Group interaction ($p < 0.05$) was also observed in mPFC. $\Delta[\text{oxyHb}]$ in mPFC in the shopping phase in Task 2 was significantly higher for the patients than for the healthy subjects ($p < 0.01$). However, there was no main effect or interaction in rPFC.

Subjective assessment. The comparison of subjective assessments between the two groups was presented in Table 5-4 and Figure 5-14. Higher scores indicated a higher load task. All three assessment items were slightly higher for the patients than for the healthy subjects. The results of ANOVA showed a significant main effect of the Task difficulty level ($p < 0.01$) and Group ($p < 0.05$) on subjective task difficulty, but no interaction. The mean score was higher for Tasks 2 and 3 than for Task 1 ($p < 0.01$). It also revealed a significant main effect of the Task difficulty level ($p < 0.01$) and Group ($p < 0.01$) on subjectively assessed efforts with no interaction. The mean score was higher for Tasks 2 and 3 than for Task 1 ($p < 0.01$), and for Task 3 than for Task 2 ($p < 0.05$). A significant main effect was observed for the Task difficulty level ($p < 0.01$) and Task difficulty level \times Group interaction ($p < 0.01$) on subjective psychological load. Patients felt a significantly heavier psychological load in Task 3 than in Tasks 1/2, and in Task 2 than in Task 1 ($p < 0.01$).

Table 5-4 Comparison of subjective assessments between healthy subjects and the patients.

Question	Task 1		Task 2		Task 3	
	Healthy subjects	Patients	Healthy subjects	Patients	Healthy subjects	Patients
	(n=6)	(n=10)	(n=6)	(n=9)	(n=6)	(n=8)
task difficulty	1.2 ± 0.4 (1 - 2)	2.7 ± 1.1 (1 - 4)	2.5 ± 0.8 (2 - 4)	3.7 ± 0.8 (2 - 5)	3.7 ± 0.5 (3 - 4)	3.9 ± 1.0 (2 - 5)
efforts made	1.2 ± 0.4 (1 - 2)	2.5 ± 1.1 (1 - 4)	2.3 ± 0.5 (2 - 3)	3.9 ± 0.9 (2 - 5)	3.7 ± 1.0 (2 - 5)	4.1 ± 0.6 (3 - 5)
psychological load	1.2 ± 0.4 (1 - 2)	2.8 ± 1.1 (1 - 4)	2.2 ± 1.0 (1 - 4)	3.3 ± 1.2 (1 - 5)	3.0 ± 1.4 (1 - 5)	3.1 ± 1.1 (1 - 4)

Result shows mean ± SD (the minimum - the maximum).

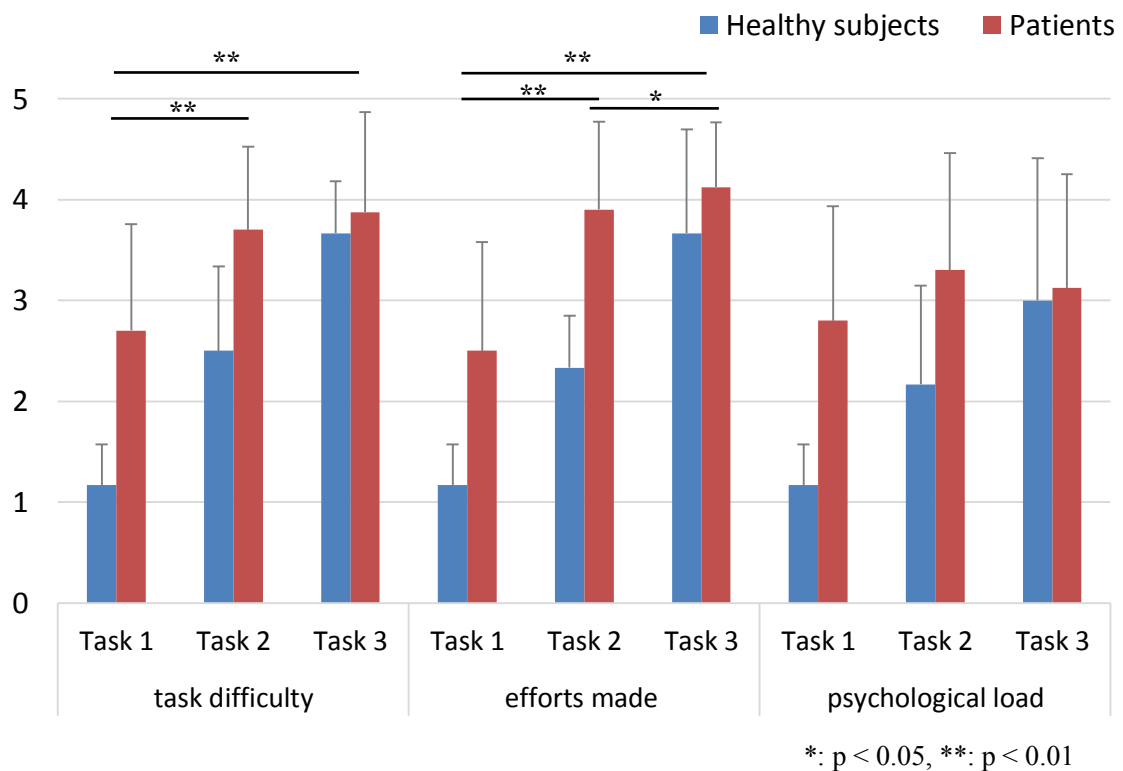


Figure 5-14 Comparison of subjective assessments between healthy subjects and the patients.

5.3.3 Discussion

The objective of this study was to investigate differences in task performance, brain activation, and subjective assessments in relation to different task difficulty levels in convalescent brain-damaged patients and healthy young subjects.

Regarding the VST-R performance, one/two patients could not accomplish Task 2/Task 3, respectively. Some patients made mistakes by buying less or more shopping items than the directions instructed beforehand. We considered these patients should start the exercise from this difficulty level. One 81-year-old patient (ID 4) needed more time to accustom herself to the virtual mall and its operation. A comparison between the two groups revealed that the mean time required to perform the test was significantly longer for the patients than for the healthy subjects. These results were consistent with our previous findings for a comparison between patient and age-matched control groups on Study 2 (Okahashi et al., 2013). We considered that these variables, including the number of purchases on VST-R, play important roles in cognitive assessment in brain-damaged patients. On the other hand, some of the times when the list was used were regarded as natural behavior; therefore, it may be possible to use VST-R in memory rehabilitation with useful compensation strategies.

Next, regarding a comparison of the VST-R performance based on three, the values and their SD of both Corrected Total time and Corrected Time in the shops were larger in the patients than in healthy subjects. The results indicate that it takes more time completing a task for the patients than for healthy subjects regardless of the task difficulty level. It might have relation to deficit of selective attention and executive functions in the patients. The values of SD were large in the patients, and we consider

they would be larger in an actual population in consideration of the fact some participants dropped out after Tasks 1 or 2 in this study. It is important that test performance is ranked in some ranks on basis of these evaluation items for the patient by using more data in a future study.

Regarding brain activation, no significant difference was observed in $\Delta[\text{oxyHb}]$ in any task for the memorizing phase between the two groups; however, $\Delta[\text{oxyHb}]$ in the shopping and/or moving phases in Task 2 in the left and medial PFC was significantly higher in the patients than in the healthy subjects. The pattern of brain activation was particularly different between the two groups in Task 2. $\Delta[\text{oxyHb}]$ was slightly higher in the patients and decreased in the healthy subjects while performing VST-R (e.g. shopping and moving phases) than in the memorizing phase of shopping items at the beginning of the test. One of the reasons for this was young healthy subjects were accustomed to using PCs in their school life so it was easy for them to operate VST-R, whereas brain-damaged patients with cognitive dysfunctions in the convalescence rehabilitation ward (mean age 61.2 years) were not familiar with PCs. These results also suggest that the difficulty levels of Tasks 2 and 3 may have been sufficient to cause brain activation in the brain-damaged patients in this study. Since our sample size was small, we need to amass more data and investigate brain activation in relation to the task level in more detail in our next study. In addition, we need to examine whole hemodynamic changes about not only $[\text{oxyHb}]$, but also $[\text{deoxyHb}]$ and $[\text{totalHb}]$ for each subject based on previous fNIRS findings (Toichi et al., 2004).

Regarding subjective assessments, patients considered all tasks to be more difficult and required a stronger effort than the healthy subjects. The patients had a

subjectively heavier psychological load in Tasks 1 and 2 (2-item and 4-item shopping task) than healthy subjects. In addition, although the healthy subjects could recognize the differences between the three task levels, the patients could not. Therefore, we consider that therapists should take subjective mental load on patients into consideration because it may be important to evaluate changes in the exercise phase for more effective rehabilitation.

The results of the present study suggest that, although large differences were not observed in the task performances or PFC responses of healthy subjects at different task levels, they could recognize the differences between the three task levels subjectively, whereas the patients could not, and this indicated that the patients could not subjectively distinguish differences in the three tasks. VST-R is applicable to convalescent patients with cognitive dysfunctions in cognitive rehabilitation, and performing a 4-item/6-item shopping task activated their PFC especially in the shopping and moving phases. A 2-item shopping task may be applied clinically by taking into consideration their behavioral errors and mental load.

In conclusion, this study applied virtual shopping with three different difficulty levels to investigate differences in task performance, brain activation, and subjective assessments in convalescent brain-damaged patients and healthy young subjects. The results obtained suggested that the two groups had not only different task performances, but also different brain activation patterns as well as different subjective assessments with an increase in the task difficulties, as described above in detail. These results are important for establishing more effective task levels for patients in the rehabilitation phase, which may not only depend on their subjective assessments, but also on more

scientific evidence, such as brain activation and/or task performance.

5.4 Summary

In this chapter, we introduced VST-R with three different task levels in order to assess daily cognitive function and described Study 5: a clinical study using this system. The objective of the present study was to investigate differences in task performance, brain activation, and subjective assessments in relation to the difficulty levels of the tasks. Subjects were asked to buy two specific items in Task 1, four items in Task 2, and six items in Task 3 at a virtual mall. The tasks were conducted and questionnaires answered by six healthy young subjects and ten convalescent brain-damaged patients. Hemodynamic changes in PFC during activation due to the tasks were examined using fNIRS.

The results obtained showed that the mean total time was significantly longer for the patients than for the healthy subjects. PFC responses to the shopping and moving phase in Task 2 were greater in the patients than for the healthy subjects. The patients subjectively evaluated Tasks 1 and 2 as more difficult than healthy subjects and also considered it to have caused a higher psychological load. Although task performance as well as PFC responses were not significantly changed in the healthy subjects, they could subjectively evaluate differences between the three task levels, whereas the patients could not, which indicated that patients could not subjectively distinguish between differences in the difficulty of the tasks performed. Taken together, the results of the present study suggest that the difficulty of the 4-item shopping task may have been sufficient to cause brain activation in the brain-damaged patients.

Chapter 6

Conclusions

6.1 Summary of this dissertation

Higher brain dysfunctions related to attention, memory, and executive functions due to aging and brain damage lead to many difficulties in everyday life. The patients have difficulties not only in the basic activities, but also many other essential activities of daily living such as shopping, housework etc. It has been reported that the results of conventional assessment methods with a paper and pencil sometimes disagree with the actual cognitive level of individuals. For such kind of assessment, it is important to observe patients in an environment that is similar to their everyday life in order to understand the problems caused by their functional impairment. Recently, VR techniques have been focused in the application of assessment of cognitive impairment. Previous studies have demonstrated that assessment of higher brain functions using VR technology has a big potential in clinical rehabilitation. However, when we applied these systems for brain-damaged patients in Japan, there were various problems as follows: some human interface like a joystick would be difficult to operate for the patients; the virtual environment and language used in these systems were foreign to Japanese patients; it seemed that some dual tasks were too complex for them.

In this dissertation, we have developed Virtual Shopping Test (VST) by using VR technology to assess realistic higher brain functions of the patients in laboratory

environment so as to overcome the limitations of conventional types of assessment in previous studies. Then, we performed four evaluation experiments on the clinical usefulness of VST in chronic brain-damaged patients and elderly adults (in Studies 1-4). After that, VST was modified to VST-R that had three different task difficulty levels. fNIRS: a non-invasive measuring technique of blood oxygenation changes was used to evaluate prefrontal cortex activity. The system could also output event signals that were synchronized with the user's inputs. We performed VST-R evaluation experiment in convalescent brain-damaged patients (in Study 5).

In VST, a Japanese virtual mall consisted of twenty shops was constructed in virtual space. Subjects executed four-items shopping tasks by simple touch screen operations. They were asked to finish buying specific items as quickly and efficiently as possible, while minimizing the use of hints as much as possible. The number of times they touched each hint/movement button, the number of items bought correctly, and the time required were adopted as evaluation items. The VST system had the following advantages: i) the virtual environmental condition similar to the real Japanese, ii) the interaction between a user and the virtual shopping mall environment, iii) human interface device operated intuitively, iv) automatic recording function of various behavioral data, and v) the dealing with predicable human errors.

First, we executed Studies 1 and 2 focused on brain-damaged patients. The objectives were to reveal 1) the significance of VST by comparing VST performance with conventional neuropsychological tests and questionnaires, 2) the difference of VST performance between age-matched control subjects and brain-damaged patients, respectively. VST and neuropsychological tests/questionnaires about attention, memory

and executive functions were conducted with ten patients, while VST and MMSE were conducted with ten age-matched control subjects. The relationship between conventional tests and VST was analyzed; the VST performance between the two groups was compared. As a result, some VST variables correlated with the scores of other cognitive assessments related to attention and everyday memory. The results demonstrated that VST could be used to evaluate the comprehensive ability of attention and memory in patients with brain damage through one test session. In addition, the number of times referring to the shopping list, the number of movements, and the total time to complete the task were all significantly larger/longer for the patients than for control subjects. Therefore, we concluded that VST can be used as an assessment tool in cognitive rehabilitation for brain-damaged patients.

Secondly, we executed Studies 3 and 4 focused on elderly people. The objectives were to reveal 1) the age differences of VST performance between healthy young and elderly subjects, 2) the parallel form reliability between VST-1 and VST-2, respectively. VST-1 was conducted with ten healthy young subjects, while VST-1 and VST-2 as parallel forms were conducted with ten elderly subjects. The behavioral data were compared between the two groups/the two forms. As a result, the total time spent on VST was significantly longer for elderly subjects than for young subjects. Additionally, there was no statistic difference between two parallel forms on the number of correct purchases and each temporal variable on VST. In conclusion, the total time spent on VST performance represented the basic difference of cognitive function between the age groups. The parallel forms of VST appeared to be equivalent measures of higher brain functions. Therefore, clinical examiners should interpret VST

performance scores considering ageing effects. The parallel forms could be used to one patient without learning effect in a retest session.

Finally, we modified this system to the version of VST (VST-R) with three different task levels and executed a clinical Study 5. The objective of this study was to investigate differences in task performance, brain activation, and subjective assessments in relation to the task difficulty levels. Subjects were asked to buy two specific items in Task 1, four items in Task 2, and six items in Task 3 at a virtual mall. These tasks and questionnaires were conducted by six healthy young subjects and ten convalescent brain-damaged patients. Hemodynamic changes in PFC during activation due to the tasks were examined using fNIRS. As a result, the mean total time spent on VST-R was significantly longer for the patients than for the healthy subjects in all tasks. PFC activation during the shopping and moving phase in Task 2 were greater in the patients than for the healthy subjects. The patients subjectively evaluated Tasks 1 and 2 as more difficult than healthy subjects and also considered it to have caused a higher psychological load. Although task performance as well as PFC responses were not significantly changed in the healthy subjects, they could subjectively evaluate differences between the tasks, whereas the patients could not, which indicated that patients could not subjectively distinguish between differences in the difficulty of the tasks performed. Taken together, the results of this study suggest that the difficulty of the 4-item shopping task may have been sufficient to cause brain activation in the patients with brain damage.

On the basis of these findings, VST appears to have basic clinical usefulness to assess higher brain functions in brain-damaged people. Their brain activation and

psychological variables are influenced by task difficulty level and should be taken into consideration with the VST performance data in cognitive rehabilitation.

6.2 Future works

In this section, we show our future directions on cognitive rehabilitation using VR technology and provide general discussions based on our research findings. Cognitive rehabilitation process consists of an assessment phase in advance and a training phase, which come in turn basically. We consider that our proposed novel VST system, which adopted a daily shopping scene in the virtual shopping mall, would be available in both phases for patients with higher brain dysfunctions caused by many kinds of diseases.

1) Establishment of VST as an assessment tool of realistic higher brain functions

We clarified the basic clinical usefulness of VST from Studies 1, 2, 3, and 4. In the next stage, to establish VST as an assessment tool of realistic higher brain functions, we need to verify the validity and reliability of VST for wide clinical application. We plan to collect more data by using this system in people with many kinds of diseases in wide generation

To be a steady method to assess higher brain functions clinically, VST would need the cutoff scores of all evaluation items for each age range to distinguish brain-damaged patients with some kinds of problem in daily life from healthy people. In addition, if we devise the effective algorithm for the total index based on raw scores of VST evaluation items (e.g. the frequency of hint/movement button use, the number of correct purchases, and the time required), this system would be used more conveniently.

2) Exploring the potential of VST as a training tool for realistic higher brain functions

When VST was modified in Study 5, we took the following three points into consideration: a tester could decide how many and what item to ask a subject to go shopping in every session; eighteen out of twenty shops in a virtual mall had different six options in each shop; there were three types of shopping mall with random shop arrangement. We consider it is possible for this system to be introduced in clinical training sessions.

Although ubiquitous networks have progressed in modern Japanese society, it is not sufficient, especially in hospital rooms and home. In such a situation, VST would be available to provide a virtual scene of shopping in a local shopping mall only by using a computer like a tablet PC. We believe our system is useful for both inpatients and patients living home to improve or maintain their higher brain functions in voluntary training sessions.

3) Clinical application of VST in extensive fields

Some previous studies has reported that rehabilitation training methods using VR technology has potential to improve IADL ability in patients with higher brain dysfunctions (Jacoby et al., 2013; Man et al., 2012; Rand et al., 2009). VR technology provides people realistic, safe, cost-effective, and interesting environment for rehabilitation of daily activities.

One of our future directions is to reveal the effective way to improve the

realistic ADL and IADL abilities by using VST in patients with various kinds of daily cognitive problems. Based on the results of Study 5, we consider it is important that clinical rehabilitation therapists examine the multiple aspects (e.g. subjects' motivation, their preference, and brain activation in relation to the task difficulty level) when they plan the training programs using VST, which should be also adjusted in accordance with individuals' progress levels.

In an unprecedented aged society, the population of elderly people with various physical and mental diseases is increasing. Not only brain-damaged patients caused by stroke and TBI in convalescent and chronic stages, but also people with dementia and MCI in every disease stage would be our intervention target of providing VST as a screening test of comprehensive cognitive ability in routine daily life and a training tool for prevention of their disease progression.

Appendix A

Screen images of shop exterior and the inside

There are screen images about ten shops. A set of a shop exterior and its inside is presented on one sheet. The following shops are presented.

- Two shops in a practice task: a bakery and a toy shop
- Four shops in VST-1: a stationary shop, a chinaware shop, a pharmacy, and a fruit and vegetable shop
- Four shops in VST-2: a shoe store, a Buddhist altar fittings store, a sporting goods shop, and a hardware store

The figure below shows the goods arrangement in each shop in VST-1 and VST-2. Each option's type is given in parenthesis.

stationary shop			chinaware shop		
fountain pen (Use)	tape (Color)	Paints (Phone)	ashtray (Shape)	rice bowl (Correct item)	bud vase (Color)
pencil (Correct item)	seal (Shape)	eraser (Set)	chopsticks (Set)	teacup (Use)	tea strainer (Phone)
pharmacy			fruit and vegetable shop		
cold tablets (Phone)	adhesive plaster (Use)	bandage (Color)	tomatoes (Set)	green Peppers (Color)	kiwi fruits (Phone)
disinfectant (Set)	mask (Shape)	gauze (Correct item)	bananas (Shape)	cucumbers (Correct item)	eggplants (Use)

(a) VST-1

shoe store			Buddhist altar fittings store		
beach sandals (Use)	sneakers (Color)	insoles (Phone)	matches (Shape)	incense sticks (Correct item)	rosary (Color)
boots (Correct item)	rubber-soled socks (Shape)	umbrella (Set)	incense holder (Set)	candle (Use)	folding fan (Phone)
sporting goods shop			hardware store		
cap (Phone)	shuttlecock (Use)	uniform (Color)	nail (Set)	saw (Color)	plane (Phone)
glove (Set)	swim ring (Shape)	ball (Correct item)	mallet (Shape)	hammer (Correct item)	screwdriver (Use)

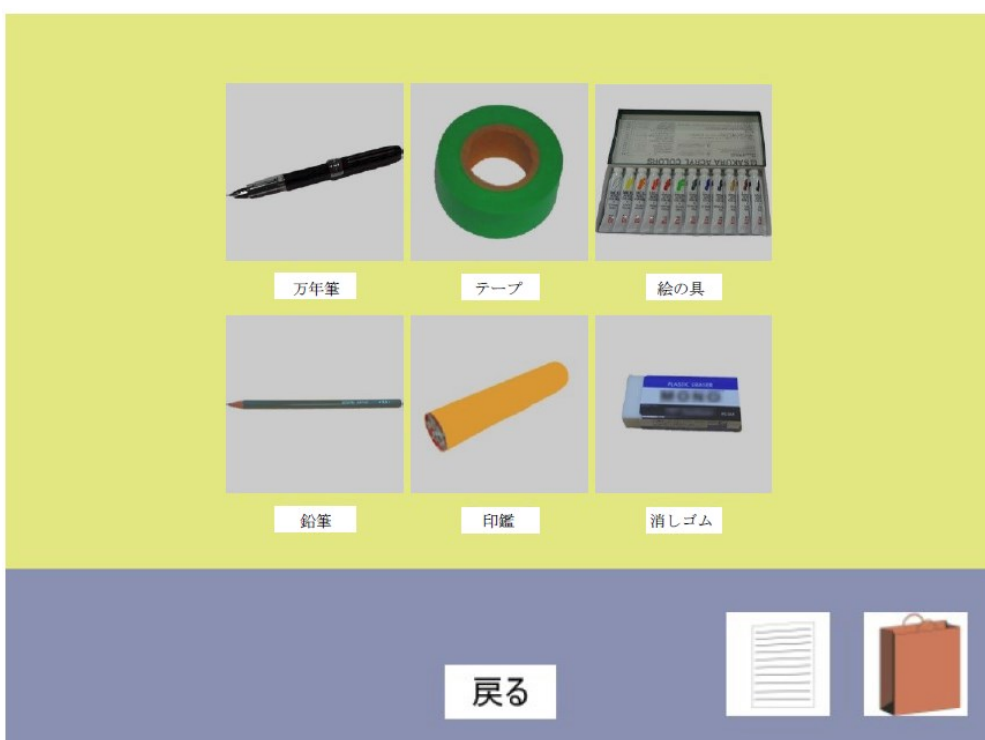
(b) VST-2



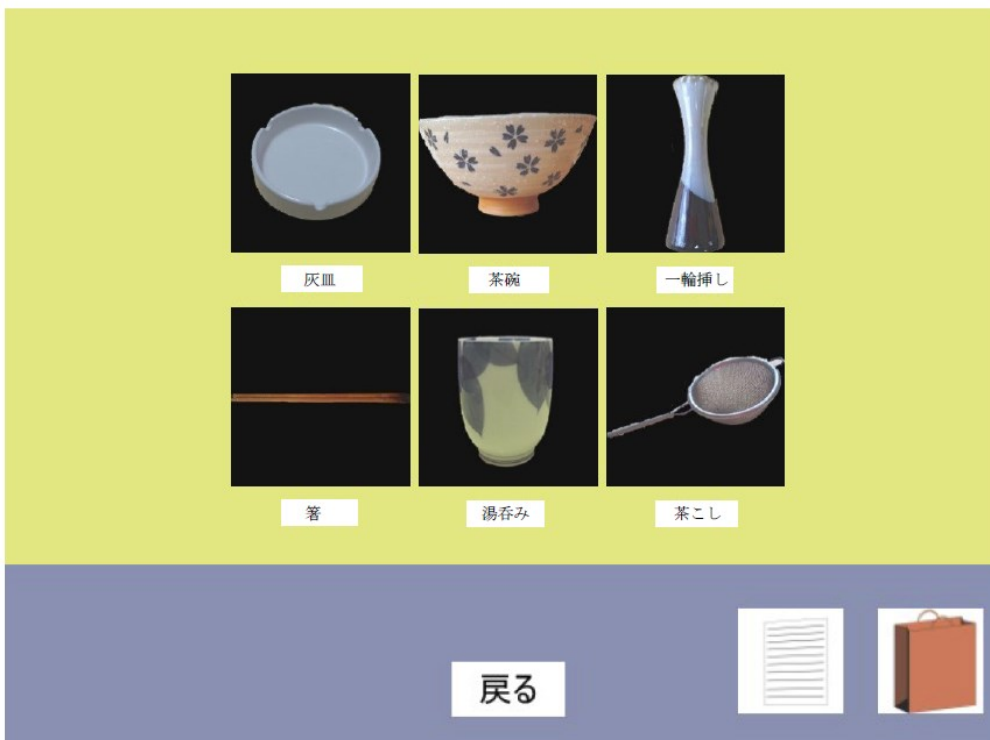
bakery



toy shop



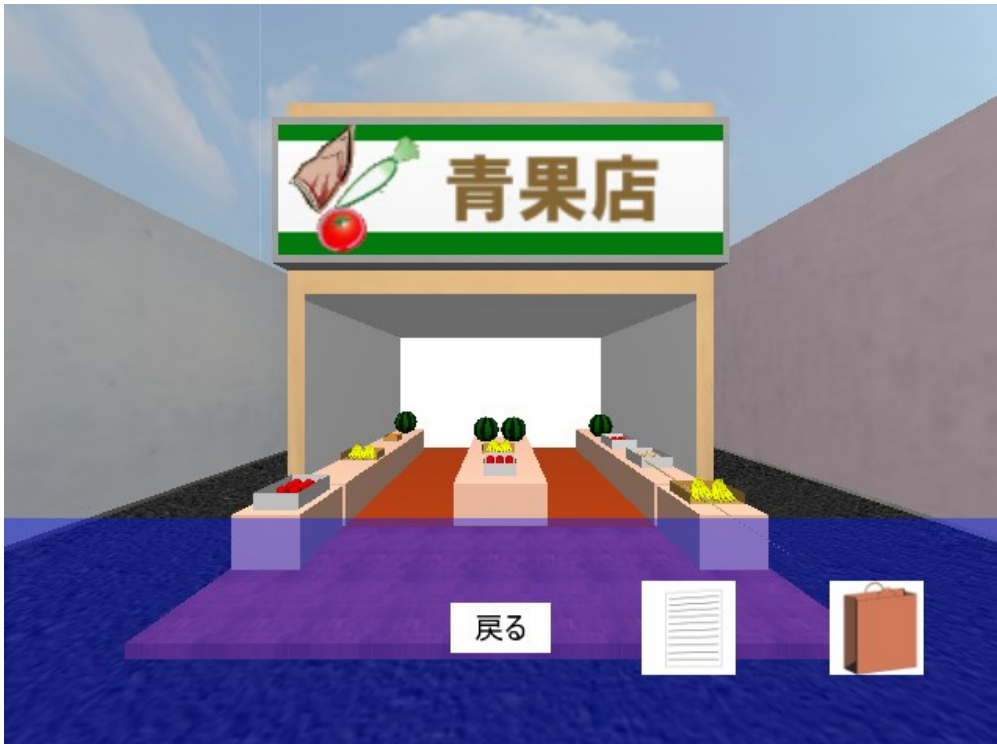
stationery shop



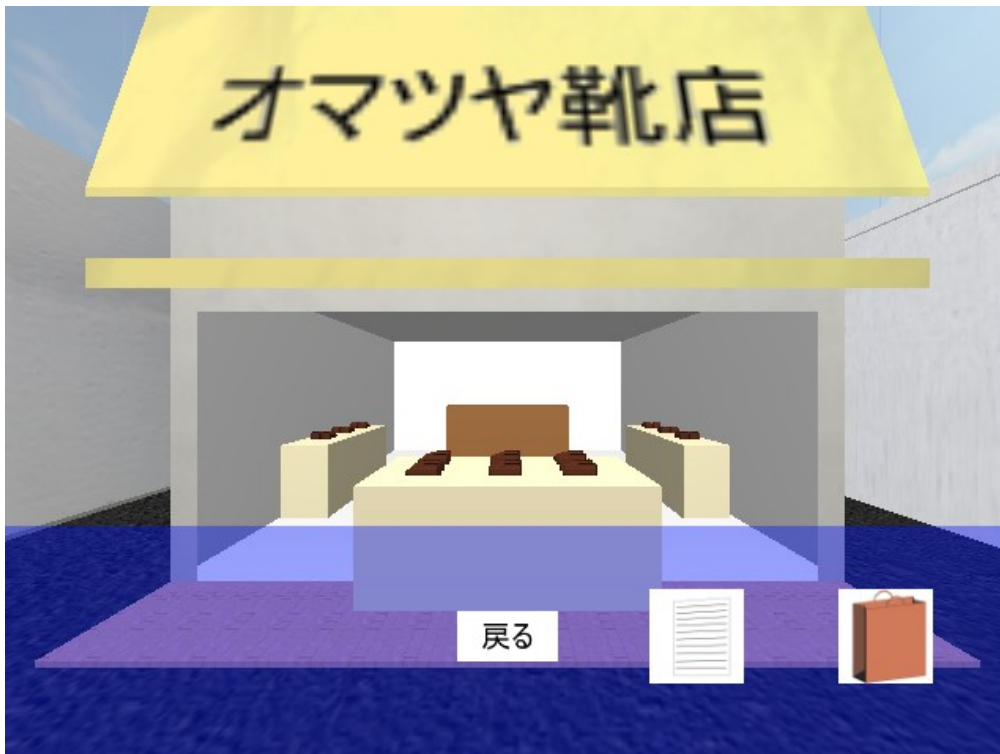
chinaware shop



pharmacy



fruit and vegetable shop



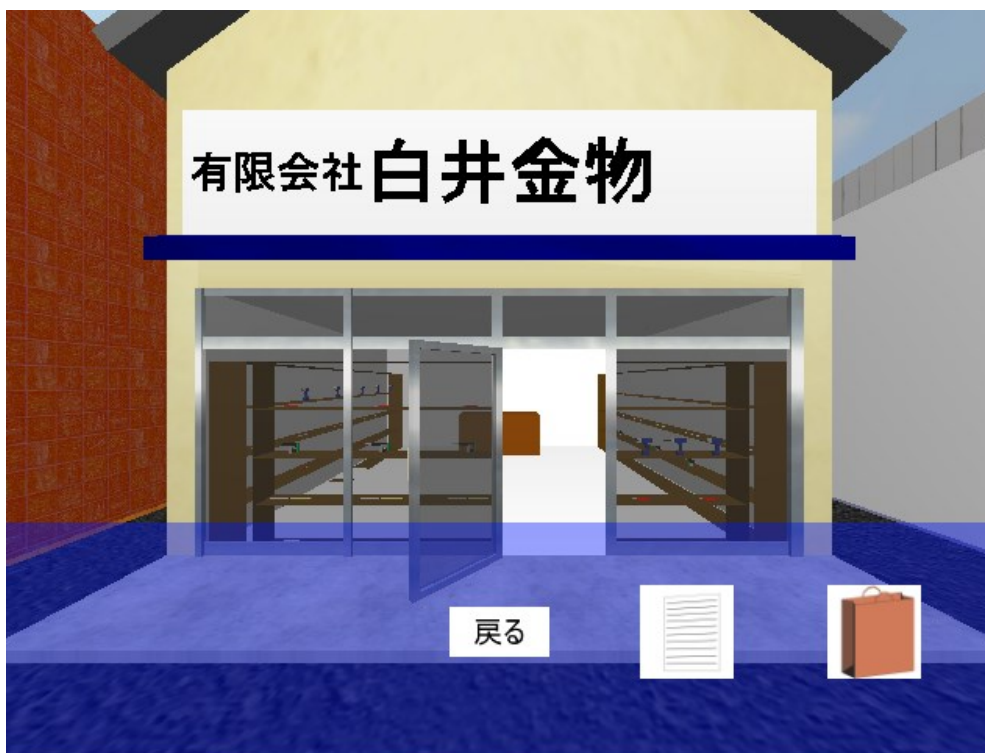
shoe store



Buddhist altar fittings store



sporting goods shop



hardware store

Appendix B

An instruction manual of VST

The tester sits on the left side of the subject and demonstrates how to perform VST as written below.

1. Tutorial session

1) Outline

Apparatus: map for the practice task

The tester explains the outline of the VST, showing the subject the map and the virtual mall on the PC screen.

Please perform a shopping task in the virtual mall on the computer screen. (The tester hands the map to the subject.)

This is a map of the virtual mall. The shop arrangement on the map is the same as the virtual mall on the screen.

2) Four basic buttons

The tester explains the operation of the buttons on the screen, comprising two arrows, a list, and a bag.

I will show you how to operate the screen. When you touch an arrow, you can move forward or turn.

[Two arrows]: By touching the upper arrow, you can move forward. By touching the lower arrow, you can turn on the same point. You can move around in the shopping mall freely by using these two buttons.

[List]: This is the shopping list. By touching it, you can check the contents of the list. After checking, you can return to the shopping task by touching the 'Return' button at the bottom of the screen.

[Bag]: This is your bag. Any items you buy will be kept inside it. You can check the contents of the bag by touching it at any time. After checking, you can return to the shopping task by touching anywhere on the screen. The list and the bag will be in the same place on the screen throughout the shopping task. You can use them whenever you need to check them.

3) The map and virtual mall

Apparatus: map for the practice task

The tester explains the map. The subject understands the map is the same as the shopping mall on the computer screen.

[Map] Please look at this map. There are twenty shops, an arcade in the center of the mall, and a station at the end of the mall. A coffee shop and a post office are located at the mall entrance next to the street. (The tester shows the subject both the map and the screen and explains this by pointing to the map.)

[Screen] Next, look at the screen in front of you. You can see that shop arrangement is the same as the map. You are currently standing at the entrance of the shopping mall. There is a coffee shop to your right, and a post office to your left.

Let's look for the shoe store. (The tester operates the screen and goes to the shoe store.)

What happens when I touch the lower button? (The tester operates the computer.)

The lower button allows you to turn. First you can see the coffee shop on your right, but by touching the lower button you can see that it is now on your left. (The tester goes back the screen at the start.)

4) Go and Turn buttons

Let's move around the mall. Firstly, try to go for the station. (The tester confirms that the subject has reached the location in front of the electric appliance shop and the stationery shop.)

Could you turn around and go to the station? (The tester confirms that the subject has reached the location in front of the bookstore and the flower shop.)

Could you turn around and go back to the start? (The tester confirms that the subject has returned to the location in front of the watch store and the chinaware shop.)

Could you turn around and go back to the station? (The tester confirms that the subject can reach the goal.)

Do you have any problems moving around in the mall?

5) How to buy an item

The tester asks the subject to choose one item and buy it in the bakery. The tester also goes into an incorrect shop and shows that the shop is closed.

I'm going to demonstrate how to buy something. I will buy a loaf of bread in the bakery. Let's go to the bakery. Once the bakery is just in front of you, please touch the picture of the shop. The view will then transfer to the front of the shop. Touching the screen once again, you can go into the bakery. There are six items in each shop, and you can choose one by touching the picture of it. If you think your choice is correct, you should touch the 'Buy' button. You can buy a shopping item during this process. (The tester shows the subject the process for entering a shop by touching the shop again.)

You can leave a shop by touching the 'return' button at any time. If you enter an incorrect shop, the word 'closed' is displayed on the screen and there will be no items available.

6) Goal

The tester shows the subject how to finish the task.

Once you finish all of the shopping tasks, go to the station. If you go through a wicket over the yellow line, a message 'Finish? / Yes or No' will appear. If you have finished all of the shopping, please touch 'Yes'. If you want to return to the mall and continue shopping, touch 'No'. This completes the tutorial in the operation of the VST. Do you have any questions?

*If necessary, the tester can provide additional explanation to the subject in order that they understand the VST operation adequately.

2. Rehearsal session

1) Comparison between the map and the virtual mall

Apparatus: map for the practice task

The tester shows the subject the map and confirms that it is the same as the shopping mall on the screen.

Let's do a practice task. (The tester shows the subject the screen and the map.) I will show you the map for the task. The arrangement of shops in the mall is the same as that on the map. Let's go shopping.

*If the subject cannot recall all of the operations from the tutorial session, the tester shows the subject how to buy items again.

2) Immediate recall

Apparatus: stopwatch, word list, word list for the recognition test

The tester shows the shopping list and reads it aloud in full. The tester then hides the list and asks the subject to recall the items orally. If the subject cannot remember all of the items on the list, the tester shows the subject the list again.

For the first session, please remember the following items to buy: a loaf of bread and a stuffed toy. (The tester shows the list for 10 seconds.)
What items should you buy? (The tester records the answer.)

*If the subject cannot recall all items, the tester shows the list for another 10 seconds, and asks the same question again.

3) Planning

Apparatus: map for the practice task, blank map for filling in, pencil, eraser

The subject plans the shopping trip and fills in the most efficient route on the map. The filled in map is submitted.

Let's plan the route through the mall to buy the items as quickly and efficiently as you can. (The subject can see the list on the screen during the planning step. After filling in the map, it is submitted.)
You should try to go shopping following your plan.

4) Cautions

The tester reminds the subject to pay careful attention during the shopping task.

Please buy all of the items required without entering other shops. You can check the list and your bag at any time, if necessary, but you should try remember their contents as much as possible. Please perform the task as quickly and precisely as you can. Let's go.

VST performance

5) Recall and recognition test

Apparatus: word list for the recognition test

If the subject could not buy the two items, the tester asks the subject to recall the items after finishing the task. If the subject is unable to answer correctly, the tester shows the subject the word list for the recognition test and asks the subject to choose the items from it.

Could you recall all the items on shopping list? (If the subject cannot answer correctly, the tester asks another question with a word list for the recognition test.)

Can you choose the items on the shopping list from the items on this list? (The tester records the answer.)

6) A question about metacognition

Please choose one option from these five about whether you could buy the items following your plan. 1) You did the shopping exactly as you planned. 2) You did shopping mostly as you planned. 3) You did shopping roughly as you planned. 4) You did not do the shopping mostly as you planned. 5) You did not do the shopping as you planned at all. (The tester records the answer.)

3. Test session

After the subject understands the operation procedure through performance of a practice task, VST-1/VST-2 is conducted.

Test stop reference

(a) If the subject does not carry out any operation for 120 seconds, the tester asks the subject whether there is any problem and gives the subject some advice if necessary. If the subject cannot continue the task, the test is stopped.

➤ Situation examples in which the tester can give hints

- The subject tries to do something, but cannot touch the screen successfully.
- The subject does not know where he/she is in the mall after using the rotation button.
- The subject forgets what to buy.
- The subject moves around to try to find a target shop, but cannot do it.

(b) If the subject cannot pass both of the recall tests and recognition test before performing the VST.

1) Comparison between the map and the virtual mall

Apparatus: map for VST-1/VST-2

The tester shows the subject the map and confirms that it is the same as the shopping mall on the screen.

Let's do a shopping task. (The tester shows the subject the screen and the map.)

Here is a map of the task. The shop arrangement in the mall is the same as in this map.

The shop arrangement is different from the practice task. Here, please buy four specific items.

2) Immediate recall

Apparatus: stopwatch, word list, word list for the recognition test

The tester shows the shopping list and reads it aloud in full. The tester then hides the list and asks the subject to recall the items orally. If the subject cannot remember all of the items on the list, the tester shows the subject the list again.

I'm going to show you what to buy, please remember all of the items.
[VST-1]: a pencil, a rice bowl, gauze, and a cucumber.
(or [VST-2]: a pair of boots, a stick of incense, a ball, and a hammer.)
(The tester shows the list for 10 seconds then asks the following question.)
What items should you buy? (The tester records the answer.)

*If the subject cannot answer all items, the tester shows the list for another 10 seconds, then repeats the question. The tester can repeat this process three times at maximum.

*If the subject still cannot recall all items correctly, the test should be usually be stopped, but the tester can decide to continue the test with the shopping list sheet available throughout depending on the subject.

3) Planning

Apparatus: map for VST-1 or VST-2, blank map for filling in, pencil, eraser

The subject plans the shopping trip and fills in the most efficient route on the map. The filled in map is submitted.

Let's plan the route through the mall to buy the items as quickly and efficiently as you can. (The subject can see the list on the screen during the planning step. After filling in the map, it is submitted.)
You should try to go shopping following your plan.

4) Cautions

The tester reminds the subject to pay careful attention during the shopping task.

Please buy all of the items required without entering other shops. You can check the list and your bag at any time, if necessary, but you should try to remember their contents as much as possible. Please perform the task as quickly and precisely as you can. Let's go.

VST performance

5) Recall and recognition test

Apparatus: word list for the recognition test

If the subject could not buy the items, the tester asks the subject to recall the items after

finishing the task. If the subject is unable to answer correctly, the tester shows the subject the word list for the recognition test and asks the subject to choose the items from it.

Could you recall all the items on shopping list? (If the subject cannot answer correctly, the tester asks another question with a word list for the recognition test.)

Can you choose the items on the shopping list from the words on this list? (The tester records the answer.)

6) A question about metacognition

Please choose one option from these five about whether you could buy the items following your plan. 1) You did the shopping exactly as you planned. 2) You did shopping mostly as you planned. 3) You did shopping roughly as you planned. 4) You did not do the shopping mostly as you planned. 5) You did not do the shopping as you plan. (The tester records the answer.)

Acknowledgements

Although only my name appears on the title page of this dissertation, a great many people have contributed to it. I owe my gratitude to all of these people who have made this dissertation possible.

First, I would like to thank my supervisor, Professor Zhiwei Luo, for his great guidance in this VR project over the past 6 years and for always having his door open for questions and discussion. His enormous knowledge of engineering and logical way of thinking have been extremely meaningful for me. His understanding, encouragement and personal guidance have provided a solid basis for the dissertation. I will treasure the experience of this project for my whole life.

I wish to express my sincere appreciation to Guest Professor Keiko Seki of Kobe University for her enthusiastic coaching. She gave me new insights to examine this problem based on neuropsychology, and the opportunity to work with her group. I warmly thank Professor Rumi Tanemura of Kobe University for her valuable clinical advice on my research. I would like to extend my gratitude to Professor Akinori Nagano of Ritsumeikan University. His detailed and constructive comments have been very helpful throughout my work. I thank Associate Professor Yuichi Togashi of Hiroshima University for his useful suggestions.

My sincere thanks are given to the official referees, Professor Kuniaki Uehara, Professor Yasuo Arika, Graduate School of System Informatics, Kobe University, for their detailed review, constructive criticism and excellent advice during the presentation of this dissertation.

My warm thanks go to Professor Toshiko Futaki, Associate Professor Maki Koyama, Department of Human Health Sciences, Kyoto University, who have

supported me and given me instructive suggestions. I also would like to thank Professor Motomi Toichi and Professor Tomohiro Kuroda of Kyoto University who gave me valuable comments in every respect.

During this work, I have collaborated with many colleagues and had a lot of productive discussions with them. Special thanks go to Yuki Yamanaka, Tatsuo Oshiumi, Hokuto Mizumoto in the CS11 Computational Robotics Laboratory; Hiromi Sakai, PhD OTR, Maki Kojima, SLP, Tomoko Tanaka, OTR, Hiromi Endo, OTR, Masumi Sawa, SLP from the Seki Laboratory, for their time and dedication to the VST development, and all who have helped me with my work in these research groups.

I am grateful to Masato Yokoyama, MD, Katsuhiko Ueno, RPT, Akiko Komae, SLP, Yohei Mori, OTR, Kyosuke Nishizawa, OTR, Fumiko Tsuzuki, SLP, Department of Rehabilitation Medicine, Nishi Memorial Port Island Rehabilitation Hospital for clinical data collection using the VST-R.

Above all, my special gratitude is due to my family for their untiring love and support. Without their encouragement and understanding it would have been impossible for me to complete this work.

Publications

This dissertation is based on the research that was previously reported in the following publications.

Journals

Okahashi, S., Seki, K., Nagano, A., Tanemura, R., Kojima, M., & Luo, Z. (2012).

Development virtual shopping test for the evaluation of cognitive function in brain-damaged patients. [in Japanese] *Higher Brain Dysfunction Research*, 32(2), 302-311. doi: 10.2496/hbfr.32.302

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Okahashi, S., Mizumoto, H., Komae, A., Ueno, K., Yokoyama, M., Nagano, A., Seki, K.,

Futaki, T., & Luo, Z. (2014). An fNIRS-based study on prefrontal cortex activity during a virtual shopping test with different task difficulties in brain-damaged patients. *Journal of Behavioral and Brain Science*, 4(6), 247-255. doi: 10.4236/jbbs.2014.46026

International Conference

Okahashi, S., Seki, K., Nagano, A., Luo, Z., Kojima, M., & Futaki, T. (2013, February).

Development of a virtual shopping test (VST) for assessment of cognitive function: parallel form reliability and effect of age. Poster session presented at

the 41st Annual Meeting of the International Neuropsychological Society, Hawaii.

Okahashi, S., Mizumoto, H., Komae, A., Ueno, K., Yokoyama, M., Nagano, A., Seki, K., Futaki, T., & Luo, Z. (2014, September). *Assessment of convalescent brain-damaged patients using a virtual shopping test with different task difficulties*. Paper session presented at the 10th International Conference on Disability, Virtual Reality and Associated Technologies, Gothenburg, Sweden. (accepted)

Domestic Conference

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Doctor Thesis, Kobe University

“Assessment of Higher Brain Functions in Everyday Life Using Virtual Reality Technology”,
142 pages

Submitted on July, 11, 2014

The date of publication is printed in cover of repository version published in Kobe University
Repository Kernel.

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