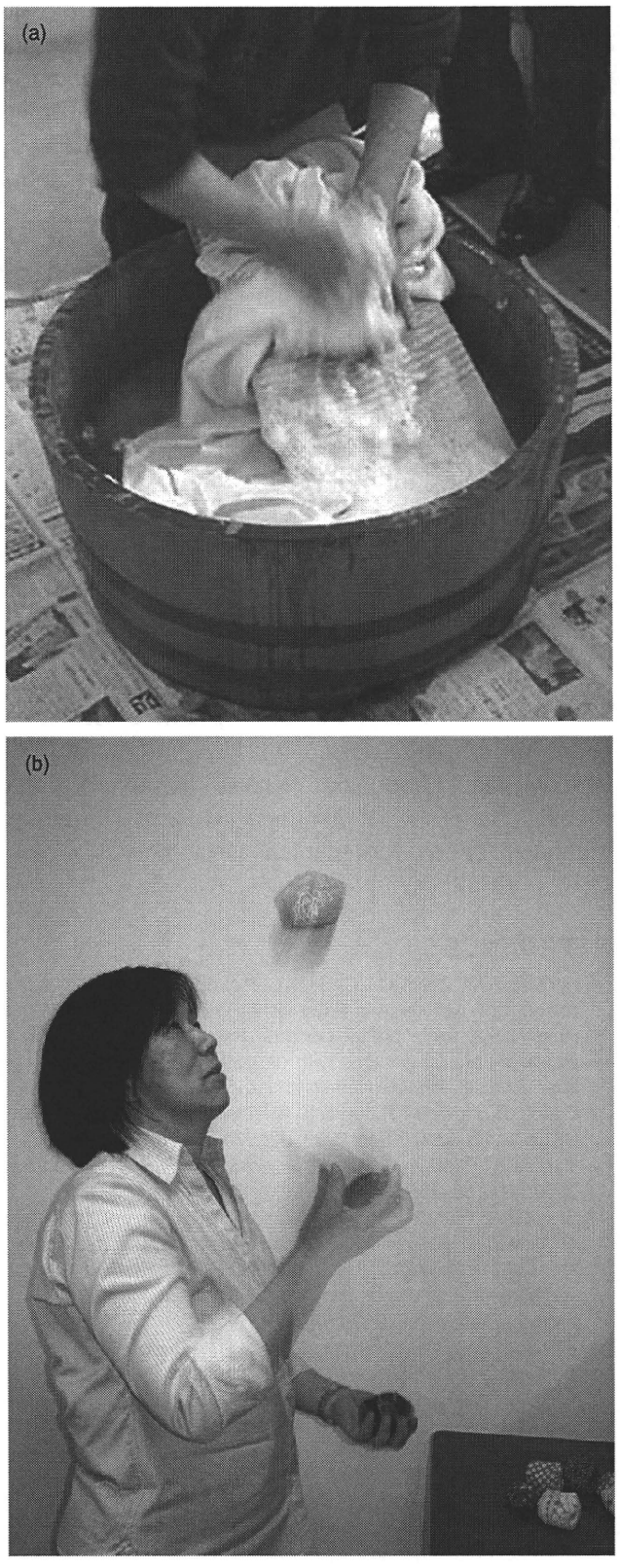

Figure 1 Activity reminiscence therapy. (a) Washing sheets using a washboard. Before electric washing machines became common, housewives did the laundry using washboards and basins. However, the younger generations rarely use washboards. Being appreciated and praised, Alzheimer's disease (AD) patients really enjoy their role of teaching and passing on their knowledge to younger generations. (b) Beanbag juggling: A beanbag is a palm-sized sack with beans inside, played with by tossing and catching (i.e. 'beanbag juggling'). Concerning the physical aspects of this activity, beanbag juggling requires rhythmic visuomotor coordination. Because the procedural memories remain robust, AD patients enjoy beanbag juggling with younger staff. Emotion-based communication over a game is enjoyable even for participants with impaired verbal skills.

ability. One of the key perspectives considering approaches to dementia is that the cognitive status does not necessarily correspond to the degree of pathological lesions in the brain. Regarding the brain's resistance to neuropathological damage, the 'cognitive reserve hypothesis' has been proposed, as described below.

The cognitive reserve refers to the observation that the degree of brain pathology or brain damage does not directly explain the clinical manifestation or cognitive performance of patients. Thus, people with a greater cognitive reserve are able to withstand a greater pathological AD burden without becoming demented by adopting alternative cognitive strategies and/or recruiting compensatory brain networks.[49–54] Increasing evidence indicates the presence of plastic changes in the synaptic efficacy in mature brains, which could be the physiological underpinning of this phenomenon.[55] A good example of 'the cognitive reserve' is the Nun study,[56] which reported non-linear associations between AD pathology in the postmortem brain and cognitive status in participants. Some participants in the study were cognitively intact, although their brains fulfilled the criteria for AD pathology. In a recent community-based study, minimal to moderate AD pathology was found in most brains of older people without dementia who were 80 years or older.[57] Enhanced cognitive ability was reported after activity reminiscence therapy intervention based on BAR principles.[58] The improvement was observed in the overall scores for immediate and delayed recall on the Wechsler Memory Scale-Revised after 1-h interventions once a week for 12 weeks.

Effects on BPSD

Behavioral and psychological symptoms of dementia often result from the relationship between patients

and their families. Patients with AD tend to overestimate their cognitive and functional abilities compared with what their families report.[59] Because of this discrepancy in evaluation of cognitive ability between patients and families, the patients may feel that they are not understood and accepted by their families, which may accelerate BPSD. In such cases, we recommend that families participate in the therapy session. By participating in the therapy, the families come to understand the underlying reasons for the patient's behavior.

Effects on daily living

Improvements in the activities of daily living (ADL) are also seen after BAR. Deficits in instrumental ADL are caused by a decline in cognitive functions such as executive function. Although disuse syndrome can account for a considerable part of the deficits in basic ADL, there remains room for beneficial effects following intervention with BAR. Patients may lose motivation due to numerous failures and reproach from their families', which suppresses brain function and accelerates disuse syndrome. Cooperation with families is indispensable to maintain enhanced motivation induced by BAR in daily living.

Family care and the QOL of both patients and their caregivers

The final effect of BAR is to make patients feel happy in their daily lives. Thus, it is crucial that patients' families understand the difficulties of living with dementia and learn how to help patients feel happy or smile by participating in BAR. At the same time, families also suffer with patients; thus, therapists should also praise and appreciate the efforts of the families. The BPSD service pack of the International Psychogeriatric Association (IPA) recommends that families and/or caregivers reward themselves for achieving certain goals to ameliorate BPSD.[60] It is desirable that therapists' attitudes towards families become their reward.

EVIDENCE FOR THE EFFICACY OF NON-PHARMACOLOGICAL TREATMENT

The efficacy of BAR should be verified on the basis of evidence. The protocol of any study investigating the efficacy of non-pharmacological treatment should reflect the characteristics of these interventions (i.e. intersubjectivity).

With regard to the outcomes, the broadening of outcome measures, including well-being, mood, and QOL, is desirable to consider the impact of non-pharmacological treatments on families and other caregivers.

For comparisons and meta-analyses among studies, it is desirable to use standardized outcome measures and protocols. In 2008, a European consensus on outcome measures for psychosocial intervention research in dementia care was published to enable meaningful comparisons between different studies and interventions.[61] We hope that the Japanese Psychogeriatric Society promotes the establishment of consensus guidelines for non-pharmacological interventions.

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TUBE FEEDING CAN BE DISCONTINUED BY TAKING DOPAMINE AGONISTS AND ANGIOTENSIN-CONVERTING ENZYME INHIBITORS IN THE ADVANCED STAGES OF DEMENTIA

To the Editor: Dysphagia, loss of the capacity for voluntary movement, speech, and continence, is one of the most serious symptoms in the advanced stage of dementia. Difficulty swallowing food is generally treated by changing the consistency of food from a hard mass to a soft paste and oral care. Recently, dopamine agonists and angiotensin-converting enzyme inhibitors (ACEIs) were reported to be effective at preventing aspiration pneumonia through increasing substance P levels, which enhances swallowing and cough reflexes.[1] We administered these drugs to some patients in the advanced stages of dementia and herein report three representative patients in whom oral food intake has been prolonged and tube feeding has been delayed for 7 months to 2 years.

CASE 1

A 67-year-old man with early-onset Alzheimer's disease (AD) in stage 7e according to functional assessment staging of AD (FAST) experienced swallowing difficulty 9 years after onset, and tube feeding was considered. He was medicated with the dopamine antagonist tiapride (25 mg) because of hyperactivity and violent behavior 2 years before; despite the disappearance of symptoms, medication had been continued. We first stopped tiapride and administered the dopamine agonist amantadine chloride (50 mg) and levodopa (100 mg). After 2 weeks, he smiled and spoke to caregivers, which surprised them. As a result of improved swallowing because of larger doses of amantadine chloride (150 mg) and levodopa (200 mg), he has maintained oral intake for 2 years; during this period, he experienced fever once, caused by aspiration pneumonia. His body weight increased from 51.4 kg (body mass index (BMI) = 20.6 kg/m^2) at the beginning of therapy to 56.3 kg (BMI = 22.5 kg/m^2) after 8 months and is now maintained at 54.5 kg (BMI = 21.8 kg/m^2) 2 years after the start of therapy.

CASE 2

An 81-year-old woman with AD in FAST stage 7e experienced swallowing difficulty 10 years after onset. She was mute, kept food in her mouth without swallowing for minutes, and started to sleep during eating. She was first medicated with the ACEI captopril (25 mg), but her body weight continued to decrease, from 46.8 kg (BMI = 22.3 kg/m^2) to 39.8 kg (BMI = 18.9 kg/m^2) over a period of 9 months. She received combined medication of captopril, amantadine chloride (150 mg), and levodopa (300 mg), and the herbal medicine Rikkunshito (5.0 g) for appetite improvement. She regained her appetite, became awake during meals, and showed increased facial expressions (smiling and laughing). Her weight has been at 39.9 kg (BMI = 19.0 kg/m^2) for 7 months, and she has experienced fever once in the last 7 months.

CASE 3

A 75-year-old bedridden woman with vascular dementia due to recurrent stroke (double hemiparesis: left > right), diabetes mellitus, and hip bone and lumbar fractures developed swallowing difficulty 16 years after her first stroke. Medication with amantadine chloride (100 mg) was started, together with a change of the antihypertensive drug from olmesartan to the ACEI imidapril (12.5 mg). Her body weight decreased from 37.1 kg (BMI = 16.9 kg/m^2) to 36.3 kg (BMI = 16.6 kg/m^2) for 20 months after the start of medication. She has experienced fever once in the last 20 months, and maintains oral intake.

We have prolonged oral food intake and delayed tube feeding by administering dopamine agonists in case 1; dopamine agonists, an ACEI, and Rikkunshito in case 2; and dopamine agonists and an ACEI in case 3. Substance P is critical for the initiation of swallowing and the cough reflex; pharmacological treatment using dopamine agonists could improve both reflexes by enhancing substance P production, whereas ACEIs lead to the inhibition of substance P breakdown,[1] although the first choice is a dopamine agonist, because as shown in cases 1 and 2, it improves the conscious state (arousal), mood (facial expression), and motivation (activity).

The traditional Japanese herbal medicine Rikkunshito was reported to enhance appetite and gastric emptying by increasing the secretion of the orexigenic hormone ghrelin.[2,3] It might be that ghrelin protects against pneumonia by suppressing gastric regurgitation.

In Japan, it is common to use long-term tube feeding introduced by percutaneous endoscopic gastrostomy (PEG), mainly with the purpose of extending life in the end stage of dementia, but PEG is not useful in preventing pneumonia because it causes the silent aspiration of contaminated saliva and regurgitated gastric secretion.[1] To delay tube feeding with PEG, dopamine agonists should be tried first for patients with dysphagia to prolong oral food intake and so help maintain their dignity. ACEIs and Rikkunshito may also be added.

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EFFECT OF MALNUTRITION ON EXECUTIVE FUNCTION IN OLDER EGYPTIANS IN GERIATRIC HOMES

To the Editor: Nutrition is an important determinant of health in elderly patients. The importance of nutritional status has been increasingly recognized in a variety of morbid conditions including cancer, heart disease, and dementia in persons aged 65 and older.[1]

Malnutrition is prevalent in elderly populations, even in the developed world.[2] The prevalence of malnutrition increases with age and is most common in institutionalized individuals.[3]

Undernutrition is associated with exacerbation of health conditions, frailty, and decline in physical and cognitive function.[4]

The aim of this study was to evaluate the effect of malnutrition on executive function in older Egyptian subjects in geriatric homes. The study was a case–control study. Participants were recruited from geriatric homes in Cairo, Egypt, and subdivided into two groups: Group 1: cases, 50 men and women aged 60 and older found to be malnourished (n = 28) or at risk of malnutrition (n = 22) according to the Mini Nutritional Assessment (MNA);[5] and Group 2: controls (matched for age and sex), 50 men and women aged 60 and older found to be well nourished according to MNA. Subjects with dementia (Mini-Mental State Examination score less than 26)[6] or depression (Geriatric Depression Scale score greater than 5)[7] were excluded from the study. Subjects with history of stroke, delirium, alcoholism, drug abuse, psychiatric disease, or thyroid disease were excluded, as were subjects with auditory or visual impairment or any organ failure.

Cognitive and executive functions were assessed using three neuropsychological tests: letter verbal fluency test,[8] animal verbal fluency test,[9] and Executive Interview 25 test (Exit25).[10] Nutritional assessment was performed using the Mini Nutritional Assessment. The mean EXIT25 score was significantly higher (impaired) in both the malnourished group ($P<.001$) and the group at risk of malnutrition ($P=.002$) than in the well-nourished group. Also letter and animal verbal fluency test scores were significantly lower in the malnourished group than in the control subjects ($P<.001$).

Elderly subjects with malnutrition or at risk of malnutrition had poorer cognitive and executive function than well nourished elderly subjects.

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SEVERE HUMAN RHINOVIRUS OUTBREAK ASSOCIATED WITH FATALITIES IN A LONG-TERM CARE FACILITY IN ONTARIO, CANADA

To the Editor: Rhinovirus (HRV) infections are one of the most common causes of viral illnesses in humans. Infection of healthy adults with HRV can lead to a self-limited upper respiratory tract illness, also known as the common cold, but it can cause more-severe disease in elderly patients, such as exacerbations of chronic lung disease, pneumonia, and death.[1,2] Several reports of HRV outbreaks in elderly patients have been described.[3–6] An outbreak of rhinovirus in a long-term care facility (LTCF) causing severe disease

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Rehabilitation for dementia using enjoyable video-sports games

The aging of society inevitably leads to an increase in the numbers of elderly with dementia who reside in nursing homes, and delaying disease progression of residents with dementia has become a big concern. Rehabilitation that focuses directly on training cognitive function (e.g. memory training) reveals what patients are unable to do. Realization of their cognitive deficits can devastate their self-confidence and lead to anxiety, depression and the lowering of self-esteem (Small *et al.*, 1997). We propose rehabilitation that encourages patients' motivation for self-improvement through social interaction based on five principles as follows: (1) the activities should be enjoyable and comfortable for patients, (2) therapists should praise the patients naturally to motivate them, (3) the activities should be associated with empathetic two-way communication to make patients feel valued and safe, (4) therapists should encourage the patients to play "social roles" to restore self-worth, and (5) error-less learning based on brain-activating rehabilitation (BAR; Yamaguchi *et al.*, in press) should be adopted wherever possible. It is suggested that the positive feelings activate those areas of the brain related to reward, which plays a critical role in motivation (Berridge *et al.*, 2003), and it is a typical social reward to be praised and appreciated in public.

Based on BAR, we tried to improve residents' cognitive function indirectly by enhancing motivation using enjoyable video-sports games in a group setting. We conducted interventions with nine elderly people with mild to moderate dementia (88.9 ± 4.9 years of age, mean ± SD; three males and six females: one with Parkinson's disease dementia, one with vascular dementia, and seven with Alzheimer's disease (AD)) residing in a nursing home. All were in the stable phase of dementia, and had been admitted to the nursing home at least three months previously. None of the participants was medicated with donepezil hydrochloride.

We used video sports-games specifically devised for rehabilitation (Hot-plus, SSD Co. Ltd, Shiga Japan). These utilize psychomotor skills, such as hand-eye coordination, require timing, and necessitate fine three-dimensional control of the limbs in space. There were essentially two types of games: those working the upper limbs, and those the lower limbs. An example of the games for upper limbs required a player to grab coins which appeared to be coming out of the TV screen. The players wore bands on their hands equipped with sensors, and when the timing and direction were accurate, they scored points. Games for the lower limbs included those which required the players to move their legs to music. Two Japanese drums were shown on the TV screen, and two balls fell slowly from the top of the TV screen. A player was required to tap his/her feet on a mat equipped with sensors, synchronizing with the balls bouncing on the drums. He/she scored when the timing was accurate. These interventions were conducted once a week for ten weeks.

General cognitive function was measured using Hasegawa's Dementia Scale-revised (HDS-R), which is similar and well-correlated with the Mini-mental State Examination. The visuospatial and constructive function was measured using Kohs block-design tests (Kohs). Behavioral changes were evaluated using the Multidimensional Observation Scale for Elderly Subjects (MOSES), with the subitems of self-care, disorientation, depression, irritability, and withdrawal. No residents had previously experienced playing the video-sports games and so to help the residents enjoy the games, the caregivers (aged 40.8 ± 12.9 years, 7 males and

Table 1. The HDS-R, Kohs and MOSES scores

SCALE	BASELINE (MEAN ± SD)	POST-INTERVENTION (MEAN ± SD)	PAIRED-T TEST (p)
HDS-R	18.89 ± 4.26	25.33 ± 2.35	0.002
Kohs	20.22 ± 15.62	37.44 ± 12.44	0.02
MOSES			
Self-care	15.18 ± 4.09	15.00 ± 3.74	0.92
Disorientation	12.01 ± 2.47	10.64 ± 2.06	0.15
Depression	12.36 ± 3.08	10.46 ± 2.58	0.13
Irritability	9.46 ± 0.82	9.00 ± 0.63	0.16
Withdrawal	15.09 ± 5.13	13.55 ± 4.53	0.46
Total	64.18 ± 7.29	58.64 ± 5.16	0.054

12 females) participated in the sessions. They were taught in advance how to maintain empathetic two-way communication with the elderly participants. They were given a communication checklist of 34 items before commencement, and they kept an observation record to reinforce empathetic communication with residents.

The HDS-R scores improved from 18.98 ± 4.26 (mean ± SD) to 25.33 ± 2.35 ($p = 0.002$, paired t-test), the Kohs test scores improved from 20.22 ± 15.62 to 37.44 ± 12.44 ($p = 0.02$), and the total MOSES scores improved from 64.18 ± 7.29 to 58.64 ± 5.16 ($p = 0.054$; Table 1). Regarding communication, the sociability of residents also showed an improvement as seen in the MOSES subitems relating to communication and social interaction – i.e. depression, irritability, and withdrawal. According to the caregivers' observation records, the residents' faces became expressive, especially with smiles. Caregivers' communication skills were also improved by self-assessment (12.92 ± 2.07 items in the checklists with 34 items listed before commencement of the sessions). Communication was not limited to verbal communication; the main purpose of communication was to enjoy exchanges of affection and empathy rather than to obtain information; thus, nonverbal communication was very important. With the aid of the games, a situation promoting communication could be easily created by playing doubles, watching others play, cheering each other on, etc.

Although it is not possible to prove a causal relationship between cognitive improvement and increased communication, a community-based study has shown that communication, i.e. social interaction in the broad sense, has a protective effect in preserving mental function in the elderly (Wang *et al.*, 2002). Furthermore, communication might at least help ameliorate the residents' disuse syndrome. Disuse syndrome keeps the residents below the mental level expected based on the degree of brain pathology or brain damage. Nursing home residents tend to be passive, apathetic and dependent on caregivers. According to a survey conducted in Japan to explore the characteristics of depressive mood in different care settings, the residents in nursing homes felt more dissatisfied, apathetic and worthless, and unwilling to stay there, compared with community-dwelling residents and the hospitalized elderly (Onishi *et al.*, 2006). A depressive and apathetic tendency leads to cognitive and functional decline in AD; the results of MOSES showed some sign of improvement with regard to depressive tendencies. The cognitive decline resulting from disuse may be a reversible change, and so residents may regain their capacities.

Inter-subjectivity is a major factor in the rehabilitation for dementia; playing video-sports games in a group setting can be effective in improving the cognitive function of elderly people with dementia, especially when performed with trained caregivers who understand the principles of BAR: namely, the importance of creating enjoyment, empathetic two-way communication, using praise, and developing social roles.

Conflict of interest

None.

Description of authors' roles

Y. Maki and H. Yamaguchi formulated the research question, designed the study, carried it out, analyzed the data and wrote the letter. K. Takahashi was the doctor in charge of the patients.

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ORIGINAL ARTICLE

Computerized visuo-spatial memory test as a supplementary screening test for dementia

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Abstract

Background: To prepare for a super-aging society, effective dementia screening tests are required. The most salient deficit appearing from the early stages of dementia/Alzheimer's disease (AD) is a deterioration in memory. The Hasegawa Dementia Scale-revised (HDS-R) and the Mini-Mental State Examination (MMSE) are widely used in Japan to screen for dementia. Both place an emphasis on memory function, but neither examines visuo-spatial memory (VSM) function, even though VSM deficits are a sensitive marker for the detection of conversion to dementia. Furthermore, brief tests of VSM that are appropriate for screening have not been standardized. Thus, in the present study, we devised a brief, computer-aided short-term VSM test.

Methods: Sixty-six aged people were evaluated. Using the Clinical Dementia Rating (CDR), it was found that 29 could be considered normal controls (NC; CDR 0), 10 had mild cognitive impairment (MCI; CDR 0.5), 15 had mild dementia (CDR 1), and 12 had moderate to severe dementia (CDR 2–3). The VSM test estimated how many locations each subject could memorize. Several numbered circles were shown on a monitor and subjects were required to memorize the location of these circles sequentially. After the numbers on the circles on the screen had disappeared, the subjects were required to indicate the circles in ascending order. A touch panel screen was used for this test to make it easier. The HDS-R was applied to subjects with MCI and dementia.

Results: The mean (±SD) VSM score in subjects with MCI (5.70 ± 0.96) was significantly lower than that in NC subjects (6.69 ± 0.82), but significantly higher than that in subjects classified as CDR 1 (4.67 ± 0.87). There was no significant difference in VSM scores between subjects classified as CDR 1 and CDR 2–3 (3.80 ± 0.80). There was a moderate significant correlation between VSM and HDS-R scores.

Conclusion: In the present study, the VSM test detected differences in VSM function among NC subjects and subjects with MCI and mild dementia. The software program for the VSM test is distributed for free so that it can be widely used.

Key words: *Alzheimer's disease, Clinical Dementia Rating, dementia, mild cognitive impairment, screening test, visuo-spatial memory.*

INTRODUCTION

With the impending retirement of the baby-boomer generation, effective methods for the prevention and early detection of dementia are urgently required to prepare for the aging of society in Japan. For earlier treatment, a better understanding of the preclinical phase of dementia is important, as well as knowledge of the course of the disease after the onset of clinical symptoms. The most salient early feature of dementia/Alzheimer's disease (AD) is memory deficit,

with dementia/AD reflecting a chronic amnestic process before the actual clinical expression of dementia.

Memory skills can be subdivided according to the type of information stored, with three types most commonly studied, namely verbal, spatial, and object information. Verbal information includes words, letters, or other materials that are primarily coded linguistically. Spatial information corresponds to information regarding the spatial positions of stimuli. Object information involves the storage of non-spatial visual features or object identity.[1] In the present study, we focused on spatial short-term memory for the various reasons. First, meta-analyses of neuroimaging data have revealed a dissociation among the brain regions related to spatial, object storage, and verbal memory; spatial memory recruits the bilateral parietal lobes more intensely than do the other two categories.[1] The bilateral parietal lobes are affected by an AD-related pathology before the onset of clinical symptoms[2] and are key structures in the conversion from amnesic mild cognitive impairment (MCI) to dementia/AD.[3] Second, longitudinal population-based studies have revealed that visuo-spatial memory (VSM) deficits are a sensitive marker of conversion to dementia.[4,5] Practically speaking, VSM deficits have a severe impact on daily life. The major complaints made by patients are of misplacing things, having to rummage around to find them, and becoming lost because they have forgotten landmarks, etc.

In the present study, we developed a short, computer-aided, short-term VSM test operated using a touch panel that is easy to operate, even for patients with dementia. We think that the VSM test may be an effective supplemental test to the standardized screening tests used in Japan to identify dementia, including the Mini-Mental State Examination (MMSE) and the Hasegawa Dementia Scale-revised (HDS-R), which is similar to and well-correlated with the MMSE.[6] The MMSE and HDS-R place an emphasis on memory function, but neither examines the VSM function. The Benton Visual Retention Test (BVRT) is commonly used as a VSM test. However, the BVRT involves factors other than visual retention, such as visual form discrimination and visual construction.[7] Furthermore, it is a time-consuming test. Most primary care doctors believe that cognitive screening for dementia is needed in medical practice, but few routinely perform such screening. The largest barrier for both doctors and patients is that the tests are time consuming,[8] so a brief test that could be used to screen for dementia would be of considerable value. Herein, we describe the brief VSM test and compare the results of this test between patients with dementia, those with MCI, and the healthy elderly.

METHODS

Sixty-six aged people (18 men and 48 women) were tested in the outpatient clinic. The only inclusion criterion was age ≥55 years. The exclusion criteria were: psychiatric diseases, delirium, verbal incomprehension (including aphasia), and motor deficits, such as paralysis, because the test uses a touch panel. The Ethics Board of Gunma University School of Health Sciences approved all procedures (no. 21–26) and informed consent was obtained from all participants or their proxies. Patients were diagnosed as having AD, dementia with Lewy bodies (DLB) or MCI on the basis of published criteria, namely the National Institute of Neurological and Communicative Disorder and Stroke, Alzheimer's disease and Related Disorders Association (NINCDS-ADRDA)[9] for AD, the third report of the DLB Consortium[10] for DLB, and a report from the International Working Group on Mild Cognitive Impairment[11] for MCI. Normal controls (NC) were identified on the basis of an interview and a questionnaire regarding the frequency of dementia-like symptoms and instrumental activities of daily living completed by their family and/or carers. Patients and some of those in the NC group underwent magnetic resonance imaging (MRI) and a set of cognitive tests (e.g. HDS-R, cube-copying test, clock-drawing test, trail-making test (TMT), and the stroop test). Of the patients with dementia, 18 had AD, six had DLB, and three had some other form of dementia. In the preset study, subjects were classified according to the Clinical Dementia Rating (CDR). In the present study, those with CDR 0.5 were regarded as MCI, even though different classifications have been proposed whereby CDR 0.5 encompasses both mild and earlier dementia[12] or it can correspond to very mild dementia.[13] We tested 29 NC subjects who corresponded to CDR 0, 10 patients with MCI (CDR 0.5), 15 patients with mild dementia (CDR 1), and 12 patients with moderate to severe dementia (CDR 2–3). Demographic data are presented in Table 1.

Visuo-spatial memory test

Participants were seated approximately 70 cm away from the screen of a 15″ touch panel connected to a PC running C++ software based on Windows XP. The VSM test measures memory capacity with regard to spatial memory configuration. We adopted the modified task of Kawai *et al.*[14] Numbered circles were displayed on the monitor for 8 s and subjects were required to memorize the location of these circles sequentially (Fig. 1a). In the first trial, three numbers (1, 2, and 3) were shown on the computer screen. After 8 s, the numbers disappeared, and three blank circles remained (Fig. 1b). Subjects were required to touch the patches sequentially in ascending order based on their memory (1, 2, 3—; Fig. 1c). There was a training session just prior to the actual test; subjects were allowed to practice twice with three numbers. Those who did not understand the task after two trials in the training session were excluded from the study. Memory capacity was measured using the staircase method. If the first response was correct, the number of stimuli increased in the second trial and so on. Alternatively, if the participant made an error, the number of stimuli decreased in the subsequent trial. When the sequence was switched from ascending to descending or vice versa, the number of stimuli was recorded as a reversal point score. The experiment was continued until four reversal points were obtained; the number of trials in one session was not fixed. The average of the four reversal point scores was used as the VSM score for that session. In the VSM test, the location of the stimuli was randomized to minimize the learning effects of repetition, and reproducibility was checked by preliminary experiments performed on 11 patients with dementia who were not included in the study itself; the tests were conducted twice at 1-week intervals and the results were correlated ($r = 0.76$).

The cut-off value was determined using the receiver operating characteristic (ROC) curve.[15] The cube-copying test and the clock-drawing test were scored as an accurate or inaccurate description. The TMT was scored as time, whereas the stroop test was scored as error rate. Results for patients with MCI and dementia were analyzed using the Japanese version of SPSS, 17th edition (SPSS, Chicago, IL, USA).

Table 1 Demographic data for the four groups

	n	Age (years)	VSM score	HDS-R score
NC (CDR 0)	29	78.3 ± 5.3	6.7 ± 0.8	ND
MCI (CDR 0.5)	10	73.7 ± 10.3	5.7 ± 1.0	27.0 ± 1.6
CDR 1	15	77.6 ± 9.3	4.7 ± 0.9	22.6 ± 3.1
CDR 2-3	12	81.9 ± 4.5	3.8 ± 0.8	12.1 ± 3.8

Unless indicated otherwise, data are given as the mean ± SD.
Normal control (NC) subjects were identified on the basis of an interview with a doctor and a questionnaire completed by their family and/or carers.
ND, not done (scores for the Hasegawa Dementia Scale-revised (HDS-R) were not obtained for NC subjects); MCI, mild cognitive impairment; CDR, Clinical Dementia Rating; CDR 1, mild dementia; CDR 2–3, moderate to severe dementia; VSM, visuo-spatial memory.

RESULTS

There were no significant differences in age or gender among the four groups (age: $P = 0.07$, one-way ANOVA; gender: $P = 0.50$, Chi-squared test).

The mean (±SD) VSM memory scores for subjects in the CDR 0 (NC), CDR 0.5 (MCI), CDR 1 and CDR 2–3 groups were 6.69 ± 0.82, 5.70 ± 0.96, 4.67 ± 0.87, and 3.80 ± 0.80, respectively (Table 1, Fig. 2). One-way ANOVA indicated the presence of significant

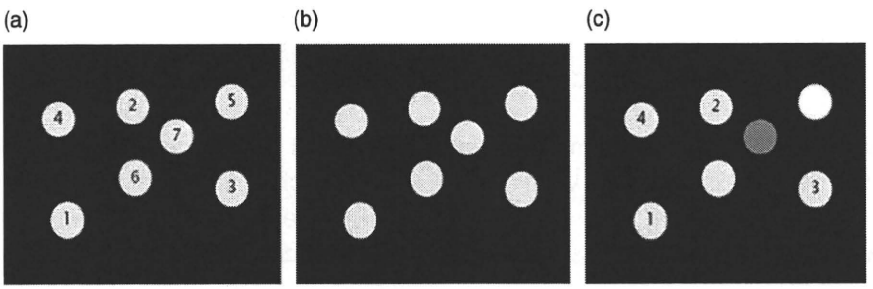

Figure 1 Example of the display seen on the touch screen for seven stimuli. (a) Seven numbered circles were shown on the touch panel screen. (b) After 8 s, the numbers disappeared. (c) Subjects were asked to touch the circles in ascending order. When subjects answer correctly, the number was displayed, but when they answer incorrectly, the circle turned red for a while and subjects could try again and continue with the test. In this case, the number was displayed in response to a correct answer. However, once the subject answer incorrectly, the trial was judged a failure and one less numbered circle (in this example, six circles) was displayed in the next trial.

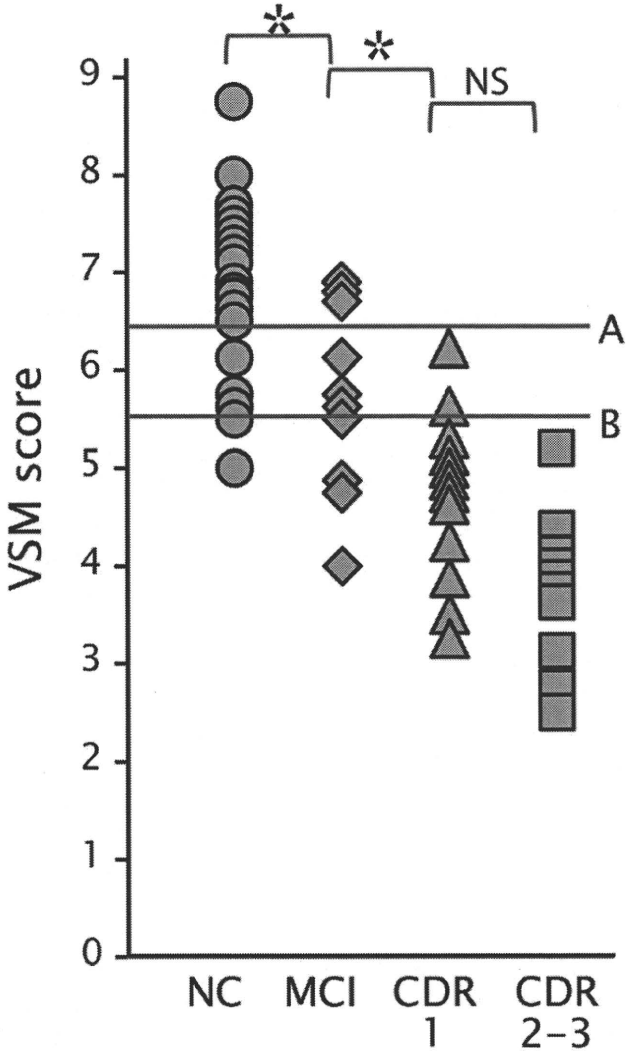

Figure 2 Cut-off points of 6.375 (A) or 5.5 (B) were evaluated for normal control (NC) subjects or patients with mild cognitive impairment (MCI). There were significant differences between the NC and MCI groups, as well as between the MCI and Clinical Dementia Rating (CDR) 1 (mild dementia) groups, whereas the difference between the CDR 1 and CDR 2–3 (moderate to severe dementia) groups did not reach statistical significance ($P = 0.06$).

differences between the four groups ($P < 0.001$). The results of post hoc analysis with Bonferroni correction indicated significant differences between the NC and MCI groups ($P = 0.01$), as well as between the MCI and CDR 1 groups ($P = 0.02$); however, the difference between the CDR 1 and CDR 2–3 groups was marginal ($P = 0.06$; Fig. 2). When the cut-off point for NC or MCI was set to 6.375, the sensitivity of the VSM test for MCI was 70% and the specificity was 76%. When the cut-off point for MCI or dementia was set to 5.5, the sensitivity of the VSM test for dementia was

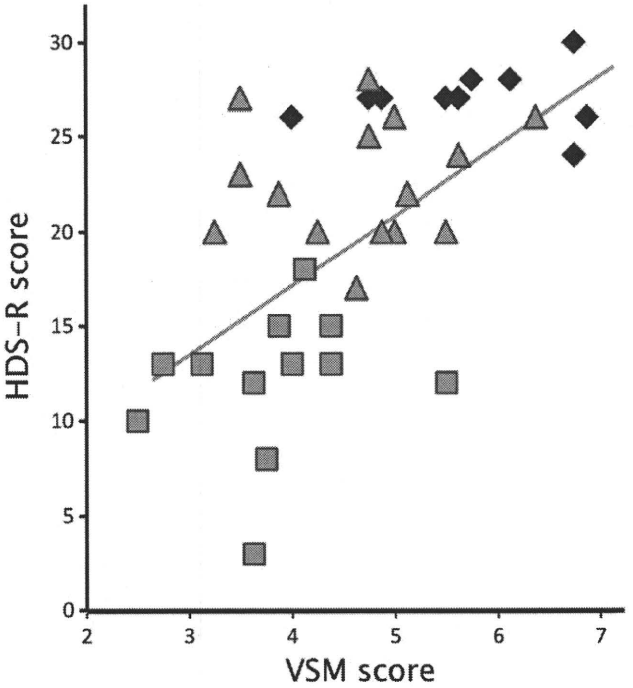

Figure 3 Correlation between scores on the visuo-spatial memory (VSM) test and Hasegawa Dementia Scale-revised (HDS-R) in subjects with mild cognitive impairment (◆), Clinical Dementia Rating (CDR) 1 (mild dementia; ▲), and CDR 2–3 (moderate to severe dementia; ■). There was a significant correlation between total scores on the VSM test and HDS-R ($r = 0.61$, $P < 0.001$). The equation for the regression line was: $y = 3.7x + 3.1$ ($r^2 = 0.37$).

93% and the specificity was 85%. Scores were not correlated with the age ($r = -0.12$).

Group averages of HDS-R scores for the CDR 0.5 (MCI), CDR 1 and CDR 2–3 groups are given in Table 1. One-way ANOVA indicated the presence of significant differences between these three groups ($P < 0.001$). The results of post hoc analysis with Bonferroni correction also indicated significant differences between MCI and CDR 1 ($P = 0.003$), as well as between CDR 1 and CDR 2–3 ($P < 0.001$). The VSM scores and HDS-R total scores were moderately correlated ($r = 0.61$; $P < 0.001$), which indicates that spatial memory deficits are correlated with the general decline of cognitive function (Fig. 3).

The sensitivity of the cube-copying test was 25% for MCI and 67% for dementia. The sensitivity of the clock-drawing test was 31% for MCI and 63% for dementia. The average VSM score of those who succeeded in the cube-copying test was 4.94, compared with an average VSM score of 3.71 for those who failed the test. The average VSM score of those

who succeeded in the clock-drawing test was 4.94, compared with an average VSM score of 3.94 for those who failed the test. There were no correlation between VSM scores and TMT scores ($r = -0.37$) or between VSM scores and stroop scores ($r = -0.33$).

The average number of trials was 10.5 in the NC group, 9.3 in the MCI group, 8.1 in the CDR 1 group, and 8.0 in the CDR 2–3 group. Almost all subjects were unfamiliar with the use of a computer, but no one refused to undergo the examination.

DISCUSSION

The brief VSM test used in the present study detected deterioration of the VSM function at the MCI level, before the onset of dementia. It was effective in evaluating individual memory function in patients with MCI and mild dementia (CDR 1), but was ineffective for subjects in the advanced stages of dementia (CDR 2 or more). There was no significant difference in VSM scores between patients classified as CDR 1 and those classified as CDR 2–3, which may have resulted from the floor effects for CDR 2–3. The trial using three numbers was easy, even for moderately demented subjects.

We paid particular attention to reducing the psychological burden of subjects. The level of difficulty can be varied according to each individual: the number of stimuli is increased only when subjects give correct answers, thus subjects are not forced to perform a task that is beyond their capacity. Because the subjects can continue the trial even if they answer incorrectly in the middle of the test (Fig. 1), they can feel a sense of accomplishment.

As for the feasibility of the VSM test in clinical practice, its brevity is an advantage. The examination time varies according to the number of trials but, generally, one session was completed within 3 min. Another advantage of the VSM test is that the results can be quantified without arbitrariness. Using the BVRT in a multiple-choice format has been proposed to facilitate quantitative evaluation of VSM and to shorten the examination time.[16] Besides, the VSM showed a higher sensitivity than the clock-drawing and cube-copying tests, which are often used in clinical practice.

There was a correlation between the results of the test and general cognitive function, as determined using the HDS-R. As a whole, the VSM function is impaired in line with the deterioration of other functions. We recommend using the VSM test as a compliment to routine screening tests, such as the HDS-R or MMSE, which lack a VSM task, to provide further information when analyzing individual profiles of cognitive function. The MMSE and HDS-R are themselves mosaics of subordinate cognitive examinations and analyzing subordinate tests should be more important than the total score.[17] In practice, it is often that other tests are also performed, such as the clock-drawing[18] and/or cube-copying tests,[19] to supplement the cognitive factors examined in the MMSE and/or HDS-R. In the present study, there was no correlation between VSM scores and TMT or stroop test scores, which are standardized tests of frontal lobe function. This emphasizes the point that the VSM test evaluates a different function from those tests and combined application of these tests should provide information regarding various aspects of each patient's cognitive function.

A limitation of the present study was that educational levels of the subjects were not considered. Performance can be influenced by the education level, as reported for the BVRT.[20]

Over all, the VSM test is effective and practical in a clinical setting. The computer program, which can be run in Windows, is available as a free download so that it can be used widely (see Acknowledgements).

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Yamaguchi Fox-Pigeon Imitation Test: A Rapid Test for Dementia

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Key Words
Dementia · Alzheimer disease · Mild cognitive impairment · Psychological burden · Gesture imitation

Abstract
Background/Aims: We herein propose a hand-gesture imitation test, consisting of a simple one-handed sign of a 'fox' and a complex two-handed sign of a 'pigeon', as a rapid, game-like test for detecting dementia/Alzheimer disease (AD) with low psychological burden. The test measures the visuomotor function, which deteriorates in the early stages of AD. ***Methods:*** We examined 88 demented subjects, 19 with mild cognitive impairment (MCI), and 53 normal controls aged 65 years or over. The subjects were classified according to the Clinical Dementia Rating (CDR). ***Results:*** The specificity of the test was 94%, and the sensitivity was 58% in CDR 0.5 (MCI), 77% in CDR 1 (mild dementia), 75% in CDR 2 (moderate dementia), and 90% in CDR 3 (severe dementia). The test could be conducted within 1 min and no subjects refused to be tested. ***Conclusion:*** This brief hand-gesture imitation test can sensitively evaluate visuomotor deficits in dementia/AD, while some subjects are unaware of their failure or even that their cognitive function is being tested. We herein describe the precise protocol for worldwide use.

Introduction

As aging is a major risk factor for dementia, the rapid aging of society leading to large increases in people with dementia will result in a heavy socioeconomic burden. Thus, the early detection and prevention of dementia are urgently required.

We propose a hand-gesture imitation test, as a rapid game-like test, evaluating the visuomotor function for dementia/Alzheimer disease (AD). Although memory deficits are a salient feature of AD, other symptoms appear from the early stages and a representative symptom is visuomotor deficit [1]. Before the onset of clinical symptoms, the bilateral parietal lobes are affected with AD-related pathology [2], and show hypoperfusion as a characteristic single-photon emission computed tomography finding [3]. Thus, gesture imitation, which requires parietal function, may be compromised even in the early stages of AD, a major cause of dementia.

Among gestures, we adopt meaningless nonsymbolic gestures to eliminate semantic components, although some studies insisted that meaningful imitation was more sensitive than meaningless imitation to detect AD [4–6]. However, meaningful imitation recruits semantic processing [7], and the semantic aspects of imitation are preserved in patients with lesions restricted to the pari-

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Table 1. Demographic data, error rate, and error patterns

Classification	CDR	Number	Age years	HDS-R	Error of 'fox' n[1]	Error of 'pigeon' n[1]	Error patterns of 'pigeon'			
							palm-palm n[2]	palm-dorsum, n[2]	dorsum-dorsum, n[2]	intermediate, n[2]
NC	0	53	78.9±5.3	–	0 (0.0)	3 (5.7)	3 (100)	0 (0.0)	0 (0.0)	0 (0.0)
MCI	0.5	19	80.7±7.4	26.5±1.3	0 (0.0)	11 (57.9)	5 (45.5)	1 (9.1)	5 (45.5)	0 (0.0)
Mild dementia	1	39	81.4±6.5	20.2±4.1	1 (2.6)	30 (76.9)	10 (33.3)	6 (20.0)	10 (33.3)	4 (13.3)
Moderate dementia	2	20	82.1±5.4	12.1±3.8	0 (0.0)	15 (75.0)	11 (73.3)	3 (20.0)	1 (6.7)	0 (0.0)
Severe dementia	3	29	81.6±4.0	7.0±5.0	9 (31.0)	26 (89.7)	0 (0.0)	11 (42.3)	12 (46.2)	3 (11.5)
Dementia total	1–3	88	81.6±5.5	14.0±7.3	10 (11.4)	71 (80.7)	21 (23.9)	20 (22.7)	23 (26.1)	7 (8.0)

Figures in parentheses represent percentage. More than half of MCI (CDR 0.5) and 4/5 of demented subjects failed to imitate 'pigeon'. The most frequent error pattern of 'pigeon' was the palm-palm pattern, especially in CDR 0.5–2. HDS-R = Hasegawa's Dementia Scale-Revised (top score is 30, as in the Mini-Mental State Examination).

[1] Errors as a percentage of the total number of attempts.

[2] Each error pattern as a percentage of the total number of errors.

etal lobe [8]. Meaningless gesture imitation examines representation of the body state [9], which is affected by parietal lobe deficits [10, 11]. Thus, we tested meaningless imitation and adjusted the difficulty level according to a previous study showing that complex meaningless gesture imitation can detect AD in the early stages, whereas simple ones cannot [12].

Here, we developed an easy and rapid test, the Yamaguchi Fox-Pigeon Imitation Test (YFPIT), which detects dementia/AD within 1 min. This game-like test reduces the psychological burden associated with ordinary cognitive tests, which often hurts the pride and self-confidence of aged people.

Methods

We tested 160 aged people: 97 in out-patient clinics and 63 in residences for seniors; 41 males and 119 females. The inclusion criterion was being aged 65 years or over. Exclusion criteria were psychiatric diseases, delirium, verbal incomprehension including aphasia, inability to walk, and motor deficits such as paralysis. The Ethics Board of Gunma University School of Health Sciences approved all procedures (No. 21–26), and signed informed consent was obtained from participants or their proxies. Subjects were diagnosed based on criteria for dementia diseases such as National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA). Normal controls (NC) were judged by interviews and questionnaires on frequent symptoms of dementia and instrumental activities of daily living, taken from their family members/carers. Patients and some NC underwent MRI and a set of cognitive tests: e.g. Hasegawa's Dementia Scale-Revised, which is similar and well-correlated with the Mini-Mental State Examination and common in Japan, the cube copying test, clock drawing test, Stroop test, trail-making test, and memory tests. The demented subjects consisted of 64 with AD, 13 with dementia with Lewy bodies, and 11 with other dementia types. In the present study, subjects were classified according to the Clinical Dementia Rating (CDR; table 1). There were no significant differences in age nor gender among the groups (age: $p = 0.11$, 1-way ANOVA; gender: $p = 0.19$, χ^2 test).

The YFPIT consists of a hand-gesture imitation of a 'fox' (fig. 1a) contiguous with a 'pigeon' (fig. 1b). The protocol is as follows:

(1) The examiner sits face-to-face with a subject.
(2) The examiner gives a simple instruction: 'Watch my hand gesture carefully and imitate it.' The instruction can be repeated if necessary.
(3) Then, the examiner makes the 'fox' sign using his/her left hand: fingers III and IV touching the thumb on flexion of the metacarpophalangeal joints with fingers II and V held up (fig. 1a).
(4) The examiner maintains the gesture for 10 s. The subject imitates the gesture concurrently with the examiner. Say nothing during the 10 s of the test. Be careful not to say the words 'fox', or the instruction.
(5) The examiner judges whether or not the subject produces the same sign within 10 s of demonstration; the subject may use either hand.
(6) For 'pigeon', the examiner gives the same instruction, and then makes a 'pigeon' sign using both hands: crossing the hands, palms facing the body, with fingers II–IV extended upward and the two thumbs crossing each other (fig. 1b).
(7) The examiner maintains the gesture without saying anything, especially the word 'pigeon' nor instructions, during the 10 s of the test.
(8) The examiner judges whether or not the subject concurrently makes the same sign within 10 seconds of demonstration.

Points for judgment are as follows:

(a) The direction of the arm and fingers II–V should be upward: hand positions in horizontal or downward directions are judged as failures (fig. 1f).

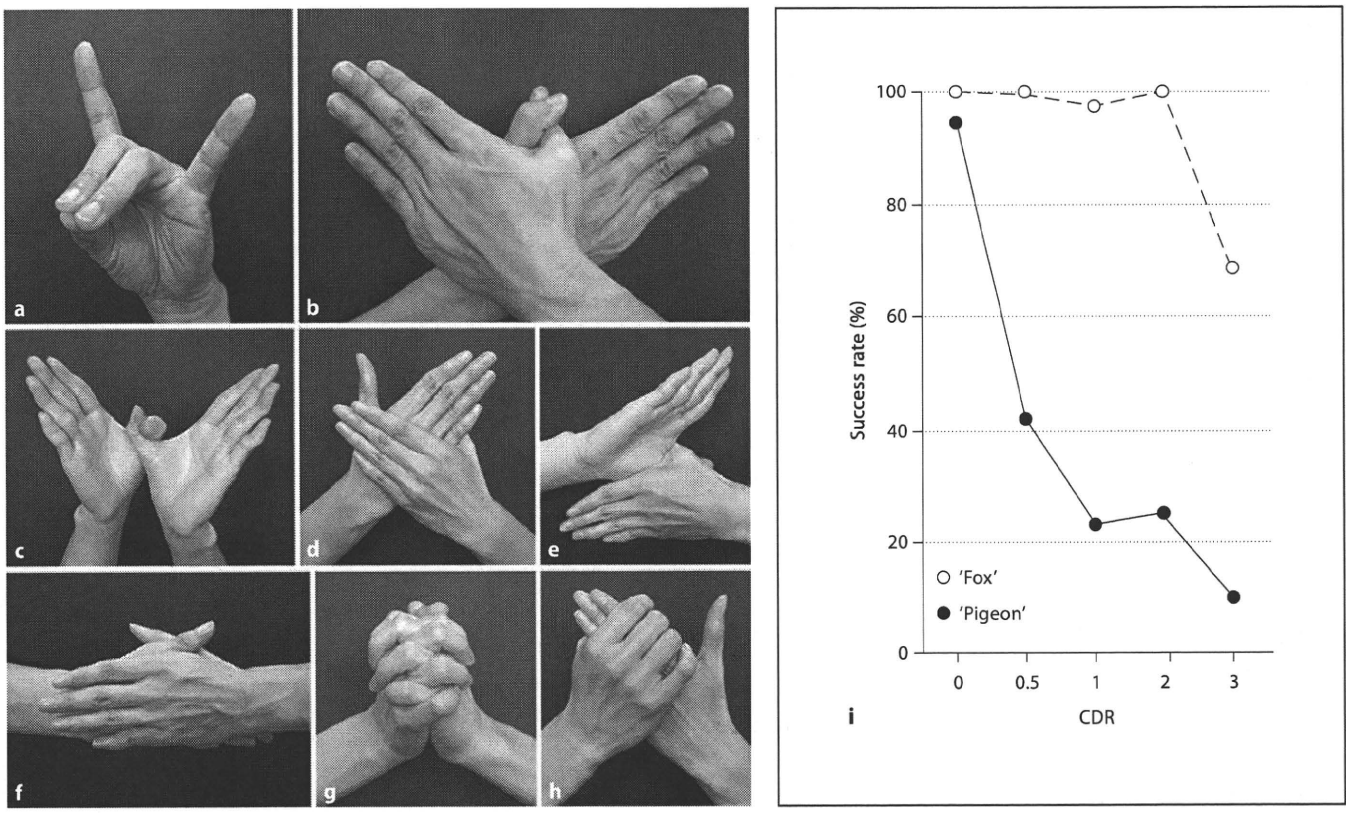

Fig. 1. Hand-gesture demonstration, error responses, and the success rate of the YFPIT according to the CDR. Examiner's demonstration of 'fox' (**a**) and 'pigeon' (**b**). Subjects' typical error patterns of palm-palm (**c**), dorsum-dorsum (**d**), and palm-dorsum (**e**). **f** Error pattern with downward direction of arms. **g**, **h** Error patterns common in CDR 3. **i** The success rate of 'fox' started to decrease at CDR 3, while that of 'pigeon' decreased at CDR 0.5.

(b) Both cases are acceptable: right hand in an outward position or vice versa.
(c) Both palms should be facing the body.
(d) Thumbs should be crossing each other.

Results

Most CDR 0–2 subjects succeeded in imitating the 'fox', whereas 31.0% of CDR 3 subjects failed. No subjects who failed to imitate the 'fox' succeeded with the 'pigeon' (fig. 1i and table 1).

On the other hand, the success rate of the 'pigeon' was 94.3% in NC (i.e. specificity), whereas more than half of the subjects with MCI (CDR 0.5) and 4/5 of demented subjects failed to imitate 'pigeon' (table 1). The error rate was not significantly influenced by age ($p = 0.17$, two-sample t test) nor gender ($p = 0.10$, χ^2). The specificity of the test was 94.3%. In comparison between NC and MCI, the sensitivity was 57.9%, the positive prediction value (PV+; positive diagnosis/test positive) was 86.2%, and negative prediction value (PV–; negative diagnosis/test negative) was 78.6%. In comparison between NC and mild dementia, the sensitivity was 76.9%, PV+ was 84.7%, and PV– was 90.9%. When subjects were limited to the 64 with AD and compared to NC/MCI, the results were similar to those obtained from all demented subjects (online suppl. table 1, www.karger.com/doi/10.1159/000289819). The number of subjects was too small to analyze the differences among the causes of dementia.

As qualitative analysis, we categorized 4 error patterns of 'pigeon' based on the direction of the hands: (1) palm-palm pattern, both palms outward (fig. 1c), (2) dorsum-dorsum pattern, both dorsa outward (fig. 1d), (3) palm-dorsum pattern, one palm and one dorsum outward (fig. 1e), and (4) other patterns. The characteristic error pattern was palm-palm, and subjects showing this error seemed not to notice it, because, from the subjects' per-

spective, they saw their dorsa as well as the dorsa of the examiner (table 1).

Regardless of the hand direction, severely demented subjects showed a tendency to fold their fingers (n = 12, 41.4% in CDR 3), e.g. bring their hands together (fig. 1g), or grip one hand with the other (fig. 1h). Inability to perform 'fox' is also observed mostly among CDR 3 subjects, and, therefore, the rate of subjects showing a folding finger pattern and/or inability to perform 'fox' was 0% in CDR 0.5, 5.1% in CDR 1 (n = 2), and 5.0% in CDR 2 (n = 1), whereas it was 58.6% in CDR 3 (n = 17).

No subjects refused to undertake the test and all finished the test within 1 min.

Discussion

Our results suggest that the YFPIT is useful to detect dementia/AD. The merits of the YFPIT are:

(1) Easy and simple, requiring 1 min.
(2) Enjoyable, like a game.
(3) Nearly half of the subjects with mild to moderate dementia showed a palm-palm pattern, and did not notice their mistakes, preserving self-confidence.
(4) Low error rate of 'pigeon' in NC (5.7%).
(5) High sensitivity for detecting dementia (80.7%).

Adding to the merits for detecting mild dementia, the YFPIT revealed the characteristics of severe dementia; more than half of CDR 3 subjects failed to imitate 'fox' and/or showed a folding finger pattern (i.e. fig. 1g, h) in 'pigeon'.

Why did the YFPIT sensitively detect dementia? The reason is that we adopted a hand gesture, 'pigeon', containing 2 components as follows. One was the component of perspective taking, which is the cognitive process when perceiving a visual scene from one's own perspective (first-person perspective, 1PP), differing from taking a view of the same scene from another person's viewpoint (third-person perspective, 3PP) [13]; 3PP recruits the bilateral parietal area more intensely than 1PP [14]. The most frequent error pattern was the palm-palm pattern, which is related to deficits of perspective taking. In the palm-palm pattern, the subjects see the dorsum of both the examiner and themselves. Another component is body midline crossing, where the hands invade the contralateral space. Making adequate gestures crossing the midline is more complex than making those limited to ipsilateral sides.

As above, with the YFPIT, we successfully detected dementia/AD in the early stages. However, a detection (error) rate of 58% in MCI (CDR 0.5) is insufficient. We do not propose that dementia should be screened with the YFPIT independently. The YFPIT can be one of the components of a test battery for dementia/AD. Questionnaires on instrumental activities of daily living from carers are also important for detecting dementia in its early stages [15]. Combination with other tests is necessary for an accurate diagnosis.

The main issue of MCI is the prognosis of conversion to AD. Imaging studies have reported that hypometabolism and/or hypoperfusion in parietal association areas have a high predictive value of conversion to AD [3], and hand-gesture imitation recruits the bilateral parietal association area. Thus, we assume that the hand-gesture imitation test is useful to predict the conversion from MCI to AD. To evaluate the prognostic role of the YFPIT in MCI, follow-up observation is needed.

Corticobasal degeneration is a progressive movement disorder with cortical and basal ganglionic dysfunction [16], and the hand-gesture imitation test is applied to evaluate the movement disorder [17]. Therefore, failure in the YFPIT can be seen in limb apraxia of corticobasal degeneration as well as ideomotor apraxia of stroke.

Our priority was to devise a simple test protocol – one easy gesture followed by a complex gesture, the difficulty of which is appropriate to distinguish dementia/AD from NC. As a result, more than half of CDR 0.5 subjects failed 'pigeon'. Gesture order is also important. We tested the simple 'fox' before the complex 'pigeon' gesture to rule out deficits caused by the incomprehension of verbal commands or visual deficits. To perform the test as a nonsymbolic imitation, we did not use the words 'fox' and 'pigeon'. Thus, the test evaluated the visuomotor but not semantic function. Previous studies revealed deficits of imitation in AD in the context of apraxia [4–7]. This hand-gesture imitation test, the YFPIT, is an effective 1-min test of dementia/AD, showing good sensitivity/specificity, even though it is quite easy, rapid, and low in psychological burden.

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