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Relative preservation of the recognition of positive facial expression "happiness" in Alzheimer disease

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ABSTRACT

Background: Positivity recognition bias has been reported for facial expression as well as memory and visual stimuli in aged individuals, whereas emotional facial recognition in Alzheimer disease (AD) patients is controversial, with possible involvement of confounding factors such as deficits in spatial processing of non-emotional facial features and in verbal processing to express emotions. Thus, we examined whether recognition of positive facial expressions was preserved in AD patients, by adapting a new method that eliminated the influences of these confounding factors.

Methods: Sensitivity of six basic facial expressions (happiness, sadness, surprise, anger, disgust, and fear) was evaluated in 12 outpatients with mild AD, 17 aged normal controls (ANC), and 25 young normal controls (YNC). To eliminate the factors related to non-emotional facial features, averaged faces were prepared as stimuli. To eliminate the factors related to verbal processing, the participants were required to match the images of stimulus and answer, avoiding the use of verbal labels.

Results: In recognition of happiness, there was no difference in sensitivity between YNC and ANC, and between ANC and AD patients. AD patients were less sensitive than ANC in recognition of sadness, surprise, and anger. ANC were less sensitive than YNC in recognition of surprise, anger, and disgust. Within the AD patient group, sensitivity of happiness was significantly higher than those of the other five expressions.

Conclusions: In AD patient, recognition of happiness was relatively preserved; recognition of happiness was most sensitive and was preserved against the influences of age and disease.

Key words: dementia, Alzheimer disease, emotional face recognition, positivity bias, aging, happiness, social interaction, morphing technology

Introduction

Deficits in the recognition of emotional facial expressions might lead to behavioral disturbances that often accompany Alzheimer disease (AD), and behavioral features are more distressing than cognitive deficits for caregivers of patients with AD (Donaldson *et al.*, 1998). Facial expressions are universally identified into six basic expressions: happiness, sadness, surprise, anger, disgust, and fear (Ekman *et al.*, 1971). The human face conveys non-verbal information about emotional states, the recognition of which is critical for appropriate social behavior.

In aged individuals, positivity recognition bias has been reported for facial expression (Mather and Carstensen, 2003; 2005). The positivity recognition bias was well-studied with memory; aged individuals remember a larger quantity of positive events than negative ones, and show more emotionally positive memory distortion for autobiographical information than younger adults do (Mather and Carstensen, 2005). Such positivity bias in aged individuals has been consistently reproduced in experimental settings of various recognition modalities such as emotional facial recognition and visual stimuli as well as memory (Mather and Carstensen, 2003; 2005; Kapucu *et al.*, 2008; Spaniol *et al.*, 2008). However, studies on emotional facial recognition in AD

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patients have produced various results. First, it is controversial whether facial recognition itself is declined or not; some studies reported preserved ability of emotional facial recognition (Bucks *et al.*, 2004; Luzzi *et al.*, 2007; Guaita *et al.*, 2009; Yamaguchi *et al.*, 2012), whereas others reported impairments (Spoletini *et al.*, 2008; Bediou *et al.*, 2009; Drapeau *et al.*, 2009). It is also controversial whether there were differences in the recognition of various emotions. Some studies reported no difference (Bucks *et al.*, 2004; Luzzi *et al.*, 2007), whereas others reported differences, e.g. selective impairment was reported in labeling the facial expression of sadness (Hargrave *et al*, 2002), and recognition of happy facial expressions was reported to be relatively preserved in comparison with angry facial expressions (Yamaguchi *et al.*, 2012). It was also reported that the most identified emotion was happiness among seven facial expressions (six basic expressions and boredom) in the moderate and severe stage of dementia (Guaita *et al.*, 2009).

The controversy may be partly due to confounding factors. Some studies have suggested involvement of confounding factors such as deficits in spatial processing of non-emotional facial features and in verbal processing to express emotions (Cadieux *et al.*, 1997; Burnham *et al.*, 2004). The deficits shown in the experiments could be due to the decline of the spatial recognition and/or verbal processing, which were prominent in AD. Thus, in the present study, we demonstrated characteristics of emotional face recognition in AD patients, by adapting a new method that eliminated the influences of these confounding factors to reveal whether the recognition of positive expressions is relatively preserved in AD.

Methods

Participants

The participants were 12 outpatients with mild AD in Clinical Dementia Rating scale (CDR) 1, 17 aged normal control (ANC), and 25 young normal control (YNC). Participants were limited to mild AD patients to eliminate the influence of difficulties of understandings of the rules. The exclusion criteria were: prosopagnosia, psychiatric diseases, delirium, and verbal incomprehension including aphasia. Those who had weak in eyesight were also excluded; all the participants could distinguish a 2-pixel gap (0.58 mm) on a 15″ monitor screen of Landolt ring from 70 cm away. Subjects were diagnosed based on the criteria for AD by NINCDS-ADRDA (Dubois *et al.*, 2007). Scores over 7 on the Japanese version of the Short Form of the Geriatric Depression Scale (Yesavage *et al.*, 1982) were also excluded because depressive tendencies could affect facial recognition. The Ethics Board of the Gunma University School of Health Sciences approved all procedures (No. 21-26), and written informed consent was obtained from all the participants.

Stimuli

Six hundred colored face images of six basic emotional expressions (happiness, surprise, anger, sadness, fear, and disgust) were used. To eliminate confounding factors related to individual difference in non-emotional facial features and ways to express emotions, we used standardized photos of four Japanese women (one neutral and six basic expression photos for each person) in database DB99 (Advanced Telecommunications Research Institute International, Inc. Nara, Japan); facial features and expressions of non-Japanese individuals could be confounding factors for Japanese. Then we made "averaged faces", which canceled individual differences. We prepared one neutral and six emotional expression (100% expression faces) averaged faces by morphing photos of four women. For grading the ability, we prepared photos of 1%–99% intermediate expression levels of each emotion by morphing neutral and 100% expression faces with weight. In this way, the images of 600 emotional averaged faces were prepared; e.g. 38% happy image was made by morphing the 100% happy image and the neutral image with a ratio of 38–62. Each image was framed by an oval to avoid the influence of hairstyle and clothing.

Experimental setting

The experimental setting is shown in Figure 1A (stimuli were in color in the experimental setting). One of the images of intermediate expression levels was displayed on the monitor of touch panel screen in the left, and six small faces of 100% expression were displayed on the right. To eliminate the confounding factor of verbal processing, the participants were required to answer by touching the 100% face that corresponded to the expression of intermediate face. Using the choice of faces instead of verbal labels, even those who had difficulties in verbal processing could answer the question.

The sensitivity of expression was measured using staircase method. The orders of six expressions were randomized using a computer program, and the first stimulus was 100% expression faces in each expression. In each expression respectively, if the response was correct, the level of stimuli increased in the next trial (ex. 38%–35% expression face).

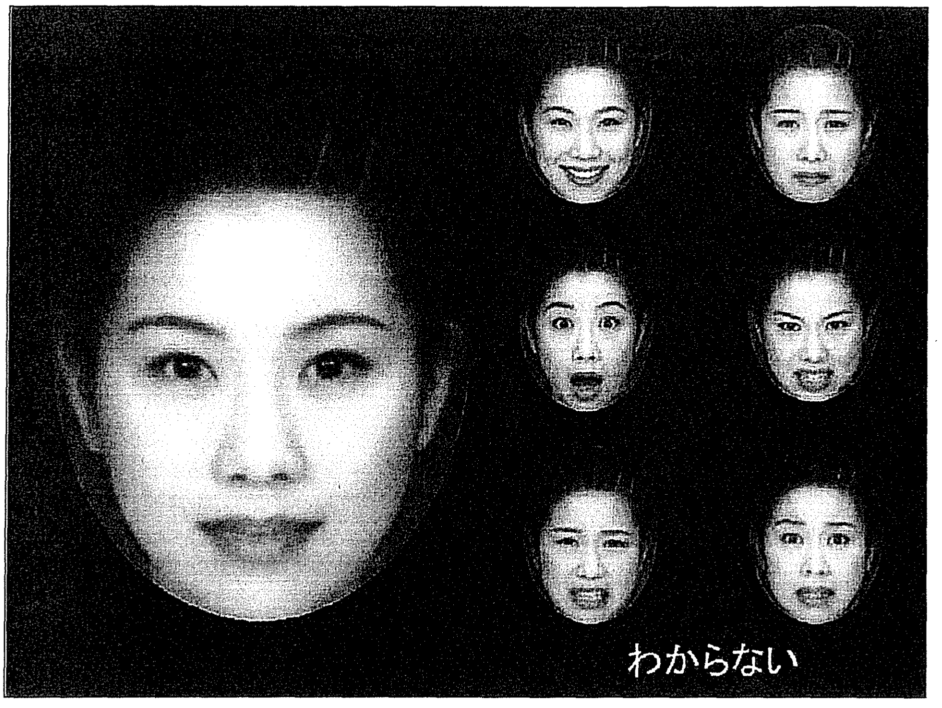

Figure 1. A stimulus shown on the monitor. On the left of the screen, 27% happy face was shown; recognition of 27% happy face corresponded to the sensitivity of 73%, which was the average sensitivity in patients with Alzheimer disease (AD). On the right, six kinds of 100% expressions were shown. The participants were required to choose and tough one of the 100% faces corresponding to the face on the left. The Japanese letters on the right bottom means to have no idea, and they could choose the option.

Alternatively if the participant made an error, the level of stimuli decreased in the subsequent trial. When the sequence was switched from ascending to descending or *vice versa*, the level was recorded as a reversal point score. The levels were changed by 15% until the first reversal point, after that, by 3%. The experiment was continued until the four reversal points were obtained. The average of the third and fourth reversal point scores was used as the sensitivity of the expression. Sensitivity was the difference calculated by subtracting expression level from 100(%); the sensitivity corresponding to 38% expression face was 62. We used the screen of a 15″ touch panel connected to a PC running C++ software based on Windows XP. Before the experimental session, a practice session was conducted. In the practice session, 100% expression images were displayed as stimuli and the participants were confirmed to be capable to match the same expression on the right, where six small faces of 100% expression were displayed as choices. The participants were also required to explain the emotion verbally to confirm that they recognized each emotion.

Statistical analysis

AD patients, ANC, and YNC were compared by using repeated-measured analysis of variance (ANOVA; 3 groups $\times$ 6 basic expressions) followed by *post hoc* testing with Bonferroni correction. According to *post hoc* analysis, significantly higher sensitivity in YNC compared with ANC was defined as age effects, and significantly higher sensitivity in ANC compared with AD patients was defined as AD effects. The data were analyzed using the Japanese version of SPSS for Windows version 19.0 (IBM Corporation, New York). Significant differences are set for two-tailed $p = 0.05$ for all analyses.

Results

The ages of the participants were 81.1±9.2 years in mild AD, 76.8±3.5 years in ANC, and 18.9±1.1 years in YNC, and there was no significant difference between age of AD patients and that of ANC by two sample *t*-test. Sensitivities of the three groups and comparisons are shown in Figure 2 and Table 1. There was a significant difference among three groups in perception of facial expressions. According to the *post hoc* analysis, both age and AD effects were observed for anger and surprise (anger: age effects $p = 0.031$, AD effects $p < 0.001$; surprise: $p < 0.001$, $p = 0.029$), whereas for happiness and fear, neither age effects nor AD effects were observed (happiness: $p = 0.138$,

Table 1. Age effects and Alzheimer disease effects

	HAPPINESS	SADNESS	SURPRISE	ANGER	DISGUST	FEAR
†YNC	86.7 ± 14.0	63.1 ± 22.9	81.1 ± 8.9	66.8 ± 15.1	55.5 ± 14.9	55.0 ± 15.3
§*YNC versus ANC*	*0.138*	*0.183*	*<0.001***	*0.031**	*<0.001***	*0.178*
††ANC	76.8 ± 16.8	48.3 ± 25.8	63.9 ± 14.3	55.0 ± 12.3	32.4 ± 19.2	43.9 ± 13.7
¶*ANC versus AD*	*1.000*	*0.048**	*0.029**	*<0.001***	*0.718*	*1.000*
AD	72.8 ± 15.8	25.3 ± 26.0	50.5 ± 18.4	23.4 ± 14.5	25.0 ± 14.6	37.3 ± 28.0

†YNC: young normal controls; ††ANC: aged normal controls; §age effects: significantly higher sensitivity of YNC in comparison with ANC; ¶AD effects: significantly higher sensitivity of ANC in comparison with AD. Both of the age and AD effects were shown by p values of intrasubject *post hoc* analysis with Bonferroni correction of 3 × 6 repeated measured ANOVA (three groups of YNC, ANC, and AD, and six expressions). $^*p < 0.05$, $^{**}p < 0.001$.

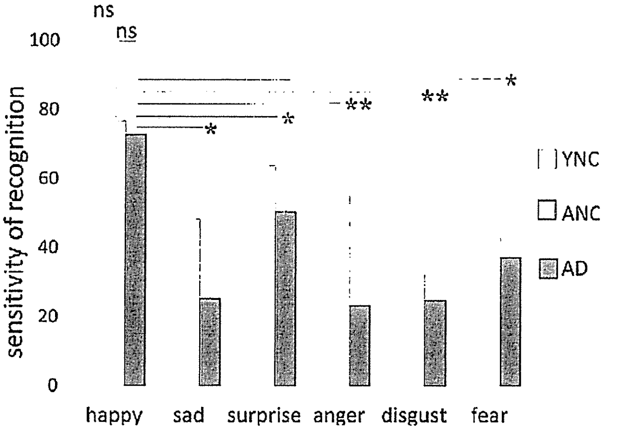

Figure 2. Results of sensitivities of the young normal controls (YNC), the aged normal controls (ANC), and the AD patients. Error bars indicate standard deviation. Regarding recognition of happy and fear faces, there was no significant difference between YNC and ANC, and ANC and AD patients. Regarding recognition of surprise and anger faces, there was significant difference between YNC and ANC, and ANC and AD patients. There was significant difference between ANC and AD in sad face recognition, and between YNC and ANC in disgust recognition. Within AD patients, sensitivity of happy face was significantly higher than that of other expressions. $^*p < 0.05$, $^{**}p < 0.001$.

$p = 1.000$; fear: $p = 0.178$, $p = 1.000$). For sadness, AD effects were observed ($p = 0.048$), whereas age effects were not ($p = 0.183$). However, for disgust, age effects were observed ($p < 0.001$), whereas AD effects were not ($p = 0.718$). Within AD patients, sensitivity of happiness was significantly higher than those of the other five expressions, and that of surprise was significantly higher than those of anger and disgust.

Discussion

This study showed that recognition of happy facial expressions was relatively preserved in AD patients. Recognition of happiness was significantly easier than recognition of five other expressions and there were no age effects or AD effects. Regarding negative expressions, age effects were observed in recognition of anger and disgust, and AD effects were observed in recognition of sadness and anger. Surprise had a neutral emotional valence and both effects were observed in surprise recognition.

The results from this study should be reliable because the task used involved a sophisticated matching task that improved on problems in previous studies to cancel confounding factors. In previous experimental settings, participants were required to match the expression of photos of different people. Thus, impairment in the matching could be a result of visuospatial dysfunctions rather than deficits in processing emotions (Ekman *et al.*, 1971). Upon misunderstanding of individual differences in facial features, the participants might fail to extract the emotional implications. The stimuli used in the present study were averaged faces with different emotional valence, where non-emotional features were shared. Thus, differences in features are directly related to emotional differences. Another merit of this matching task was to eliminate the cognitive process to convert perception to abstract verbal expression; abstract thinking and verbal recognition also decline in AD patients. The use of images of Japanese individuals for Japanese participants also eliminated irrelevant cognitive load. Social recognition, including emotional facial expression, has sociocultural implications, and expression of facial emotions could be influenced by cultural backgrounds (Ekman *et al.*, 1987; Shioiri *et al.*, 1999).

Adding to canceling confounding factors, another advantage of this method is the precise measurement of the sensitivity by using the intermediate level of expressions. In the often used experimental settings, the participants were required to classify the photos of typical emotional faces (100% in the present study) by emotional expression. According to a meta-analysis of 17 studies on emotion recognition and aging, the average of the stimuli of one emotion was around 7. Concerning happiness recognition, the magnitude of the difference between young and aged subjects is potentially masked by a ceiling effect, with young subjects scoring 98% or better in 15 out of 17 studies (Ruffman *et al.*, 2008). Such ceiling effects could exist in the experiments comparing aged subjects and AD patients, thus more sensitive tests with subtle stimuli are desirable. In the present study, we applied 1%–99% intermediate levels of expression, which enabled precise measures of sensitivity.

After eliminating the confounding factors of deficits in spatial processing of non-emotional facial features and in verbal processing to express emotions, positivity bias in ANC was shown, in that recognition of happiness was spared in comparison with YNC. In AD patients, recognition of happiness was spared in comparison with ANC. Hargrave *et al.* (2002) reported that AD patients showed selective impairment in labeling facial expressions of sadness compared with ANC. The results were not identical, as there were differences in the methods used to eliminate the confounding factors of facial features of different people. Hargrave *et al.* (2002) tried to remove the factors by analysis. The experimental setting involved matching the emotion displayed on the reference face with one of six simultaneously presented alternatives, and all seven photographs were faces of different people. A multivariate analysis of covariance (MANCOVA) model was adapted using each subject's score on the facial identity matching task as a covariate. The advantage of the present study is eliminating the confounding factors at the experimental phase.

The mechanism of positivity recognition bias in aged individuals and AD patients remains unproven. Positivity bias in aged individuals was explained by lifetime perspective motivational changes; as the time perspective is reduced, current emotional goals associated with well-being become more important (Carstensen *et al.*, 1999). Consequently, aged individuals would tend to allocate more cognitive resources to improve emotion regulation, and their information processing was characterized by a positivity bias (Mather and Carstensen, 2005; Mather and Knight, 2005; Brassen *et al.*, 2011). Within this framework, positivity bias in facial emotional recognition could be explained by shifts in attention allocation for positive stimuli (Mather and Carstensen, 2005; Goeleven *et al.*, 2010).

Concerning such allocation of cognitive resources to emotion regulation, capacities of cognitive resources should be considered. Mather and Knight reported that aged individuals with superior cognitive abilities were more likely to exhibit positivity bias (Mather and Knight, 2005). In line with the report, the positivity bias should be reduced in AD patients with cognitive decline. However, the experiment was conducted on memory, and if the allocation occurred only in the remembering phase, and not the memorizing phase, the explanation could not be applied to facial recognition. Goeleven *et al.* (2010) suggested that increased age is associated with reduced allocation of resources to negative stimuli, and the explanation could also be true in AD patients.

The present study showed decreases of negative emotion recognition and relatively preserved positive recognition. Our results are in line with the conclusions based on the meta-analysis of Murphy and Issacowitz, which revealed an age-related decrease of negativity preference as compared to an increased positivity preference (Murphy and Isaacowitz, 2008). The above explanations are still hypotheses, and specifying the interaction between cognitive decline and emotion processing would be a valuable topic for future research.

Regarding study limitations, it is possible that recognizing happy facial expressions was easier, as this was the only positive emotion in the study. The differentiation of the four negative expressions, sadness, anger, disgust, and fear, was more difficult. Thus, the results should be confirmed in an experimental setting using stimuli with three facial expressions: happiness, a negative emotion, and a neutral expression.

This study showed that recognition of happy facial expressions was relatively preserved in AD patients; the results could be generalized to other ethnicity because emotional facial recognition is basically universal. These experimental results may be useful if they are implemented in a way to improve the daily life of AD patients. Caregivers should take advantage of cues from happy facial expressions to provide beneficial care.

Conflict of interest

None.

Description of authors' roles

Y. Maki designed the study, collected and analyzed the data, and wrote the paper. H. Yoshida designed the study and did the computer programming for the task. T. Yamaguchi collected and analyzed the data. H. Yamaguchi supervised the study and wrote the paper.

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Pitfall Intention Explanation Task with Clue Questions (Pitfall task): assessment of comprehending other people's behavioral intentions in Alzheimer's disease

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ABSTRACT

Background: In Alzheimer's disease (AD) patients, deficits in contextual understanding and intentions/beliefs of other people (theory of mind; ToM) cause communication problems between patients and caregivers. To evaluate deficits of contextual understanding/ToM, we developed the Pitfall Intention Explanation Task with Clue Questions (Pitfall task).

Methods: We recruited 26 healthy older adults in clinical dementia rating (CDR) 0, and 62 outpatients: 12 with amnestic mild cognitive impairment (aMCI) in CDR 0.5; 36 mild AD in CDR 1; and 14 moderate AD in CDR 2. The Pitfall task consists of a single-frame cartoon that shows a character's intention and seven serial questions that provide clues for contextual understanding/ToM.

Results: The total score (0–7) was decreased with progression of AD (CDR 0, 5.4 ± 2.6; CDR 0.5, 3.7 ± 2.7; CDR 1, 1.9 ± 3.1; CDR 2, 0.0 ± 0.0; respectively). In CDR 0, two-third of the participants responded correctly without clue questions. In CDR 0.5, one-third of the participants responded correctly without clue questions, and half of them understood with the help of the clue questions. In CDR 1, one-fourth of the participants responded correctly without clue questions, and the clue questions did not increase the correct response. In CDR 2, none responded correctly. Additionally, the Pitfall task provided the chance for patients' families to observe patients' responses.

Conclusion: Contextual understanding/ToM, a kind of social cognition, was impaired with progression of AD. The Pitfall task evaluates the function quickly with low burden for memory function, and may provide helpful clues for caregivers to achieve good communication with AD patients.

Key words: dementia, carers, behavioral and psychological symptoms of dementia (BPSD), cognitive assessment, family therapy

Introduction

Evaluating communication problems between caregivers and patients is important, when caring for Alzheimer's disease (AD) patients. These problems could potentially arouse feelings of anxiety, and lead to conflict in their relationship, depression, social isolation, and caregiver burden (Potkins *et al.*, 2003; Savundranayagam *et al.*, 2005). Furthermore, communication problems trigger behavioral and psychological symptoms of dementia (BPSD) in AD patients (Gitlin *et al.*, 2007). Therefore, education for caregivers to attenuate communication problems is effective in reducing BPSD (Ripich *et al.*, 1998; Gitlin *et al.*, 2007). Thus, in AD patients, it is important to assess the communication problems, one of the social skill deficits, in order to provide information to caregivers for appropriate care with attenuated communication problems.

Communication skills include both linguistic and non-linguistic skills. Linguistic communication skills, such as subtle spontaneous language, idiosyncratic pragmatic skill, linguistic changes in verbal expression, and referential communication, were reported to decline from the mild cognitive impairment (MCI) stage or very early stage of AD (Carlomagno *et al.*, 2005; Forbes-McKay and Venneri, 2005; Cuetos *et al.*, 2007; de Lira *et al.*, 2011). Therefore, the ability to comprehend complex references or difficult phrases

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(e.g. understanding the story line of a TV drama or a complex conversation) is impaired with progression of AD. We have also reported impaired comprehension of figurative proverbs, which is associated with disinhibition, excuse, and confabulation in patients with dementia (Yamaguchi *et al.*, 2011).

Social cognition, one of the higher cerebral functions, includes recognition of emotions, theory of mind (ToM), and behavioral regulation, and its deficits may cause communication problems. The ToM, which requires both linguistic and non-linguistic skills, is reported to be preserved in mild to moderate AD, because failure in false-belief task, a representative ToM test, is secondary to impairment of other functions such as memory (Gregory *et al.*, 2002; Zaitchik *et al.*, 2004; Fernandez-Duque *et al.*, 2009). The ToM tasks were originally developed for children (Baron-Cohen *et al.*, 1985). Therefore, we tried to develop a kind of ToM task for AD, where memory function is impaired.

We focused on deficits in contextual understanding and intentions/beliefs of other people (ToM), rather than linguistic aspects. As a brief task available in a clinical setting, we developed a new cognitive task, the Pitfall Intention Explanation Task with Clue Questions (Pitfall task), to assess the ability for contextual understanding/ToM by explanation of a character's behavioral intentions/beliefs in a cartoon. The task consisted of a single-frame cartoon and seven clue questions to help contextual understanding/ToM step-by-step. We hypothesized that we could demonstrate decline of contextual understanding/ToM with AD progression qualitatively and quantitatively by using a kind of ToM task associated with low burden for memory function.

Methods

Participants

Healthy older adults (n = 26) were recruited from community dwellers who participated in the "Prevention of mental decline project" in Takasaki City, Gunma, Japan, and outpatients who visited the Geriatrics Research Institute and Hospital, Gunma, Japan. These participants were judged as normal, corresponding to clinical dementia rating (CDR) 0 based on the results of cognitive tests and medical interviews by a neurologist specializing in dementia.

We recruited 62 participants, who were diagnosed as having amnestic MCI (aMCI) or AD in an outpatient clinic. All the participants were classified according to CDR by the neurologist. The criteria of aMCI, mild AD, and moderate AD were CDR 0.5 (n = 12), CDR 1 (n = 36), and CDR 2 (n = 14), respectively. In this study, the AD patients were diagnosed based on the criteria of the National Institute of Neurological and Communicative Disorders and Stroke and Alzheimer's Disorders and Related Disorders Association (NINCDS-ADRDA) (Dubois *et al.*, 2007). Similarly, the aMCI patients were diagnosed based on a previous study (Petersen, 2007). CDR 0.5 was regarded as MCI, although a different classification was proposed, whereby CDR 0.5 encompasses both mild and earlier dementia (Reisberg *et al.*, 2008) or very mild dementia (Grundman *et al.*, 2004). Exclusion criteria were: problems with alcoholism, motor deficits such as paralysis, or neurological and psychiatric disorders other than the primary diagnosis of AD or aMCI.

The demographic data and clinical characteristics are shown in Table 1. All the participants reported normal or corrected-to-normal vision, and they were unaware of the purpose of the experiment. The Ethics Board of Gunma University School of Health Sciences approved all procedures (nos. 21–27), and signed informed consent was obtained. All the participants underwent the Mini-Mental State Examination (MMSE) (Folstein *et al.*, 1975).

Procedure

In the present study, we developed a new task. The task consisted of a single-frame cartoon (19 cm long and 25.5 cm wide), which was drawn on A4-size paper, and seven serial questions (Figure 1). The Q2–Q6 are clue questions. The cartoon depicts a scene of a misbehaving child: the person in the center is hiding behind a tree and imagines that the other person (on the left) falls into a pitfall (top right circle).

Protocol

1. The cartoon is placed in front of the sitting participant.
2. The examiner asks the participant whether the participant can see all parts of the cartoon or not, and then asks seven simple questions:
   - Q1: "What is happening in this cartoon?"
   - Q2: "What do you think this person on the left is doing?" (The examiner gives instructions by pointing to the leftmost person.)
   - Q3: "What is this person in the center doing?" (Pointing to the center person.)
   - Q4: "What is this?" (Pointing to the top right circle.)
   - Q5: "What is this?" (Pointing to the bottom left pitfall.)
   - Q6: "What do you think is going to happen to the person on the left?" (Pointing to the leftmost person.)

Table 1. Demographics and clinical characteristics

	ALL	CDR 0[a]	CDR 0.5[b]	CDR 1[c]	CDR 2[d]
Number	88	26	12	36	14
Male/female	30/58	11/15	6/6	12/24	1/13
Age, year	77.1 ± 6.5	73.2 ± 6.3	74.4 ± 5.0	79.2 ± 5.8	81.0 ± 5.5
Education, year	10.4 ± 2.7	12.5 ± 2.4	9.5 ± 2.8	9.5 ± 2.1	9.8 ± 2.4
MMSE	22.4 ± 5.9	28.9 ± 1.3	25.0 ± 3.2	19.9 ± 3.3	14.1 ± 3.1
Total task score	2.9 ± 3.2	5.4 ± 2.6	3.7 ± 2.7	1.9 ± 3.1	0.0 ± 0.0

Note: CDR – Clinical dementia rating; MMSE – Mini-Mental State Examination. Data are presented as mean ± SD.
[a]Healthy older adult.
[b]Amnestic mild cognitive impairment (aMCI).
[c]Mild AD.
[d]Moderate AD.

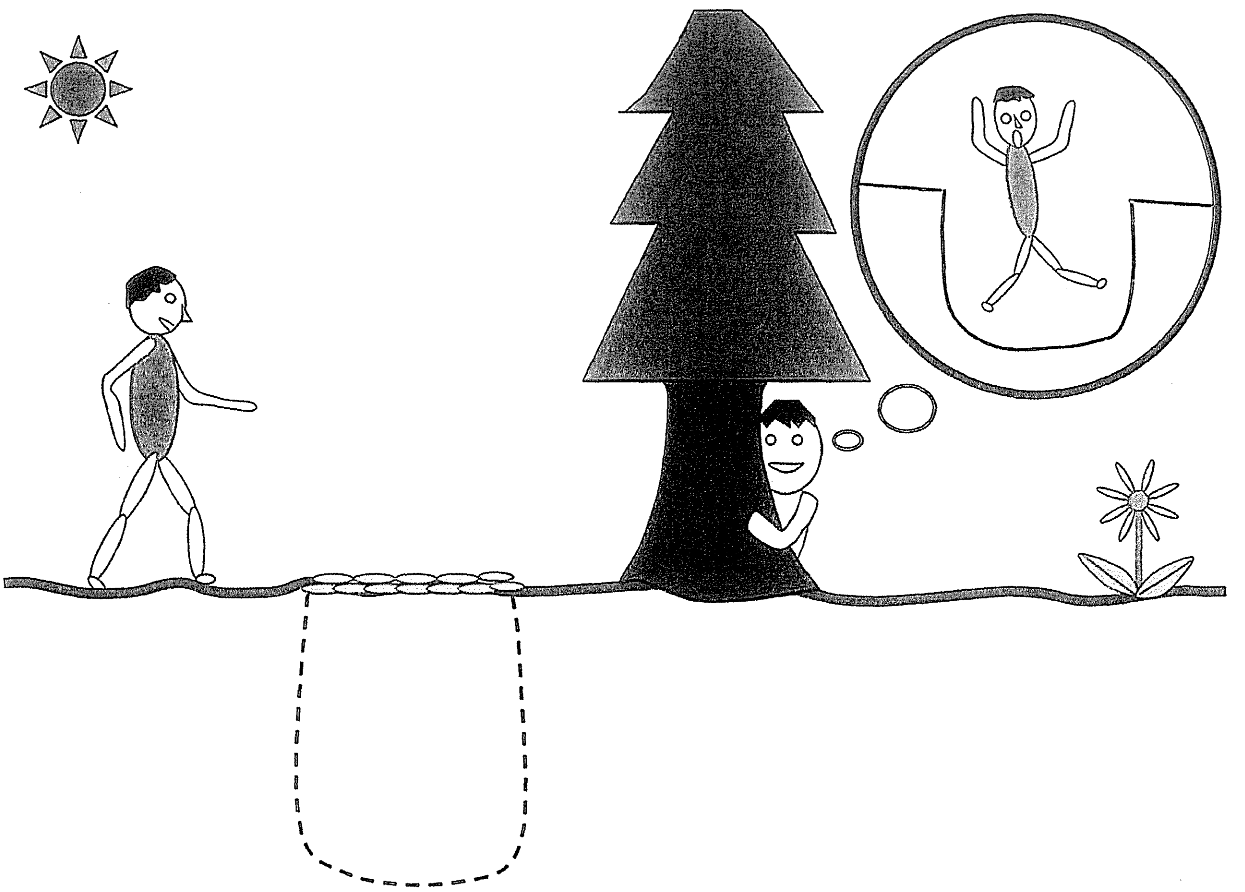

Figure 1. The cartoon for the Pitfall Task. The single-frame cartoon depicts a scene of a misbehaving child: the person in the center is hiding behind a tree and imagines that the other person (on the left) falls into a pitfall (top right circle).

Q7: "What do you think the person in the center intends to do?" (Pointing to the center person.)

3. If the participant says nothing within 30 sec or does not understand the question, skip the question. The participant is required to respond within 1 minute for each question.
4. The examiner records the response.
5. If visual loss is suspected, the participant's visual impairment can be checked by pointing to the flower and the sun, and asking the participant what they are.

Guideline for scoring

The total task score is 0–7 points (1 point for each question), and the score is determined by whether each question is responded to correctly or not. Some examples are as follows:

Q1: If the participant can explain the scene correctly, with terms such as "Mischief" or "Pitfall," the score is 1 point. If the participant does not explain the correct context, for example "There are three children playing hide-and-seek" or "Walking and resting under the shade of a tree," the score is 0 points.
Q2: If the response is similar to "He (or she) is walking and does not know about the hole" or "He is walking and does not know about the pitfall," the score is 1 point.
Q3: If the response is similar to "He (or she) is looking at another child who is walking and does not know about the pitfall, and is imagining that the other (left) child will fall into the pitfall," the score is 1 point.
Q4: If the response is similar to "This is an image of his (center child's) expectation," the score is 1 point.
Q5: If the response is similar to "Pitfall" or "A trap for the child on the left," the score is 1 point.
Q6: If the response is similar to "Fall into a pitfall" or "Walk into a trap," the score is 1 point.
Q7: If the response is similar to "He (or she) wanted to surprise his (or her) friend (or another person) with a pitfall that he (or she) made" or "He (or she) is annoying his (or her) friend (or another person) with a malicious and intentional act (or with a pitfall)."

Data analyses

We calculated the total task scores, and analyzed the number of correct responses and the effect of clue questions for each CDR group. Furthermore, the participant's responses were analyzed qualitatively.

To analyze the CDR group differences of the total task scores, we used analyses of covariance (ANCOVA) with covariates of age, educational years, and genders to exclude these effects. *Post hoc* analysis for each CDR group was conducted with Bonferroni correction in all 88 participants. We also analyzed by further adding MMSE scores as covariates. We examined the relationship of the total task scores with MMSE scores by Pearson's product–moment correlation coefficient in all 88 participants. We did not assess test–retest reliability because of learning effects. All statistical analyses were performed with the Japanese version of SPSS 19.0 for Windows (IBM Com., New York, NY). The results are reported at a significance level of $p < 0.05$.

Results

The total score and its relationship with cognitive tests

The demographic data and the total score for all the participants are shown in Table 1. The total task score (mean ± SD) in CDR 0 (5.4 ± 2.6, n = 26) was the highest of the four CDR groups, and next was that in CDR 0.5 (3.7 ± 2.7, n = 12). The mean total score decreased further in CDR 1 (1.9 ± 3.1, n = 36), and no patients scored any points in the CDR 2 (0.0 ± 0.0, n = 14). The total task score decreased significantly with progression of AD, as demonstrated by ANCOVA with covariates of age, educational years, and genders ($F_{6,81} = 10.65$, $p < 0.001$). The results of a *post hoc* analysis with Bonferroni correction indicated a significant difference between CDR 0 and CDR 1, and between CDR 0 and CDR 2 ($p = 0.004$, $p < 0.001$; respectively; Figure 2). Even when the MMSE score was further added to the covariates, the total task score decreased significantly with progression of AD ($F_{7,80} = 9.19$, $p < 0.001$), and significant differences were shown between CDR 0 and CDR 1 and between CDR 0 and CDR 2 on *post hoc* analysis ($p = 0.02$, $p = 0.02$; respectively).

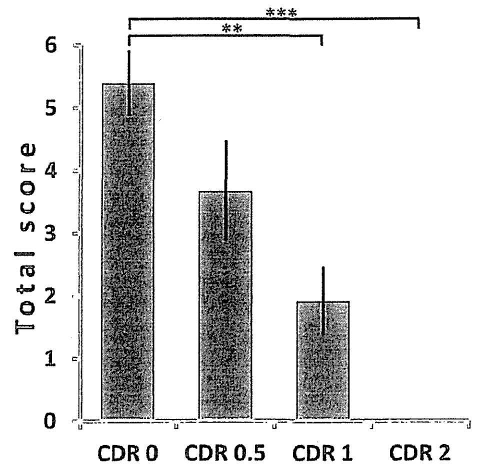

Figure 2. The total scores in the CDR groups. Total score (mean ± SE) was decreased with progression of AD (CDR 0, 5.4 ± 0.5; CDR 0.5, 3.7 ± 0.8; CDR 1, 1.9 ± 0.5; CDR 2, 0.0 ± 0.0; respectively). $^{**}p < 0.01$, $^{***}p < 0.001$ (ANCOVA with covariates of age, educational years, and genders).

The correlation between the total task scores and MMSE scores in all participants (n = 88) was significant and moderate ($r = 0.51$, $p < 0.001$).

When did participants understand the context?

The question at which participants understood the context of the cartoon was analyzed in each CDR group (Figure 3).

In CDR 0, two-third of the participants (65.4%, n = 17) responded correctly from the first question (Q1), and some understood at Q2 (3.8%, n = 1), Q4 (7.7%, n = 2), Q5 (3.8%, n = 1), and Q6 (7.7%, n = 2). The correct response increased up to 88.5% (23/26) at Q7.

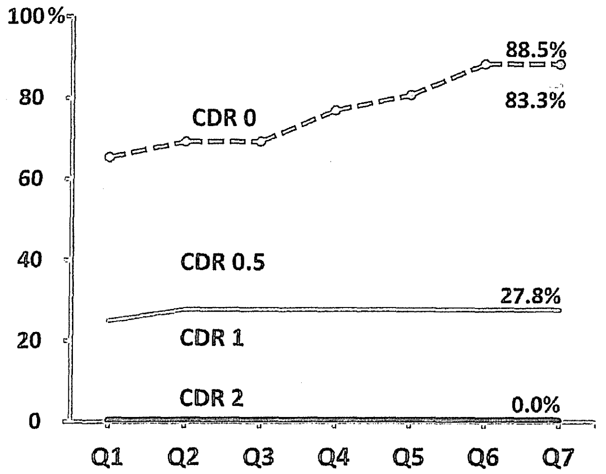

Figure 3. Rate of correct response (contextual understanding/ToM). In CDR 0, most of the participants understood the context from the first question (Q1). In CDR 0.5, the rate of correct response at Q1 was one-third, and the rate increased between Q4 and Q6. In CDR 1, one-fourth of the participants understood at Q1, and the rate did not increase with the clue questions. In CDR 2, none of the participants responded correctly.

In CDR 0.5, the rate of correct response at Q1 was only one-third (33.3%, $n = 4$). Many participants understood at Q4 (8.3%, $n = 1$), Q5 (16.7%, $n = 2$), and Q6 (25.0%, $n = 3$) with the exclusion of two participants (16.7%) who did not understand. The rate of correct response increased between Q3 and Q6, and finally became 83.3% (10/12). The rate of correct response at the last question (Q7) in CDR 0.5 was comparable with that in CDR 0.

The result in CDR 1 was interesting. Although a quarter of participants understood the context at first Q1 (25.0%, $n = 9$), none understood at Q3–Q7. They did not understand with the help of clue questions, except one participant who understood the context at Q2. Thus, the rate of correct response did not increase with each clue question, and was maintained at 27.8% (10/36) to the last question in CDR1.

In CDR 2, none of the participants understood the context at any question.

Characteristic incorrect responses in each CDR group

At Q1, the most common incorrect response in CDR 0 to CDR 1 was an explanation of the interrelation between the two characters in the cartoon; the typical response was "They are playing hide-and-seek" or "He is looking for his friend who is hiding behind the tree." The ratio of this type of response to all the incorrect responses decreased with progression of AD (66.7% of incorrect responses in CDR 0, $n = 6$; 62.5% in CDR 0.5, $n = 5$; 44.4% in CDR 1, $n = 12$; 7.1% in CDR 2, $n = 1$; respectively) (Figure 4a). In contrast, incorrect responses that lacked interrelation between the characters, such as "There is a child" or "There is a flower" increased with progression of AD (11.1% of incorrect responses in CDR 0, $n = 1$; 12.5% in CDR 0.5, $n = 1$; 18.5% in CDR 1, $n = 5$; 28.6% in CDR 2, $n = 4$; respectively) (Figure 4a). These responses did not include interrelation between the two characters. Participants in CDR 2 had difficulty in seeing the cartoon as a whole.

The characteristic incorrect responses at Q2–Q6 reflected a part of the cartoon; for example,

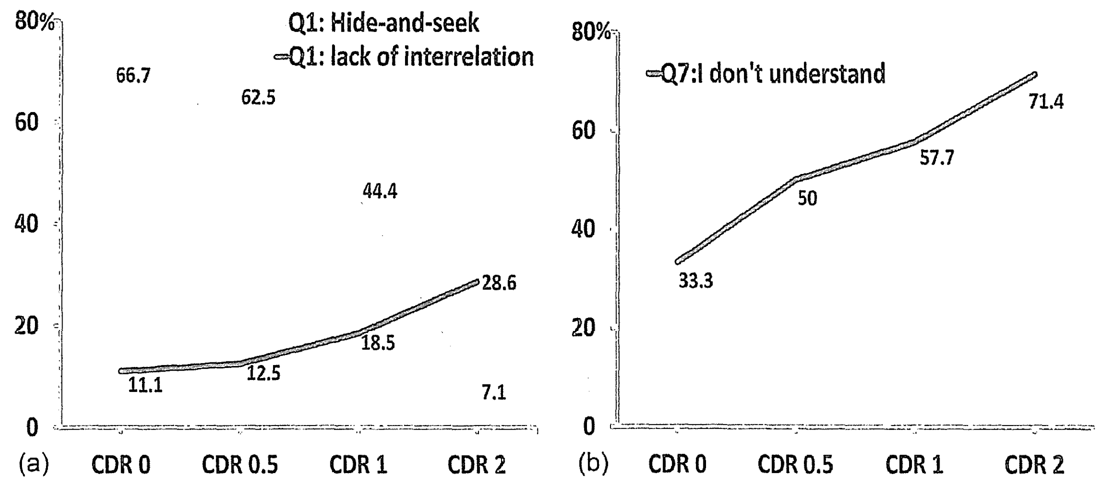

Figure 4. The ratio of response to all incorrect responses for Q1 and Q7. (a) At Q1, the ratio of incorrect response of "Hide-and-seek," which indicated an interrelation between the two characters in the cartoon, decreased according to AD progression, whereas explanations that lacked interrelation between the two characters increased. (b) At Q7, the ratio of incorrect response of "I don't understand" to total incorrect response increased according to AD progression, and was prominent at CDR2.

"Walking or jogging" in Q2, "Climbing a tree" in Q3, and "Throwing one's arms in the air in celebration" in Q4. However, no interrelation between each character was described. Furthermore, for Q5, many participants who failed to understand the context of the cartoon responded such as "A hole in the ground" or "Hole," but not "Pitfall." Similarly, for Q6, they provided responses such as "He is just walking" or "He is walking through the park (without any change)," even though they described a hole in Q5.

For Q7 (Figure 4b), the most common incorrect response was "I really don't understand it" or "Hmmm…I can't make any sense of this" (3.8% of incorrect responses in CDR 0, $n = 1$; 50.0% in CDR 0.5, $n = 1$; 55.7% in CDR 1, $n = 15$; 71.4% in CDR 2, $n = 10$). Many participants in CDR 2 said "I don't understand" without thinking, whereas the participants in CDR 1 provided several possibilities as the response.

Discussion

Findings of the present investigation

In the present study, the total score of the Pitfall task in mild (CDR1) to moderate (CDR2) AD participants was significantly lower than that in healthy older adults (CDR 0). Even when the MMSE score was further added to the covariate of ANCOVA, the total task score also decreased significantly with progression of AD. Furthermore, the Pitfall task showed mild correlation with the MMSE score, indicating that the Pitfall task partly reflects comprehensive cognitive function, but mostly reflects a kind of social cognitive function.

As previously noted, there is considerable agreement that communicative disability is a prominent symptom of AD, and studies have focused on various aspects of linguistic skill disorders (Carlomagno *et al.*, 2005; Forbes-McKay and Venneri, 2005). These studies often used the picture description task, such as the Cookie Theft Picture, which was originally developed for aphasia (Goodglass and Kaplan, 1983) to assess linguistic changes in verbal expression or subtle spontaneous language decline, but not to assess intentions/beliefs of characters in the cartoon (ToM) (Bschor *et al.*, 2001; Carlomagno *et al.*, 2005; Cuetos *et al.*, 2007).

Some studies showed that AD patients succeeded in first-order false–belief tasks, but failed in second-order false–belief tasks, and suggested that any deficits on ToM testing are secondary to impairment in other functions such as memory and/or verbal skills (Gregory *et al.*, 2002; Zaitchik *et al.*, 2004; Fernandez-Duque *et al.*, 2009). However, it is possible that the second-order false–belief task was too difficult, because the sentences used are complex and require memory and other cognitive functions. Our current task was designed to minimize these factors.

In the course of developing the Pitfall task, we tried several single-frame cartoons including other people's intentions/beliefs, and determined the task and clue questions based on a difficulty level where most healthy older adults perform contextual understanding/ToM without clue questions. The task is brief, easy to administer in the outpatient clinic, and less stressful for patients than conventional cognitive tests.

The Pitfall task is associated with seven serial questions, which gradually provide clues to understand the whole context: the Q1 is not a clue question, Q2 and Q3 are clues about the character's objective context, Q4–Q6 are clues to understand the whole context of the cartoon, and Q7 is a direct question of the character's intention.

In this study, most of the participants in CDR 0 understood the context at Q1 without clue questions. In contrast, about half of the participants in CDR 0.5 understood with helpful clues (Q4–Q6), suggesting that social skills such as contextual understanding/ToM start to become impaired from the aMCI stage. Many of the participants in CDR 0.5 understood the context at Q4–Q6, suggesting that the clues for aMCI patients may promote contextual understanding/ToM, including understanding of other people's intentions. Although, about one-fourth of the participants in CDR 1 understood the context at Q1 or Q2, none of the remaining participants understood at Q3–Q7. Furthermore, no participants in CDR 2 understood the context of the cartoon. Thus, contextual understanding/ToM is mildly impaired in early AD patients and impaired more severely with progression of AD.

There is evidence that visuospatial attention declines in early AD (Parasuraman *et al.*, 2000). A study by Rösler *et al.* (2005) suggested reduced efficiency of visual search in AD, which is caused by reduced control of attentional zoom and disengagement of attention from peripheral targets. Thus, some of the incorrect responses in the present study may have been related to deficits of visual attention or simultanagnosia, which is associated with parieto-occipital damage (Huberle and Karnath, 2010).

Using the findings of the Pitfall task for AD care

The communication problems between caregivers and patients trigger BPSD (Potkins *et al.*, 2003; Gitlin *et al.*, 2007). Moreover, family education, which attenuated communication problems, was effective in reducing BPSD (Ripich *et al.*, 1998; Gitlin *et al.*, 2007).

According to the current results of the Pitfall task, we recommend promising strategies for caregivers to provide appropriate explanations or helpful clues for AD patients. The majority of aMCI patients had difficulty in understanding context without explanation. If the patients understand the context with clue questions, a simple explanation may be effective. In the current study, some participants in CDR 0 and CDR 0.5, who did not understand the context, quickly understood after the examiner's explanation and said things such as "He falls into a hole...... Oh! I see!" or "This is a pitfall! The other child is playing a funny trick on him!". However, in CDR 1 and CDR 2, only a few participants understood the context, even after the examiner's explanation. If mild (CDR1) and moderate (CDR 2) AD patients fail to understand the context with clue questions, detailed explanations or clues could cause confusion. The current study indicated that social reasoning skills were considerably poorer in patients with mild AD and further deteriorated in patients with moderate AD. These findings suggest that caregivers should provide simple explanations for patients in the milder stages of AD, and factual information with minimal explanation for patients in the moderate stages of AD.

In the present study, we allowed patients' families to observe the patients' responses during the task. The family caregivers showed various responses; some expressed feelings of shock and disappointment on seeing the results or reprehended the patients' mistakes, while other caregivers nodded encouragingly with a warm smile even if the patient responded with incorrect responses or did not understand. We observed some communication problems between caregivers and patients through caregivers' responses to patient's mistakes during the Pitfall task. The Pitfall task could provide helpful clues to assist caregivers for better understanding of communication problems in AD patients.

As limitations, the Pitfall task assessed only one narrow area of social cognition. Vasse *et al.* (2010) suggest in their systematic review that there is insufficient evidence of communication strategies for people with dementia. Effective use of the Pitfall task in successful care should be demonstrated in our future study.

Conflict of interest

None.

Description of authors' roles

T. Yamaguchi designed the study, collected the data, carried out the statistical analysis, and wrote the paper. Y. Maki collected the data and wrote the paper. H. Yamaguchi supervised the design of study, collected the data, and wrote the paper.

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Author Contributions: T. Strandberg had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: T. Strandberg. Acquisition of data: T. Strandberg, Pitkala, Tilvis. Analysis and interpretation of data: T. Strandberg, A. Strandberg, Pienimaki, Pitkala, Tilvis. Drafting of the manuscript: T. Strandberg, Pienimaki. Critical revision of the manuscript for important intellectual content: T. Strandberg, A. Strandberg, Pienimaki, Pitkala, Tilvis. Statistical analysis: T. Strandberg. Obtained funding: T. Strandberg, Tilvis. Administrative, technical, or material support: Pitkala, Tilvis.

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INTERVENTION USING A COMMUNITY-BASED WALKING PROGRAM IS EFFECTIVE FOR ELDERLY ADULTS WITH DEPRESSIVE TENDENCIES

To the Editor: Dementia has become a socioeconomic burden in Japan because of the increasing elderly population, and delaying the onset of dementia would significantly reduce its incidence. Under the Japanese public Long-Term Care Insurance Act, municipality-led interventions for the prevention of mental decline are encouraged in accordance with the concept of community-based rehabilitation.[1] A previously reported randomized controlled trial demonstrated the efficacy of a walking program in preventing mental decline in elderly individuals with subjective memory complaints, and significant benefits were shown ina categorical word fluency test related to frontal lobe function.[2]

This intervention aimed at producing synergetic effects of aerobic exercise and social interaction based on the five principles of brain-activating rehabilitation for dementia: maintaining a pleasant atmosphere, enhancing participants' motivation and self-directed thinking, maintaining interactive communication, providing social roles for participants, and providing positive feedback for learning.[3] It has been reported that aerobic exercise such as walking is beneficial for prevention of mental decline, as well as for slowing the progression of dementia.[4] A rich social network and interaction may protect against mental decline,[5] whereas social isolation is associated with risk of mental decline.[6] Social isolation and loneliness is fundamentally associated with depression in senile individuals.[7] Thus, the previous study was continued with a larger population, and the relationship between participants' depressive tendency and improvement in word fluency tests was reviewed.

The intervention participants were 138 community residents aged 65–80. Based on a medical examination, 106 participants had no cognitive decline (normal controls, NC), and 32 were diagnosed with mild cognitive impairment (MCI). All participated in a 90-minute intervention program conducted once a week for 12 weeks. The intervention was conducted as described previously.[2] The program consisted of a 30-minute exercise period and 60 minutes of small-group work with five to eight participants. Evaluation was conducted twice: at a baseline assessment before the intervention and at a postintervention assessment. Function of word fluency was measured using a categorical test of "animals," and depressive tendency was measured using a self-completed questionnaire

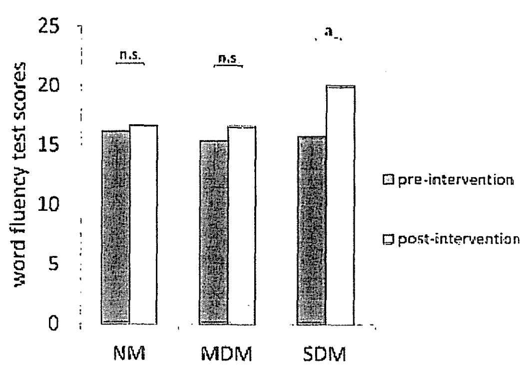

Figure 1. Results of word fluency test. Participants were classified into three groups according to Geriatric Depression Scale score; a score of 0–4 indicated normal mood (NM), 5–9 indicated a mild tendency toward depressed mood (MDM), and 10–15 indicated a severe tendency toward depressed mood (SDM). A higher score on the word fluency test indicates improvement. $^{a}P < .001$.

from the Geriatric Depression Scale (GDS);[8] a score of 0–4 indicated normal mood (NM), 5–9 indicated a mild tendency toward depressed mood (MDM), and 10–15 indicated a severe tendency toward depressed mood (SDM).

The effects of the intervention were analyzed in the participants whose attendance rate was greater than 80%. There were 117 participants (mean age ± standard deviation 72.4 ± 4.3, 11.9 ± 2.6 years of education; 36 male and 81 female; 91 NC and 26 MCI). Participants were divided into three groups according to baseline GDS score (79 NM, 31 MDM, 7 SDM). Scores on a word fluency test and GDS were analyzed using two by three analysis of covariance with covariates of age, sex, and years of education: two terms for pre- and postintervention and three groups for NM, MDM, and SDM. The Japanese version of SPSS for Windows version 19.0 (IBM Corp., New York, NY) was used, and statistical significance was set as $P < .05$. The ethics board of Gunma University School of Health Sciences approved all procedures, and written informed consent was obtained from all participants.

The results of the word fluency test were significantly different between the groups ($F(2,111) = 5.345$, $P = .006$), and within-subject post hoc analysis showed significant improvement only in the SDM group (NM, preintervention 16.2 ± 4.2, postintervention 16.7 ± 4.9, $P = .13$; MDM, preintervention 15.4 ± 3.8, postintervention 16.6 ± 4.7, $P = .06$; SDM, preintervention 15.7 ± 2.9, postintervention 20.0 ± 3.7, $P < .001$; increase indicated improvement; Figure 1). In addition, the attendance rate of each SDM participant was greater than 80%, and depressive mood was ameliorated. The GDS results were significantly different between the groups ($F(2, 111) = 8.304$, $P < .001$), and within-participant post hoc analysis showed amelioration in MDM and SDM (NM, preintervention 1.6 ± 1.4, postintervention 2.0 ± 2.1, $P = .16$; MDM, preintervention 6.4 ± 1.4, postintervention 5.5 ± 2.0, $P = .02$; SDM, preintervention 11.0 ± 1.0, postintervention 8.9 ± 2.5, $P = .003$; decrease indicated amelioration).

These results suggest that this intervention provided dual benefits in cognitive function and amelioration of depressive mood in community residents with depressive tendencies. Presenile depressive states are common in elderly individuals, and depressive state and withdrawal related to depressive mood have been found to be risk factors for dementia. Thus, this intervention may be worthwhile for community-based rehabilitation programs. The intervention reported here involved a small group of subjects, although the intervention is continuing, and the results will be confirmed in a larger population as well as longitudinal follow-up of participants.

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Anosognosia: Patients' Distress and Self-awareness of Deficits in Alzheimer's Disease

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Abstract

We aimed to study how patients with mild cognitive impairment (MCI) and Alzheimer's disease (AD) suffer from awareness of their deficits. Self-awareness was assessed using the Anosognosia Questionnaire for Dementia in 12 pairs of MCI outpatients and caregivers, 23 with mild AD, and 18 with moderate AD. The discrepancy between patient's and caregiver's evaluation (anosognosia) became greater as AD progressed. The predictors of patients' distress, shown by multiple linear regression analyses, were awareness of decline in intellectual or social functioning; self-awareness of deficits in remembering appointments in MCI; in remembering appointments, writing, mental calculation, and understanding the newspaper in mild AD; and in mental calculation and doing clerical work in moderate AD. Caregivers assumed the predictors of patients' distress differently: awareness of deterioration of memory in MCI and mild AD, and basic activities of daily living in moderate AD. Understanding patients' disability from patients' perspective is required for successful care.

Keywords

Alzheimer's disease, anosognosia, self-monitoring, self-awareness, empathy

Introduction

Deficits in self-awareness of disease, anosognosia, has been recognized as one of the typical symptoms in Alzheimer's disease (AD).[1] The unawareness of impairment is manifested in several domains, including memory and other cognitive functions, and psychological and behavioral functions.[2-4] As for neural substrates of self-awareness, previous research has identified involvement of posterior dorsomedial regions of the parietal lobe including the precuneus and the temporoparietal junction, as well as the prefrontal cortex, in experiments with healthy volunteers.[5-7] The experiments in patients with AD showed that those areas are related to deficits in self-awareness[8-10] and decline of regional cerebral blood flow is observed from the early stages of disease.[11-13] The finding is consistent with the symptomatic changes occurring as neurodegeneration progresses; self-awareness gradually deteriorates as the disease progresses.[4,14]

These neuropsychological findings are beneficial if they are implemented to care for patients with AD. Previous studies reported that behavioral and psychological symptoms of dementia (BPSD) could be caused by deficits of self-awareness.[15-17] From the caregivers' perspective, BPSD increases caregiver distress.[18] However, it is essential to understand the perspective of patients for treatment and care of BPSD.[19,20] To our knowledge, few studies have tried to elucidate the awareness of the deficits from the patients' perspective. For a better understanding of patients' perspective, we assessed the self-awareness of patients and analyzed their distress caused by self-awareness of their deficits. To understand the discrepancy, we also assessed caregivers' perspectives of patients' abilities and how the caregivers assessed patients' distress. We hypothesized that patients retain self-awareness of deficits partially and/or insufficiently and feel distressed by self-awareness at least in the early stage of AD, which the caregivers' might assess differently. The BPSD could result from such misunderstanding of how patients feel, rather than objective assessment of function. It would contribute to beneficial care of

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Table 1. Demographic Data[a]

CDR	n	Gender, n (M, F)	Mean ± SD Age, years	Education, years	MMSE
0.5	12	(2, 10)	74.8 ± 5.0	10.5 ± 2.3	26.9 ± 1.5
1	23	(9, 14)	79.6 ± 7.8	9.4 ± 2.1	19.9 ± 4.1
2	18	(3, 15)	82.3 ± 17.8	9.4 ± 3.5	12.5 ± 5.7

Abbreviations: CDR, Clinical Dementia Rating scale; M, male; F, female; MMSE, Mini-Mental State Examination; SD, standard deviation.
[a] There were no significant differences among groups in age ($P = .193$), gender ($P = .185$, chi-square test), or education ($P = .535$). Scores on MMSE were significantly different among groups ($P < .001$).

patients with AD to understand patients' distress related to self-awareness of deficits.

Methods

The participants were 53 pairs of outpatients and their caregivers: 12 amnesic patients with Clinical Dementia Rating scale (CDR) 0.5, 23 with mild AD (CDR 1), and 18 with moderate AD (CDR 2). Demographic data are shown in Table 1. The exclusion criteria were psychiatric diseases, delirium, and verbal incomprehension including aphasia. Participants were diagnosed based on the criteria for AD by National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA),[21] and mild cognitive impairment (MCI) by the report of the International Working Group on Mild Cognitive Impairment.[22] The CDR 0.5 was regarded as MCI, although a different classification was proposed whereby CDR 0.5 encompasses both mild and earlier dementia[23] or it corresponds to very mild dementia.[24] Patients with CDR 0.5 were limited to those free from objective symptoms of other types of dementia such as dementia with Lewy bodies or frontotemporal dementia. Patients with scores over 7 on the Japanese version of the Short Form of the Geriatric Depression Scale,[25] which has a full score of 15, were also excluded because depressive tendency could affect self-evaluation.[26,27] The ethics board of the Gunma University School of Health Sciences approved all procedures (No. 21-27), and written informed consent was obtained from participants.

Anosognosia was evaluated by the questionnaire discrepancy method, which compares patient's self-report with that of a caregiver.[28] The patients and caregivers were required to answer the same questions about the function of the patients independently. The caregivers' assessment was considered as the objective standard and discrepancy was analyzed between the patients' and the caregivers' assessment.

We chose the Japanese version of the Anosognosia Questionnaire for Dementia (AQ-D),[3,29,30] which contains questions asking awareness of deficits on intellectual functioning (22 items), and mood and behavior domains (8 items). Each item of the AQ-D was evaluated on 0 to 3 scales: *never* (0 point), *sometimes* (1 point), *usually* (2 points), or *always* (3 points). Lower scores of the patients meant deficits of awareness in comparison with those of the caregivers. Self-awareness for each item was analyzed by one-sample *t* test. Summed scores of the 2 domains were compared among CDR groups using 1 × 3 analysis of variance ([ANOVA]; 3 groups according to CDR). The caregivers' scores were analyzed in the same fashion. Discrepancy of each item was evaluated by paired *t* test. Scores of the 2 domains were summed up, and those summed scores were compared among CDR groups using 2 × 3 repeated measured ANOVA (the patients and their caregivers in pairs and 3 groups according to CDR).

To understand patients' perspective, how patients feel distressed by self-awareness of deficits was analyzed as below. The patients' scores of mood and behavior domain were regarded as their distress from the patients' perspective.[31] The predictors of scores of mood and behavior domain were analyzed using multiple linear regression analyses. The dependent variables were summed scores of mood and behavior domains (8 items), and the candidates of predictors were chosen among items in intellectual functioning domain. All the 22 items in intellectual functioning domain were assessed by one sample *t* test, and those items with statistical significance ($P < .05$) were entered in a stepwise fashion into multiple linear regression analyses. The caregivers' assessment was analyzed in the same fashion to show how the caregivers assessed the patients' distress.

The patients were also tested using the Mini-Mental State Examination. All analyses were conducted using the Japanese version of SPSS for Windows version 19.0 (IBM Corporation, New York). Significance was set as $P < .05$.

Results

Self-awareness of the Patients

In intellectual functioning domain, patients' assessments were 8.5 ± 4.9 in CDR 0.5, 11.6 ± 6.7 in CDR 1, and 7.2 ± 4.1 in CDR 2 (Table 2). There was a significant difference among the groups ($P = .042$); however, self-evaluation of patients in CDR 2 was not significantly different from that of patients in CDR 0.5 (Figure 1).

The results of each item are shown in Table 2. In CDR 1, patients were aware of their problems in all the 16 items where discrepancy was observed. Concerning 2 items of problems with orientation in the neighborhood (#11) and mental calculation (#15), patients' awareness was not significantly different from that of caregivers.

In CDR2, patients were not aware of their problems in remembering telephone call (#3), understanding conversations (#4), signing one's name (#5), understanding the newspaper (#6), writing (#9), handling money (#10), orientation in the neighborhood (#11), practicing favorite hobbies (#13), communicating with people (#14), bladder control (#17), understanding the plot of a movie (#18), orientation in the house (#19), doing home activities (#20), and feeding oneself (#21), although caregivers noticed the patients' deficits.

In mood and behavior domains, patients' assessments were 3.3 ± 3.0 in CDR 0.5, 3.4 ± 2.9 in CDR 1 and 4.6 ± 4.0 in CDR 2 (Table 2). The results of each item are shown in Table 2.

Table 2. The Results of Each Item

		CDR	Caregivers[a] Mean ± SD	Patients[b] Mean ± SD	Disc[c] *P* value	Pred. C[d]	Pred. P[e]
Intellectual functioning domain							
1	Problems with remembering dates	0.5	1.17 ± 0.83[g]	0.92 ± 0.67[g]	.429		
		1	1.91 ± 0.79[h]	1.30 ± 0.76[h]	.016[f]		
		2	2.61 ± 0.50[h]	1.11 ± 0.76[h]	<.001[h]		
		0.5	0.42 ± 0.51[f]	0.25 ± 0.45	.166		
2	Problems with orientation in new places	1	1.17 ± 1.03[h]	0.74 ± 0.92[g]	.047[f]		
		2	1.78 ± 1.00[h]	0.78 ± 0.73[h]	.004[g]		
		0.5	0.50 ± 0.67[f]	0.33 ± 0.49[f]	.551		
3	Problems with remembering telephone call	1	1.43 ± 0.79[h]	0.65 ± 0.71[h]	<.001[h]		
		2	2.06 ± 1.11[h]	0.17 ± 0.38	<.001[h]		
		0.5	0.58 ± 0.67[f]	0.33 ± 0.49[f]	.389		
4	Problems with understanding conversations	1	1.13 ± .63[h]	0.52 ± 0.59[h]	.002[g]		
		2	1.78 ± 0.88[h]	0.11 ± 0.47	<.001[h]		
		0.5	0.08 ± 0.29	0.00 ± 0.00	.339		
5	Problems with signing your name	1	0.22 ± 0.42[f]	0.17 ± 0.49	.747		
		2	1.33 ± 1.14[h]	0.00 ± 0.00	<.001[h]		
		0.5	0.25 ± 0.45	0.58 ± 0.67[f]	.166		
6	Problems with understanding the newspaper	1	1.00 ± 0.95[h]	0.43 ± 0.51[h]	.020[f]		.221[f]
		2	1.94 ± 0.94[h]	0.11 ± 0.32	<.001[h]		
		0.5	0.75 ± 0.97[f]	0.58 ± 0.79[f]	.551		
7	Problems with keeping belongings in order	1	1.61 ± 0.99[h]	0.43 ± 0.66[g]	<.001[h]		
		2	2.44 ± 0.70[h]	0.22 ± 0.43[f]	<.001[h]		
		0.5	1.50 ± 0.80[h]	0.83 ± 0.39[h]	.005[g]	.555[f]	
8	Problems with remembering where things were left	1	1.78 ± 0.80[h]	1.04 ± 0.64[h]	.001[g]	.352[g]	
		2	2.33 ± 0.77[h]	0.83 ± 0.51[h]	<.001[h]		
		0.5	0.67 ± 0.89[f]	0.33 ± 0.49[f]	.166		
9	Problems with writing	1	0.96 ± 0.71[h]	0.52 ± 0.79[g]	.022[f]	.934[h]	.533[h]
		2	2.17 ± 0.86[h]	0.28 ± 0.75	<.001[h]		
		0.5	0.50 ± 1.00	0.25 ± 0.62	.082		
10	Problems with handling money	1	1.04 ± 1.07[h]	0.35 ± 0.71[f]	.015[f]		
		2	2.06 ± 1.00[h]	0.11 ± 0.47	<.001[h]		
		0.5	0.33 ± 0.89	0.08 ± 0.29	.389		
11	Problems with orientation in your neighborhood	1	0.65 ± 0.83[g]	0.30 ± 0.56[f]	.103		
		2	1.39 ± 1.14[h]	0.11 ± 0.32	<.001[h]		
		0.5	0.67 ± 0.89[f]	0.50 ± 0.52[g]	.504		.766[g]
12	Problems with remembering appointments	1	1.78 ± 0.95[h]	0.78 ± 0.67[h]	<.001[h]		.388[g]
		2	1.94 ± 0.80[h]	0.56 ± 0.62[g]	<.001[h]		
		0.5	0.17 ± 0.39	0.25 ± 0.45	.674		
13	Problems with practicing favorite hobbies	1	0.83 ± 0.94[h]	0.39 ± 0.72[f]	.038[f]	−.309[f]	
		2	1.67 ± 0.97[h]	0.28 ± 0.75	<.001[h]		
		0.5	0.08 ± 0.29	0.25 ± 0.45	.339		
14	Problems with communicating with people	1	0.74 ± 0.69[h]	0.35 ± 0.49[g]	.025[f]		
		2	1.39 ± 0.92[h]	0.00 ± 0.00	<.001[h]	−.471[h]	
		0.5	0.42 ± 0.67	0.83 ± 0.39[h]	.054		
15	Problems with mental calculations	1	1.17 ± 0.89[h]	1.22 ± 0.80[h]	.852		.322[g]
		2	1.83 ± 1.10[h]	0.83 ± 1.15[g]	.022[f]		.523[g]
		0.5	0.75 ± 0.87[f]	0.58 ± 0.51[g]	.638		
16	Problems with remembering shopping lists	1	1.65 ± 0.93[h]	0.74 ± 0.81[h]	<.001[h]		
		2	2.22 ± 0.81[h]	0.50 ± 0.71[g]	<.001[h]		
		0.5	0.17 ± 0.58	0.00 ± 0.00	.339		
17	Problems with bladder control	1	0.39 ± 0.84[f]	0.13 ± 0.34	.186		
		2	1.00 ± 1.03[g]	0.00 ± 0.00	.001[g]	.382[g]	
		0.5	0.25 ± 0.45	0.42 ± 0.51[f]	.438		
18	Problems with understanding the plot of a movie	1	1.09 ± 0.67[h]	0.52 ± 0.51[h]	.006[g]		
		2	1.67 ± 1.03[h]	0.11 ± 0.32	<.001[h]		
		0.5	0.00 ± 0.00	0.00 ± 0.00	–		
19	Problems with orientation in the house	1	0.13 ± 0.34	0.00 ± 0.00	.083		
		2	0.94 ± 1.11[g]	0.00 ± 0.00	.002[g]		

(continued)

Table 2. (continued)

		CDR	Caregivers[a] Mean ± SD	Patients[b] Mean ± SD	Disc[c] P value	Pred. C[d]	Pred. P[e]
20	Problems with doing home activities	0.5	0.92 ± 1.16[f]	0.42 ± 0.67	.166		
		1	1.09 ± 1.04[h]	0.22 ± 0.42[f]	.001[g]		
		2	2.06 ± 0.94[h]	0.11 ± 0.32	<.001[h]		
21	Problems with feeding oneself	0.5	0.42 ± 1.00	0.00 ± 0.00	.175		
		1	0.17 ± 0.49	0.04 ± 0.21	.266		
		2	1.00 ± 1.14[g]	0.06 ± 0.24	.004[g]	.490[h]	
22	Problems with doing clerical work	0.5	0.92 ± 1.16[f]	0.75 ± 0.97[f]	.504	.439[f]	
		1	1.52 ± 1.08[h]	0.74 ± 1.10[g]	.002[g]		
		2	2.33 ± 0.84[h]	0.94 ± 1.35[g]	.002[g]	.574[h]	.439[f]
	Sum	0.5	11.50 ± 10.48[h]	8.50 ± 4.87[h]	0.389		
		1	23.48 ± 9.68[h]	11.61 ± 6.66[h]	<.001[h]		
		2	39.94 ± 14.65[h]	7.22 ± 4.14[h]	<.001[h]		
Mood and behavior domains							
23	More rigid and inflexible about decisions	0.5	0.75 ± 0.87[f]	0.58 ± 0.90[f]	.339		
		1	1.57 ± 0.90[h]	0.61 ± 0.72[g]	<.001[h]		
		2	2.06 ± 0.80[h]	0.94 ± 1.21[g]	.003[g]		
24	More egotistical and self-centered	0.5	0.92 ± 0.90[g]	0.58 ± 0.67[f]	.266		
		1	1.39 ± 0.94[h]	0.26 ± 0.45[f]	<.001[h]		
		2	1.56 ± 0.86[h]	0.67 ± 0.97[f]	<.001[h]		
25	More irritable	0.5	0.50 ± 0.67[f]	0.58 ± 0.51[g]	.723		
		1	0.96 ± 0.93[h]	0.39 ± 0.58[g]	.020[f]		
		2	1.22 ± 0.88[h]	0.83 ± 1.04[g]	.149		
26	More frequent crying episodes	0.5	0.08 ± 0.29	0.42 ± 0.51[f]	.104		
		1	0.48 ± 0.79[g]	0.43 ± 0.66[g]	.770		
		2	0.67 ± 0.84[g]	0.83 ± 0.99[g]	.636		
27	Laughing inappropriately	0.5	0.08 ± 0.29	0.17 ± 0.39	.586		
		1	0.17 ± 0.39[f]	0.22 ± 0.52	.770		
		2	0.39 ± 0.61[f]	0.06 ± 0.24	.029[f]		
28	Increased sexual interest	0.5	0.00 ± 0.00	0.17 ± 0.39	.166		
		1	0.13 ± 0.34	0.09 ± 0.29	.665		
		2	0.11 ± 0.32	0.06 ± 0.24	.579		
29	Less interest in favorite activities	0.5	0.50 ± 0.67[f]	.42 ± 0.51[f]	.723		
		1	1.00 ± 0.85[h]	.65 ± 0.93[g]	.088		
		2	1.61 ± .92[h]	.61 ± 1.04[f]	.001[g]		
30	More depressed	0.5	.83 ± 0.83[g]	.42 ± 0.67	.096		
		1	1.13 ± 0.87[h]	0.70 ± 0.76[h]	.038[f]		
		2	1.33 ± 0.69[h]	.56 ± 0.92[f]	.012[f]		
	Sum	0.5	3.67 ± 2.77[h]	3.33 ± 2.99[h]	0.768		
		1	6.83 ± 3.41[h]	3.35 ± 2.92[h]	<.001[h]		
		2	8.94 ± 2.60[h]	4.56 ± 4.00[h]	<.001[h]		

Abbreviation: SD, standard deviation; CDR, Clinical Dementia Rating scale.
[a] Scores of caregivers were analyzed by one-sample *t* test, and statistically significance was denoted.
[b] Scores of caregivers patients were analyzed by one-sample *t* test, and statistically significance was denoted.
[c] Discrepancy between caregivers' and patients' assessment, showing severity of anosognosia; discrepancy was evaluated by paired *t* test.
[d] Predictors of distress in caregivers were analyzed by multivariate regression model, and statistically significant standardized beta value was shown in the column.
[e] Predictors of distress in patients were analyzed by multivariate regression model, and statistically significant standardized beta value was shown in the column.
[f] $P < .05$.
[g] $P < .01$.
[h] $P < .001$.

Caregivers' Evaluation

Caregivers' assessments were 11.5 ± 10.5 (mean ± standard deviation) in CDR 0.5, 23.5 ± 9.7 in CDR 1 and 39.9 ± 14.7 in CDR 2 in intellectual functioning domain (Table 2 and Figure 1), and they were 3.7 ± 2.8 in CDR 0.5, 6.8 ± 3.4 in CDR 1, and 8.9 ± 2.6 in CDR 2 in mood and behavior domains (Table 2).

Anosognosia: Discrepancy Between Caregivers' and Patients' Assessment

In intellectual functioning domain,discrepancy between caregivers' and patients' assessment was significantly different among groups ($P < .001$), and post hoc analysis showed that caregiver's assessment was significantly higher than patients' assessment in the CDR 1 and CDR 2 groups ($P < .001$ in both