Analysis of the Clock-Reading Ability in Patients with Cognitive Impairment: Comparison of Analog Clocks and Digital Clocks

（認知機能障害を有する患者における時計を
読む能力の分析:
アナログ時計とデジタル時計の比較）

下 坂　桃 代

主論文

Journal of Alzheimer's Disease 87 (2022) 1151–1165
DOI 10.3233/JAD-215471
IOS Press

Analysis of the Clock-Reading Ability in Patients with Cognitive Impairment: Comparison of Analog Clocks and Digital Clocks

Momoyo Shimosaka[a,*], Hiroyuki Nishimoto[b] and Ayae Kinoshita[a]
[a]*Department of Human Health Sciences, Graduate School of Medicine, Kyoto University, Kyoto, Japan*
[b]*Liaison Healthcare Engineering, Kochi Medical School, Kochi University, Japan*

Accepted 18 March 2022
Pre-press 12 April 2022

Abstract.
Background: Time disorientation is one of the main symptoms observed in patients with dementia; however, their clock-reading ability has not been fully reported.
Objective: This study aimed to investigate the clock-reading ability of both digital and analog clocks in patients with dementia. We newly devised the clock-reading test (CRT) and the number-reading test (NRT) to assess cognitive factors that may affect clock-reading ability. Furthermore, the discriminating power of the CRT was calculated.
Methods: 104 participants were categorized based on their Mini-Mental State Examination (MMSE) scores as follows: subjective cognitive decline ∼ mild cognitive impairment (SCD∼MCI, $N = 43$), early Alzheimer's disease (AD) ($N = 26$), and middle-to-late AD ($N = 35$). Their cognitive abilities were evaluated using the clock-drawing test (CDT), CRT, and NRT.
Results: Cognitive decline leads to impairment of clock-reading ability which is more pronounced in the analog clocks than digital ones. This deficit in clock-reading is attributed to a loss of semantic memory regarding clocks at all stages. Additionally, visuospatial dysfunction and reduced ability of number recognition may lead to deficit in clock-reading in the advanced stage of AD. The discriminating power of the CRT (analog) (AUC = 0.853) was high enough to detect cognitive decline.
Conclusion: Digital clocks are more readable by patients with dementia. Since reading clocks is closely associated with daily life, the CRT has proved to be a useful tool. A decline of analog clock-reading may be an early detector for the onset of dementia in elderly patients.

Keywords: Alzheimer's disease, clock test, cognitive impairments, dementia, neuropsychological tests

INTRODUCTION

Cognitive decline or dementia has become one of the major concerns in rapidly aging societies. To some extent, the progression of the disease can be prevented or delayed using early intervention; therefore, early diagnosis is essential for maintaining the quality life of people with cognitive decline.

Among the diseases that cause dementia, Alzheimer's disease (AD) is one of the most prevalent forms of dementia in developed countries [1, 2]. AD is a neurodegenerative disease characterized by slowly progressive course of cognitive and functional decline. The hallmark pathologies of AD are extracellular accumulation of amyloid-β-containing plaques and intracellular development of tau-containing neurofibrillary tangles [3]. This

*Correspondence to: Momoyo Shimosaka, Department of Human Health Sciences, Graduate School of Medicine, Kyoto University, Kawara-machi 53, Shogoin, Sakyo-ku, Kyoto City, Kyoto 606-8507, Japan. Tel.: +81 75 751 3969; E-mail: shimosaka.momoyo.28x@kyoto-u.jp.

neurodegenerative process in AD is estimated to start 20–30 years before the dementia symptoms emerge [2], which is then followed by mild cognitive impairment (MCI) phase. The clinical phase of MCI is an intermediate state between normal aging and very earlier dementia. Subjects with MCI have objective memory impairment beyond that expected for age, but their activities of daily living are essentially intact [4, 5]. They also have a high likelihood of progressing to dementia at a rate of 10–15% per year [6, 7]. When cognitive impairment becomes apparently sufficient for interfering with daily activities, the patient is diagnosed with dementia [5]. As for AD, signs of dementia are characterized by progressive episodic memory impairment, challenges in planning and solving problems, confusion with time or place, trouble understanding visual images and spatial relationships, difficulty completing daily tasks at home or work, new problems with words when speaking or writing, decreased poor judgement, and so on [1]. It is now well-established that impairment in the encoding of new episodic memories is typical of the earliest stages of the disease. Deficits in semantic memory, language, executive function, verbal short-term memory, and perceptual and spatial functions then follow this initial amnesic stage [8].

In order to evaluate the degree of cognitive decline, the Mini-Mental State Examination (MMSE) is one of the most widely used cognitive screening instruments for dementia, covering various domains of cognitive functions [9, 10]. It assesses orientation to time and place, immediate and delayed recall, attention and calculation, language, copying figures, and the ability to follow simple verbal and written commands. The MMSE has a maximum score of 30 points, and a score of 23 or less has generally been accepted as indicating the presence of cognitive impairment [9].

One of the main symptoms of dementia is disorientation, which is a state of mental confusion, including losing track of time, place, and people; as the disease progresses, orientation to these three becomes disturbed, mostly in this order. Disorientation to time is often observed in the early stage of cognitive decline, such as in patients with amnestic MCI due to AD [3, 11–14]. Therefore, questions such as "What is today's date?", "Month?", "Day of the week?", and "Year?" of the MMSE are reported to be strong predictors of subsequent cognitive decline [15–17]. If time perception is compromised in dementia patients, it leads to a lot of confusion, such as not being able to adhere to medication, keep promises, and plan family events. Thus, temporal disorientation may become a common cause of concern in patients and their relatives [14].

In order to deal with disorientation non-pharmaceutically, an approach called reality orientation (RO) is used, providing dementia patients with a greater understanding of their surroundings. In this approach, the environment, including dates and locations, is frequently pointed out by caregivers. As such, RO can benefit those living with dementia when used appropriately [18–20]. From this perspective, placing a calendar or a clock around the patients may be a useful approach to support them on the condition that they can recognize date and time correctly. Further, innovating a novel clock may help patients restore temporal orientation for some time, as reported in a case study by Coetzer [21]. Since time perception is an essential cognitive function for human beings, we need to evaluate the ability of dementia patients to read the time and develop easily readable clocks for them.

According to the previous literature, the clock-drawing test (CDT), one of the most widely used neuropsychological screening tools, reflects the various functions of the brain, including time perception [22]. The CDT is a popular screening tool for dementia [23]; it is used either by itself or as part of a brief battery in routine clinical practice. Previous studies showed that the CDT is highly and significantly correlated with the MMSE and other neuropsychological batteries in patients with cognitive decline. Thus, it is considered to be useful in detecting and monitoring cognitive impairment [23, 24]. Although the CDT is not a sensitive tool to detect very mild cognitive decline, it has a high diagnostic value for detecting moderate to severe dementia in patients [25, 26].

The task of clock drawing is a complicated one, as it requires various cognitive and motor functions. Both the frontal and parietal cortical areas play a role in drawing a clock, as confirmed by a functional magnetic resonance imaging study in normal subjects [27]. The task of drawing a clock can be affected by impairment of visuospatial ability including space perception, constructional skill, executive function, language processing, and semantic memory [28]. If these cognitive functions decline, we assume that deficits in reading a clock may also be expected. Tuokko et al. [22] developed a novel composite clock test that included three types of clock-related tasks (clock-drawing test, clock-setting test, and clock-reading test). They examined them with normal elderly and AD patients, reporting that the functionally relevant components of clock setting and clock reading combined with clock drawing made the composite clock test particularly useful as a screening tool for AD [22].

What must be noticed is that the task of "clock reading" is a more common behavior than the task of "clock drawing" in daily life. The clock-reading test (CRT) requires no goal-directed, planned behavior, no comparisons between different stimuli, and no manual activity [29]. Tuokko et al. [22] have also suggested that clock reading is more dependent on abstract conceptualization than on constructional skills and may remain intact despite constructional deficits. When compared with the task of "clock drawing," the task of "clock reading" is thought to be less dependent on executive function and more related to other functions such as semantic memory and visuospatial function.

In contrast to episodic memory, which is typically disturbed even in MCI and the earliest stage of AD, semantic memory is culturally rather than personally shared and is not temporally specific [30]. Semantic competence is required for the comprehension of test instructions and for the activation of clock number concepts [29]. Rouleau et al. [31] have suggested that conceptual deficits, in which a subject demonstrates a misrepresentation of the clock or difficulty in setting the hands, may occur because of loss of semantic knowledge concerning the meaning and attributes of analog clocks. They also suggested that conceptual deficits were related to the severity of the patients' dementia. Furthermore, according to Yamamoto et al. [32], the frequency of conceptual deficits in MCI was significantly lower than that in the AD/vascular dementia/mixed dementia groups, and significantly higher than that in the normal elderly group. Thus, patients with AD are more likely to make errors that reflect a deficit in adequately representing the attributes, features, and meaning of a clock than the normal elderly [31, 33]. It is also assumed that early AD patients' deficits in the clock test are mainly determined by reduced access to semantic memory regarding the appearance and functionally of a clock [28].

Deficit of visuospatial cognition is one of the major symptoms of dementia, which is further impaired as the disease progresses [34]. When such patients read an analog clock, they may not be able to capture the positional relationship between the clock hands and digits because of this deficit. So, the subscale of the intersecting pentagon copying task in the MMSE is commonly used to assess visuospatial function. Accurately copying two interlocking pentagons involves the transformation of visual information into a motor plan, known as visuomotor integration [35].

Deficits in these cognitive functions, such as semantic knowledge and visuospatial function, make it difficult to read a clock accurately. Other than these well-reported cognitive functions, patients may not be able to recognize the number itself on the clock display. Reading a clock is premised on being able to read number itself, therefore, we hypothesized that deficits in number recognition may also be related to clock-reading difficulties in patients with dementia. To the best of our knowledge, no studies have ever focused on number recognition in the task of clock reading for the patients with cognitive decline.

Furthermore, clock-reading ability may depend on what types of clocks are used in the test. A previous study reported that patients who were unable to recognize clock faces with analog displays could correctly recognize clock faces with digital displays [36], suggesting that visuospatial-coded information about time seems to be processed differently between analog and digital clocks. Although little is known about the topographic correlations of the cortical processing of analog and digital displays in reading clocks, Ebenbichler et al. [37] previously examined healthy human controls by electrophysiological methods, revealing a difference of cortical substrate between when subjects read digitally-presented time displays and analog displays. This disparity led us to ask which is easier to read, traditional analog clocks or a digital ones, for patients with cognitive impairment.

Since electronic devices have become increasingly prevalent over time, we need to evaluate the influence of digital clocks in interpreting the result of a clock test. Ilardi et al. [38] reported that even some healthy controls were affected by daily exposure to digital displays when they were asked to draw a conventional analog clock; some placed numbers in increments of five on the analog clock face instead of placing numbers from 1 to 12. Therefore, the presence of digital contamination in the clock test ought to be more carefully analyzed. As such, it is considered that the contents of the semantic knowledge of analog clocks and digital clocks are different [39]. With respect to analog clocks, the semantic knowledge means 1) the appearance of clock, 2) meaning of clock face symbols, 3) functionality of clock hands, and 4) converting the number pointed to by clock hands to time. On the other hand, the semantic knowledge for digital clock is composed of 1) the concept of 24-hour notation, 2) meaning of AM/PM, and 3) appearance of the clock (wherein the colon is used to partition the hour and minute values) [39]. If this is the case, we need to evaluate the influence of digital contamination on clock "reading" as well.

Koreki et al. [40] recently performed a CRT with digital clocks (CRT-digital) as well as with analog clocks (CRT-analog), showing that digital clocks are easier to read for patients with dementia. This result is interesting in that most of the dementia patients born before the advent of digital clocks might be more comfortable with digital clocks. According to their research, which examined patients with various types of dementia, AD patients showed a particularly faster decline in reading ability of analog than digital clocks. However, how this clock-reading ability decreases as the disease progresses has not yet been examined. Therefore, in this study, we would like to investigate the ability to read analog and digital clocks at various stages of AD progression and clarify the factors for being unable to read clocks in each stage to better help maintain the patients' quality of life.

This study presents an analysis to compare the reading ability of conventional analog clocks with that of digital ones, especially in patients with AD. Furthermore, we aim to investigate the causes of deficit in clock-reading ability. For this purpose, we examined the relationship between cognitive decline and performance on a CRT, which we devised for this study, compared the ability to read analog and digital clocks. Next, we evaluated the visuospatial ability and the ability of number recognition and semantic knowledge about analog clocks in order to analyze the factors that may affect clock-reading ability.

Lastly, we calculated the detective value of CRT, discriminating dementia patients from non-dementia persons, and compared it with that of the CDT. If the CRT has the same discriminatory power as the CDT, it may be a more useful everyday screening tool.

METHODS

Subjects

A total 104 patients with subjective or objective cognitive impairment were included. All patients were outpatients who visited the Memory Clinic, Kyoto University Hospital, between July 2018 and December 2019.

Patients with AD or MCI were diagnosed by a neurologist based on the National Institute on Aging-Alzheimer's Association workgroup (NIA-AA) diagnostic criteria and Petersen's criteria, respectively, while SCD was defined as self-experienced decline in cognitive functions, especially memory, without formal deficits on neuropsychological testing. For MCI, we chose patients who showed amnestic MCI, since it is considered to be an earlier stage of AD.

Exclusion criteria were as follows: 1) patients with local brain lesion such as cerebrovascular diseases; 2) patients who face difficulty doing tasks because of impaired hearing or visual acuity; and 3) patients who could not carry out clock-reading tasks because of aphasia.

All the participants examined were classified into three groups based on their performance on the MMSE. The MMSE subscales consist of an orientation score (orientation to time and place), memory score (word registration and word recall), attention score (Serial 7s), language score (naming, repetition, following commands, reading, and writing), and construction score (copying pentagons). We also collected data of the MMSE subscales, since a previous study has reported that the MMSE subscales are also clinically useful measures, providing information on memory, orientation, and construction ability of the patients [41]. Although the MMSE alone is perceived to be insufficient for the staging of dementia, its scores are used in this study for convenience. The staging is defined as follows: the participants with scores$\geq$ 24 are defined as subjective cognitive decline $\sim$ mild cognitive impairment (SCD$\sim$MCI), those with 20–23 as early stage of AD (early AD), and those with$\leq$ 19 as middle-to-late stages of AD (middle-to-late AD) [9].

Procedure

All the participants were administered MMSE by a professional clinical psychologist. In addition to MMSE, CDT, CRT, and number-reading test (NRT) were administered by one examiner. The NRT and CRT were particularly devised for this study.

Clock-drawing Test (CDT)

The participants were provided with a blank A4 sheet of paper and asked to draw the circle of a clock face and the numbers in their appropriate positions and then to place the hands "10 minutes past 11 o'clock." Scoring of the CDT was according to the Rouleau method [42]: 10 points for a perfect clock and 0 points when unable to make any reasonable representation of a clock. This scoring method is designed to independently assess the accuracy of the

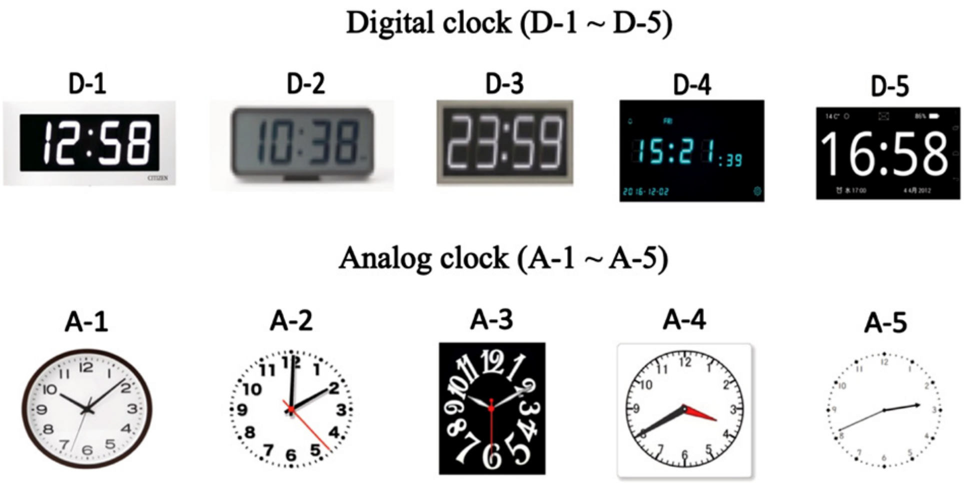

Fig. 1. The actual clock face used in this study. Digital clock (D-1∼D-5) and Analog clock (A-1∼A-5) for CRT.

clock face representation (maximum score: 2 points), the layout of the numbers (maximum score: 4 points), and the position of the hands (maximum score: 4 points); higher scores reflected better performance [42].

In general, conceptual errors reflect a loss or a deficit in accessing knowledge of the attributes, features, and meaning of a clock [31]. For the qualitative analyses of the types of errors on the CDT, conceptual errors regarding analog clocks were recorded by the examiner. The following type of errors were classified into conceptual deficits in the present study: a) misrepresentation of the time on the clock (the hands are either absent or inadequately represented); b) misrepresentation the clock itself (only a clock face without numbers or inappropriate use of numbers); c) the time is written (in letters or numbers) besides the "11" or between "10 and 11" on the clock or hands are either absent or pointed toward "10" and/or "11"; and d) no reasonable or understandable attempt at drawing.

Clock-reading test (CRT)

To measure patients' clock-reading abilities, 10 clock faces indicating different time (5 analog clocks and 5 digital clocks) were presented on a tablet display for five seconds per clock face, and the subjects were asked to read the clock time (the hour number and the minute number). Each clock face showed a different time. The actual clock faces used in this study are shown in Fig. 1. Previously, the CRTs developed by Schmidtke et al. [29] used analog clocks without numbers on clock face. In this study, we chose clocks with numbers that we often see in our daily routines, since this CRT is expected to be an early detector of cognitive decline in daily life. The scoring for the CRT was assigned as follows: one point for the correct answer and zero points for the wrong or no answer. Thus, the CRT has a maximum score of 10 points: 5 points for the digital clock and 5 points for the analog clock.

Number-reading test (NRT)

To measure participants' recognition of number, 20 numbers were presented on a tablet display at random and the participants were asked to read them. These 20 numbers consist of 11 "seven-segment digital font" numbers and 9 "graphic design number font" ones. The seven-segment digital font is widely used for calculators, electronic meters, digital clocks, and other digital devices, whereas several types of graphic design number font are usually used for conventional analog clock faces. For testing, one-digit numbers of both fonts were presented for two seconds and two-digit numbers were presented for three seconds. Representative numbers used in this study are shown in Supplementary Figure 1. The scoring for this NRT was assigned as follows: one point for correct answers and zero for wrong or no answers. Thus, the NRT has a maximum score of 20 points: 11 points for the seven-segment digital font and 9 points for the graphic design number font.

Statistical analyses

Statistical analyses were performed using JMP Pro (version 15.2.0) and R statistical package (version 4.0.2, R Foundation for Statistical Computing). Statistical significance in this study was defined when the p-value was less than 0.05.

One-way analysis of variance (ANOVA) was chosen to assess group differences for age and MMSE score, while Spearman's rank correlation coefficients were calculated to assess the relationship between MMSE and CRT. The nonparametric Kruskal-Wallis test was applied to detect group differences in the CDT, CRT, and NRT. For *post hoc* comparisons, we used the Steel–Dwass test. Chi-square tests were applied for categorical data for 1) the detection of differences in gender distribution and 2) the detection of differences in each clock face (D-1∼D-5, A-1∼A-5). The Wilcoxon rank sum test was chosen to assess differences in the scores of CRT in patients with conceptual deficits regarding analog clocks and those without conceptual deficits. The nonparametric Wilcoxon signed-rank test was chosen to assess 1) the difference in CRT scores between analog clock and digital clock and 2) the difference in the scores of CRT (analog) and CRT (digital) in patients with conceptual deficits regarding analog clocks.

A discriminant analysis was performed with CDT, CRT (analog), and CRT (digital) as predictor variables for differentiating non-dementia patients (MMSE scores $\geq$ 24, corresponding to MCI and SCD patients in this study) from dementia patients (MMSE scores< 23). The Receiver Operating Characteristic (ROC) analysis was used to identify each optimal cutoff point for the CDT, CRT (analog), and CRT (digital). Subsequently, their sensitivities, specificities, positive predictive value, and negative predictive value were calculated. The Youden index was used to determine the optimal cutoff point. The sensitivity of the CRT refers to its ability to correctly identify those individuals who have been classified as having dementia according to MMSE. Specificity refers to the CRT's ability to correctly identify those individuals who have previously been classified as non-dementia persons (SCD∼MCI). The diagnostic accuracy of CDT and CRT were calculated at the area under the curve (AUC). The DeLong's test for two correlated ROC curves was applied to compare the AUC of the ROC curves.

Ethical approval

The study's protocol approval was granted by the Ethics Committee of Kyoto University Hospital (R1243). Oral and written informed consent was obtained from participants and their caregivers. They were informed of their freedom to withdraw from the study.

RESULTS

Demographic characteristics of the participants

The characteristics of the subjects and mean MMSE scores of the 3 groups are shown in Table 1. The SCD∼MCI group consisted of 43 subjects who had scores of 24–30 on the MMSE. The early AD group consisted of 26 subjects who had scores of 20–23 on the MMSE. The middle-to-late AD group consisted of 35 subjects who had scores of 0–19 on the MMSE. As to the CDT, we could not get a depiction from seven participants (two participants were in the early AD group and five were in the middle-to-late AD group), the total being 97 in CDT. The ANOVA of the mean age ($F[2, 101] = 0.95$, $p = 0.38$) did not show any significant group differences. The 3 groups also did not differ in gender distribution ($\chi^2[2] = 3.23$, $p = 0.20$).

Results of CRT and CDT

Reading time performance of digital and analog clocks

We first evaluated the participants' clock-reading abilities in both digital and analog clocks. As to digital clocks, the percentages of the correct answers for all type of tested clocks were as follows: D-1:88.5%; D-2:84.6%; D-3:74.0%; D-4:76.0%; and D-5:78.8%. These five digital clocks did not statistically differ in the number of correct answers ($\chi^2[4] = 9.59$, $p = 0.05$). As for analog clocks, the percentages were as follows: A-1:65.4%; A-2:71.2%; A-3:63.5%; A-4:66.3%; and A-5:59.6%. Moreover, the results of these five analog clocks did not differ ($\chi^2[4] = 3.25$, $p = 0.52$). Since there is no significant difference in the correct answer rate of each clock, the scores of the analog and digital clocks are totaled.

Correlation between cognitive decline and CRT performance

We examined whether the ability of reading a clock may be correlated with cognitive decline detected by the MMSE. Spearman's correlation coefficients between the MMSE and CRT (both analog and digital) are shown in Table 2. There were significant correlations between the total scores of the MMSE and the scores of the CRT (analog) ($r = 0.76$, $p < 0.0001$) and CRT (digital) ($r = 0.77$, $p < 0.0001$). Moreover, all of the subscales of the MMSE were significantly correlated with the scores of CRT (both analog and digital; Table 2).

Table 1
Demographic characteristics of the participants

		SCD ~ MCI	early AD	middle-to-late AD
Number, n	**Total**	43	26	35
Gender	**Male**	18	9	7
	Female	25	17	28
Age, y		79.2 (6.04)	80.3 (10.0)	81.6 (7.5)
MMSE	**Total [Range: 0–30]**	26.4 (1.88)	22.0 (1.02)	13.5 (4.4)
	Subscale			
	Orientation score			
	Time score [0–5]	4.02 (0.83)	2.19 (1.60)	0.83 (0.98)
	Place score [0–5]	4.84 (0.37)	4.31 (0.84)	1.94 (1.64)
	Memory score			
	Words registration [0–3]	2.98 (0.15)	2.96 (0.20)	2.63 (0.81)
	Words recall [0–3]	1.98 (1.03)	0.84 (0.93)	0.03 (0.17)
	Attention score			
	Serial 7s [0–5]	3.86 (1.10)	3.23 (1.61)	1.37 (1.19)
	Language score			
	Naming [0–2]	2.0 (0)	2.0 (0)	1.71 (0.67)
	Repetition [0–1]	0.88 (0.32)	0.92 (0.27)	0.43 (0.50)
	Following commands [0–3]	2.86 (0.35)	2.77 (0.43)	2.54 (0.61)
	Reading [0–1]	1.0 (0)	1.0 (0)	0.86 (0.36)
	Writing [0–1]	1.0 (0)	0.92 (0.27)	0.54 (0.51)
	Construction score			
	Copying pentagons [0–1]	1.0 (0)	1.0 (0)	0.69 (0.47)

Characteristics of subjects and mean (standard deviations: SD) on the MMSE (total score and its subscale). MMSE, Mini-Mental State Examination; SCD~MCI, patients with subjective cognitive decline ~ mild cognitive impairment; early AD, patients with early stage of AD; middle-to-late AD, patients with middle-to-late stages of AD.

Table 2
Spearman's rank correlation coefficient between MMSE score and performance of CRT

		CRT (analog)	CRT (digital)
MMSE	**Total**	0.76 **	0.77 **
	Subscale		
	Orientation score	0.59 **	0.66 **
	Memory score	0.63 **	0.55 **
	Attention score	0.62 **	0.50 **
	Language score	0.61 **	0.75 **
	Construction score	0.56 **	0.67 **

Spearman's rank correlation coefficient between MMSE (total score and its subscale) and score of CRT. MMSE, Mini-Mental State Examination; CRT (analog), clock-reading test (analog clock); CRT (digital), clock-reading test (digital clock). $^{**}p < 0.0001$.

Group differences in CRT and CDT

The means and standard deviations (SD) in CDT and CRT are calculated and shown in Table 3. As the cognitive function declines, the score of CRT decreases in the same way as the score of CDT. The early AD patients performed significantly worse compared to SCD~MCI patients in CDT, CRT (analog), and CRT (digital). The scores of CRT (both analog and digital) in the middle-to-late AD group were significantly lower than those in the early AD group.

Comparison of analog and digital clock-reading ability

We then investigated the ability of reading clocks and compared the results of analog and digital clocks. As shown in Fig. 2, the scores of digital clocks were significantly higher than those of analog clocks in the SCD~MCI group (Z = 3.42, p = 0.0006) and early AD group (Z = 3.44, p = 0.0006). In contrast, no significant difference between the scores of analog and digital clocks could be detected in the middle-to-late AD group (Z = 1.50, p = 0.13).

Cognitive factors affecting clock-reading ability

Results of the NRT

The results of the CRT led us to ask what factors affect the ability of reading clocks in patients with cognitive decline. We, thus, investigated what cognitive factors decrease the ability of clock "reading." We first examined whether patients were able to recognize numbers correctly, since number-recognition

Table 3
Means and standard deviations (SD) for the CDT and CRT

	CDT			CRT (analog)			CRT (digital)		
	mean (SD)	95%CI	Rank score mean	mean (SD)	95%CI	Rank score mean	mean (SD)	95%CI	Rank score mean
SCD∼MCI	9.12 (1.29)	[8.31, 9.92]	64.70	4.56 (0.80)	[4.14, 4.98]	74.03	4.95 (0.30)	[4.54, 5.36]	66.97
early AD	7.17 (2.70)	[6.09, 8.25]	43.94	3.19 (1.67)	[2.65, 3.73]	49.37	4.54 (0.90)	[4.01, 5.07]	56.29
middle-to-late AD	4.73 (3.84)	[3.77, 5.70]	30.55	1.71 (1.69)	[1.25, 2.18]	28.37	2.49 (2.17)	[2.03, 2.94]	31.91
$\chi 2$	28.39			47.75			40.81		
p	<0.0001			<0.0001			<0.0001		
Pairwise comparison	Rank score mean difference	Z	p	Rank score mean difference	Z	p	Rank score mean difference	Z	p
SCD∼MCI									
early AD	16.10	3.39	<0.0001	18.00	3.95	0.0002	8.39	3.03	0.0069
middle-to-late AD	24.11	4.93	0.002	32.83	6.64	<0.0001	25.14	5.98	<0.0001
early AD									
middle-to-late AD	9.49	2.22	0.068	14.08	3.12	0.0052	15.72	3.70	0.0006

Mean (standard deviations: SD) on the MMSE (total score and its subscale). The nonparametric Kruskal-Wallis test was applied to detect group differences in the CDT, CRT (analog), and CRT (digital). For *post hoc* comparisons, we used the Steel-Dwass test. Continuity correction is applied to the rank score mean difference. MMSE, mini-mental state examination; CDT, clock-drawing test; CRT, clock-reading test (analog clock / digital clock); SCD∼MCI, patients with subjective cognitive decline ∼ mild cognitive impairment; early AD, patients with early stage of AD; middle-to-late AD, patients with middle-to-late stages of AD.

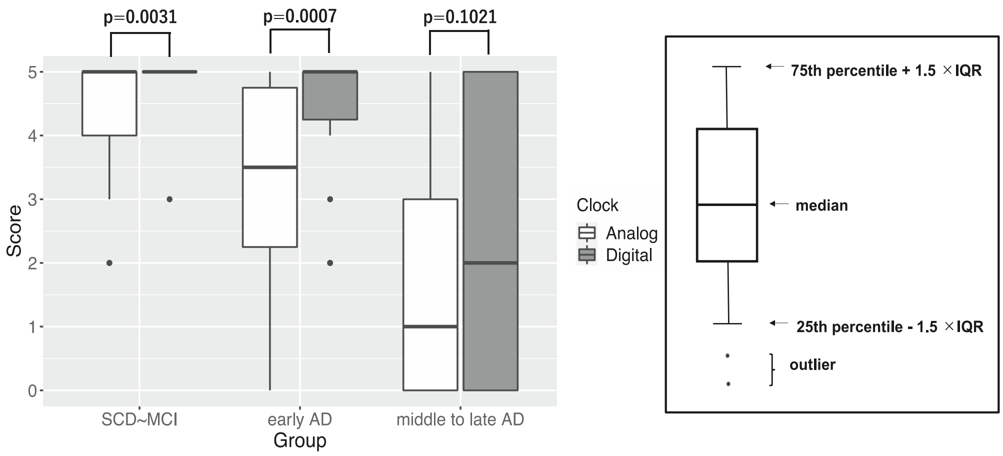

Fig. 2. The comparison of analog clocks and digital clocks for CRT. Score of the CRT (analog clock/digital clock) in SCD∼MCI, early AD, and middle-to-late AD. The nonparametric Wilcoxon signed-rank test was applied. CRT, clock reading test (analog clock/digital clock); SCD∼MCI, patients with subjective cognitive decline ∼ mild cognitive impairment; early AD, patients with early stage of AD; middle-to-late AD, patients with middle-to-late stages of AD; IQR, interquartile range.

ability has not been investigated in past literature. As the seven-segment display of digital numbers is widely used for digital clocks, we examined the patients' ability to recognize numbers correctly in both seven-segment digital font and graphic design number font. The means and SD in the NRT are shown in Fig. 3A. The middle-to-late AD patients performed significantly worse than the SCD∼MCI patients in the reading task of both seven-segment ($Z = 3.38$, $p = 0.0021$) and graphic design numbers ($Z = 2.94$, $p = 0.014$), whereas early AD patients and SCD∼MCI patients performed well when recognizing numbers, indicating that number-recognition ability was decreased in the patients of the middle-to-late AD group, which may have affected clock reading. As to the seven-segment font, a significant group difference was detected between the early AD and middle-to-late AD groups ($Z = 2.72$, $p = 0.0018$), although it was not observed for the graphic design number font ($Z = 2.19$, $p = 0.07$). This result raises the possibility that seven-segment numbers are not easily recognizable for advanced AD patients.

A

	seven- segment font [Range: 0-11]			graphic design number font [Range: 0-9]		
	mean (SD)	95%CI	Rank score mean	mean (SD)	95%CI	Rank score mean
SCD~MCI	10.93 (0.26)	[10.37, 11.49]	58.12	9.0 (0)	[8.72, 9.28]	55.50
early AD	10.92 (0.37)	[10.20, 11.65]	57.77	9.0 (0)	[8.64, 9.36]	55.50
middle to late AD	9.37 (0.32)	[8.75, 9.99]	41.69	8.34 (1.61)	[8.03, 9.28]	46.59
χ2	15.65			12.42		
p	0.0004			0.002		
Pairwise comparison	Rank score mean difference	Z	p	Rank score mean difference	Z	p
SCD~MCI						
early AD	0.216	0.10	0.99	0	0	1
middle to late AD	12.28	3.38	0.0021	6.66	2.94	0.014
early AD						
middle to late AD	9.42	2.72	0.018	5.20	2.19	0.07

B

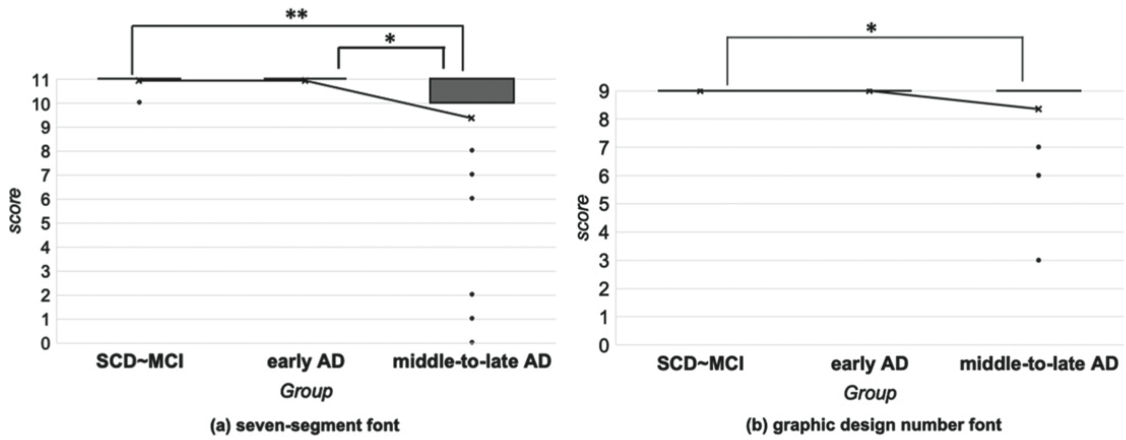

Fig. 3. The results of Number Reading Test. A) Means and standard deviations (SD) for Number Reading Test. Mean (standard deviation: SD) on the NRT. The nonparametric Kruskal-Wallis test was applied to detect group differences in the NRT. For *post hoc* comparisons, we used the Steel-Dwass test. Continuity correction is applied to the rank score mean difference. NRT, number reading test (seven-segment font/graphic design number font); SCD∼MCI, patients with subjective cognitive decline ∼ mild cognitive impairment; early AD, patients with early stage of AD; middle-to-late AD, patients with middle-to-late stages of AD. B) Group difference in the performance of the Number Reading Test. Score of the NRT (seven-segment font/graphic design number font) in SCD∼MCI, early AD, and middle-to-late AD. The × markers in the box represent the mean value. *$p < 0.05$, **$p < 0.01$.

Loss of semantic knowledge

Next, we evaluated another factor that might affect clock-reading ability. Loss of semantic knowledge about analog clocks was examined by the presence of conceptual errors detected by CDT, as previously reported [31]. The percentage of patients with conceptual deficits about analog clocks in our study are shown in Fig. 4A, with 16.3% in the SCD∼MCI,

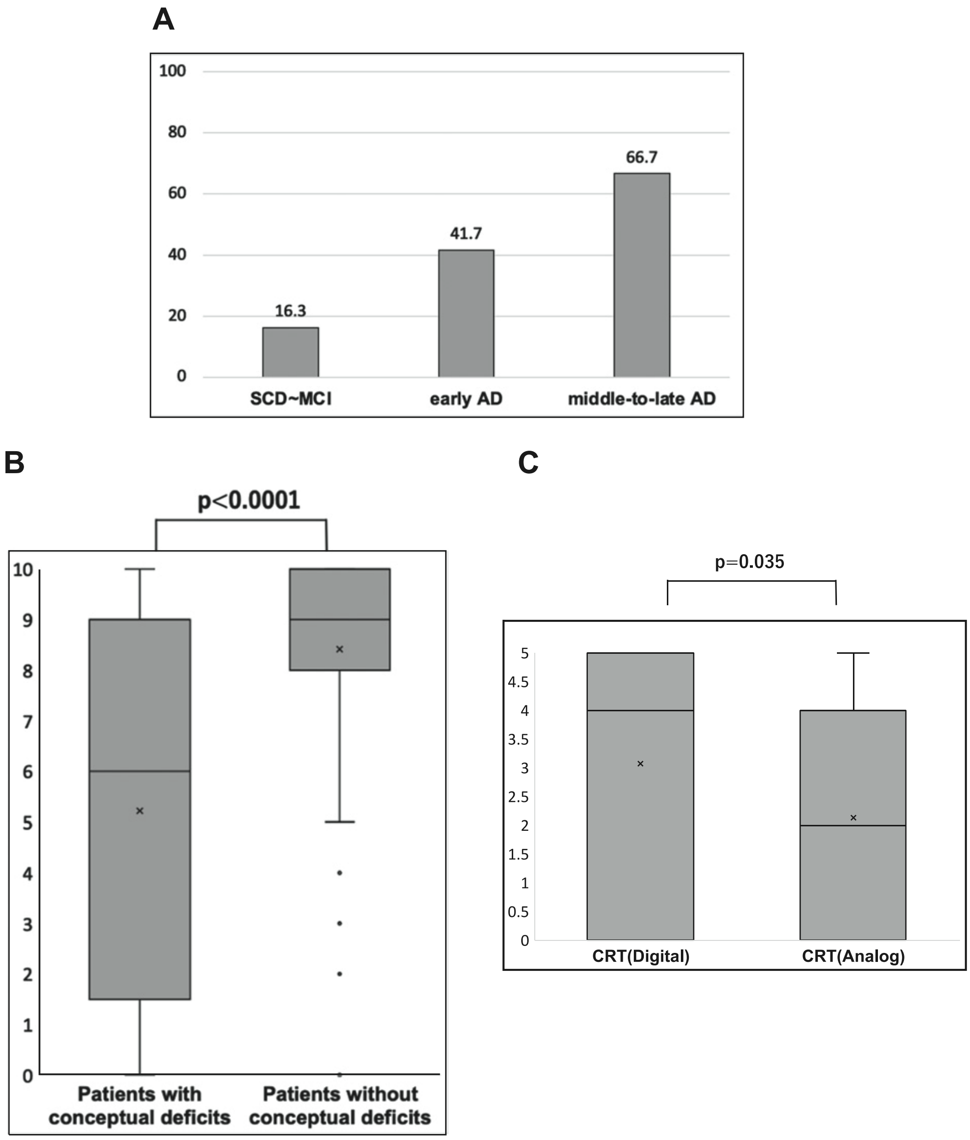

Fig. 4. The effect of conceptual deficit on CDT/CRT. A) Percentage of the patients whose depiction in CDT had conceptual deficits. SCD∼MCI, patients with subjective cognitive decline ∼ mild cognitive impairment; early AD, patients with early stage of AD; middle-to-late AD, patients with middle-to-late stages of AD. B) The comparison of the score CRT (analog and digital) in patients with/without conceptual error. The Wilcoxon rank sum test was applied. C) The comparison of the score of CRT (analog) and CRT (digital) in patients with conceptual error. The nonparametric Wilcoxon signed-rank test was applied. CRT, clock-reading test (analog clock/digital clock). The × markers in the box represent the mean value.

41.7% in the early AD, and 66.7% in the middle-to-late AD groups.

Then, we compared the cognitive functions and clock-reading abilities of patients with and without conceptual deficits about analog clocks. The scores of the total MMSE and its subscales (orientation score, attention score, memory score, language score, construction score) in patients with conceptual deficits were significantly lower ($p < 0.0001$) than those in patients without conceptual deficits, indicating that patients with conceptual errors have more severe cognitive deficits. As shown in Fig. 4B, the mean score of CRT (analog and digital) in patients with conceptual deficits was 5.22 (SD: 0.49), while the mean score of CRT without conceptual deficits was 8.42 (SD: 0.36), indicating that the score in participants with conceptual deficits was significantly lower than the score in patients without conceptual deficits ($Z = -4.83$, $p < 0.0001$).

Further, we asked which clocks were more readable for those with conceptual deficits. As shown in Fig. 4C, these patients' mean score of CRT for digital clocks was 3.08 (SD: 2.18) and that for analog clocks was 2.14 (SD: 1.84). The score of CRT (digital) was significantly higher than that of CRT (analog) ($Z = 2.11$, $p = 0.035$), clearly demonstrating that digital clocks are more readable for patients with conceptual errors. Collectively, since the contents of the semantic knowledge differ between analog and digital clocks, patients with conceptual deficits involving analog clocks may be able to read digital ones.

Deficits in visuospatial ability

Next, we examined whether other domains of cognitive function such as visuospatial function may affect clock reading in AD, since visuospatial function is known to be associated with the CDT scores. We picked up a subscale "copy pentagon" in the MMSE, which is used to assess visuospatial function. The score of this subscale decreased only in the middle-to-late AD group, as shown in Table 1. We then examined the relationship between visuospatial function and clock-reading ability. The Spearman's rank correlation coefficients with the subscale of "copy pentagons (construction score)" in the MMSE were $r = 0.56$ ($p < 0.0001$) and $r = 0.67$ ($p < 0.0001$) for performance in the CRT (analog) and CRT (digital), respectively, as shown in Table 2. Further, the relationship between the CRT and MMSE scores (total score and its subscale) in the middle-to-late AD group is shown in Supplementary Table 1. The correlation coefficient with "copy pentagon (construction score)" were $r = 0.59$ ($p = 0.0002$) and $r = 0.58$ ($p = 0.0002$) for CRT (analog) and CRT (digital) respectively, which were larger values than that of other subscales in the middle-to-late AD group.

Predictive value of CRT in evaluating cognitive decline

Finally, we compared the predictive abilities of the CRT and the CDT. If the predictive value of the CRT is comparable to that of the CDT, the former will be a useful tool for detecting cognitive decline, which can be used more easily.

The AUC, cutoff point, sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and ROC curves are shown in Fig. 5. The ROC curve analyses show that CRT (analog) produced discrimination of suspected dementia patients from non-dementia persons (diagnosed as SCD∼MCI) (AUC: 0.853), which produced a higher discrimination ability than CRT (digital) (AUC: 0.737). To our surprise, the discriminating power of CRT (analog) is higher than that of CDT (AUC: 0.795) in our study. A significant difference was detected only between CRT (analog) and CRT (digital) ($Z = -3.005$, $p = 0.003$). There were no significant differences between the discriminating power of CDT and CRT (digital) ($p = 0.334$) and between CDT and CRT (analog) ($p = 0.267$). This result suggests that testing reading ability of analog clocks may be able to discriminate dementia patients from non-dementia persons more effectively than CDT, although this difference was not significant.

DISCUSSION

The present study was designed to test the clock-reading abilities in patients with cognitive decline. The task of "clock reading" is a common behavior in daily life; however, little is known about the reading abilities of dementia patients. Recently, Koreki et al. [40] reported similar findings as ours. They evaluated clock-reading ability of both analog clocks and digital clocks. According to them, digital clocks are easier to read for patients with dementia. However, we believe that our paper has contributed further novel findings to the field. We not only compared the reading ability of digital and analog clocks, but also calculated the detective values both of CRT (analog) and CRT (digital). Further, we investigated and analyzed the factors that may reduce clock-reading ability, such as number-reading ability, semantic knowledge about analog clocks, and visuospatial function. We then used various designs of clocks often seen in daily life, which makes our results more generalizable for detecting patients' cognitive function.

Clock-reading ability in patients with cognitive decline

First, we found that there is a significant correlation between clock-reading ability and the scores of the MMSE. As with the CDT, which is widely used for screening dementia, the scores of the CRT decrease with a decline in cognitive abilities. Clock-reading ability for both digital and analog clocks decreases even in early AD patients compared with non-dementia (SCD∼MCI) persons, as shown in Table 3. Thus, the CRT, especially CRT (analog), may have discriminating power for cognitive decline, which was also verified by the result of ROC curve (Fig. 5).

A

Test		AUC [95%CI]	Cutoff Point (Youden Index)	Sensitivity	Specificity	PPV	NPV
CDT		0.795 [0.710, 0.879]	8.50	0.654	0.814	0.818	0.648
CRT	**Digital**	0.737 [0.671, 0.803]	4.55	0.492	0.977	0.968	0.575
	Analog	0.853 [0.785, 0.922]	4.46	0.853	0.698	0.80	0.769

B

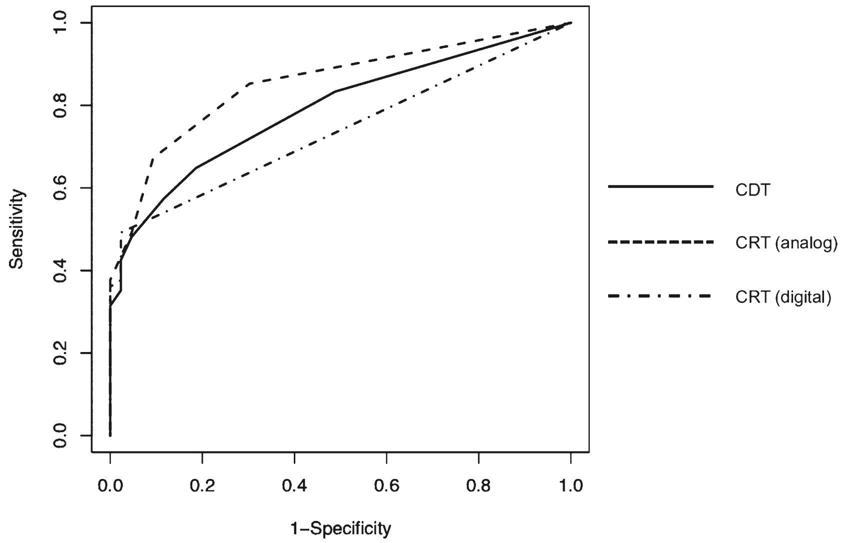

Fig. 5. Predictive value of CRT. A) AUC, Cutoff Point, Sensitivity, Specificity, PPV, and NPV for CDT and CRT. Predictive value of CDT and CRT in evaluating cognitive decline. CDT, clock-drawing test (Rouleau scoring method); CRT, clock-reading test (analog clock/digital clock); AUC, area under the curve; 95%CI, 95% confidence interval; PPV, positive predictive value; NPV, negative predictive value. B) ROC curve. Receiver operating characteristic (ROC) curves for the CDT, CRT (analog), and CRT (digital) in differentiation between non-dementia (SCD∼MCI) and suspected dementia.

Intriguingly, when analog and digital clocks were compared, the average score of reading analog clocks was significantly lower than that of digital ones, even in the SCD∼MCI and early AD groups. This result suggests that analog clock reading is disturbed earlier than digital reading, which is consistent with Koreki et al.'s result, as they calculated the digital-analog score gap and showed that there was a significant difference between the score gap and the score of the MMSE. We also tried to calculate this score gap in each group and found that it was biggest in the early AD group, which corresponds to the results of comparison of analog and digital clock-reading ability shown in Fig. 2. In the group of middle-to-late AD, there is no significant difference between analog and digital clocks, probably because they could not read either of them correctly. However, a larger SD in the scores of digital clocks may suggest that some patients in this group can still read digital clocks correctly.

Factors affecting clock-reading ability in patients with cognitive decline

Next, we analyzed the factors that affect the analog and digital clock-reading ability of patients with cognitive decline. We attribute the decreased ability of clock reading to several factors that we speculate from this study: number-reading ability, semantic knowledge, and visuospatial function.

Our study investigated whether participants could recognize numbers of the clock face (display) properly to see if number-reading ability is associated with the CRT. The results showed that number-reading ability was decreased only in the middle-to-late AD group, which may affect clock-reading ability in advanced AD cases, regardless of the type of clock. Considering that patients with mild cognitive decline (in the early AD group) could read numbers properly, the reduced ability of reading clocks in early AD patients did not attribute to deficits in number recognition.

We then found that the score of CRT in patients whose depiction in CDT had conceptual deficits regarding analog clocks was significantly lower than the score in patients without conceptual deficits, suggesting that loss of semantic knowledge about analog clocks could be one of the factors that reduces clock-reading ability. We also found that loss of semantic knowledge about clocks (both analog and digital) is considered to be a cause of error in the CRT at all stages, including middle-to-late AD as well as MCI and early AD. As stated before, analog clock reading depends more on abstract conceptualization than constructional skills [22]. According to a previous study by Leyhe et al. [43], semantic memory concerning complex knowledge about the functionality of an analog clock decreases in the early impairment stage. Later, additional deficits concerning the functionality of the minute hand and the meaning of the clock face symbols begin to accumulate. Additionally, semantic knowledge of the hour hand and the appearance of the clock is lost in the advanced stage of AD. These previous literatures support our study that the loss of semantic knowledge about clocks (both analog and digital) could be a factor that reduces clock-reading ability at all stages of AD.

Moreover, patients with conceptual deficits about analog clocks had significantly higher scores in CRT (digital) than CRT (analog), suggesting that even if patients have loss of semantic knowledge of analog clocks, some could still read digital clocks correctly. This observation may be attributed to the fact that the contents of the semantic knowledge differ between analog and digital clocks. From these results, we conclude that patients with conceptual deficits about analog clocks should be advised to use digital ones.

A deficit of visuospatial cognition also could be a factor affecting clock-reading ability [44]. When patients read an analog clock, they need to capture the positional relationship between the clock hands and digits; however, it becomes difficult to recognize the angle of lines because of visuospatial dysfunction that arises as the disease progresses [45]. In this study, the scores of "copy pentagons" in the MMSE, which is thought to represent visuospatial function, decreased only in the middle-to-late AD group, as shown in Table 1. As expected, we found that the score of "copy pentagons" in the MMSE is significantly related to analog clock-reading ability. It is known that visuospatial function is impaired in dementia in the later stage [34], which may lead to a decrease in analog clock-reading ability in cases of advanced dementia.

Discriminating power of clock-reading test for cognitive decline

Since telling time is a common task in daily life, and clock-reading ability is necessary for maintaining temporal orientation, we explored whether clock-reading ability may be an early indicator of detecting cognitive decline. As shown in Fig. 5, the AUC of CRT (digital) was smaller and the AUC of CRT (analog) was greater than that of CDT, suggesting that CRT (analog) showed a high discriminating power for dementia patients in our study. This point is clinically important since analog clock-reading ability may be an early detector of cognitive decline in the daily life of elderly patients. Therefore, when the elderly have difficulty in working out the time on the traditional analog clock face, it may be a warning sign of cognitive decline that is as sensitive as the CDT.

Strengths and limitations

This study presents novel insights into the clock-reading ability of both digital and analog clocks in patients with cognitive decline of various degrees. We further investigated the cognitive factors that may affect reading clocks. From this research, we propose that digital clocks may be more readable than analog clocks for patients with dementia. The limitation of this study is that the patients were recruited from one hospital and with an AD background. In order to further generalize this result, more patients from various hospitals and facilities should be collected, and future studies including other types of dementia (i.e., dementia with Lewy bodies) are needed to make this clock-reading test more useful.

ACKNOWLEDGMENTS

This study was supported by research grants from the Mitsubishi Foundation (Project No. 203180600017), the Takata Foundation (Project No. 203190600065), and the Kyoto University GAP Fund

Program (2020). The funding sources did not have any specific involvement in this study. We would like to thank Mr. Mitsukazu Okuda for providing the materials and for his critical reviews.

Authors' disclosures available online (https://www.j-alz.com/manuscript-disclosures/21-5471r2).

SUPPLEMENTARY MATERIAL

The supplementary material is available in the electronic version of this article: https://dx.doi.org/10.3233/JAD-215471.

REFERENCES

[1] Alzheimer's Association (2020) 2020 Alzheimer's disease facts and figures. *Alzheimers Dement* **16**, 391-460.
[2] Blennow K, de Leon MJ, Zetterberg H (2006) Alzheimer's disease. *Lancet* **368**, 387-403.
[3] El Haj M, Kapogiannis D (2016) Time distortions in Alzheimer's disease: A systematic review and theoretical integration. *NPJ Aging Mech Dis* **2**, 1-5.
[4] Petersen RC (2004) Mild cognitive impairment as a diagnostic entity. *J Intern Med* **256**, 183-194.
[5] Albert MS, DeKosky ST, Dickson D, Dubois B, Feldman HH, Fox NC, Gamst A, Holtzman DM, Jagust WJ, Petersen RC, Snyder PJ, Carrillo MC, Thies B, Phelps CH (2011) The diagnosis of mild cognitive impairment due to Alzheimer's disease: Recommendations from the National Institute on Aging-Alzheimer's Association workgroups on diagnostic guidelines for Alzheimer's disease. *Alzheimers Dement* **7**, 270-279.
[6] Petersen RC (2003) Mild cognitive impairment clinical trials. *Nat Rev Drug Discov* **2**, 646-653.
[7] Petersen RC, Smith GE, Waring SC, Ivnik RJ, Tangalos EG, Kokmen E (1999) Mild cognitive impairment - Clinical characterization and outcome. *Arch Neurol* **56**, 303-308.
[8] Perry RJ, Watson P, Hodges JR (2000) The nature and staging of attention dysfunction in early (minimal and mild) Alzheimer's disease: Relationship to episodic and semantic memory impairment. *Neuropsychologia* **38**, 252-271.
[9] Tombaugh TN, McIntyre NJ (1992) The Mini-Mental State Examination: A comprehensive review. *J Am Geriatr Soc* **40**, 922-935.
[10] Folstein MF, Folstein SE, McHugh PR (1975) "Mini-mental State": A practical method for grading the cognitive state of patients for the clinican. *J Psychiatr Res* **12**, 189-198.
[11] Ashford JW, Kolm P, Colliver JA, Bekian C, Hsu LN (1989) Alzheimer patient-evaluation and the Mini-Mental State-Item characteristic curve analysis. *J Gerontol* **44**, P139-P146.
[12] Grand JH, Caspar S, MacDonald SW (2011) Clinical features and multidisciplinary approaches to dementia care. *J Multidiscip Healthc* **4**, 125-147.
[13] Manning C (2004) Beyond memory: Neuropsychologic features in differential diagnosis of dementia. *Clin Geriatr Med* **20**, 45-58.
[14] Dumurgier J, Dartigues JF, Gabelle A, Paquet C, Prevot M, Hugon J, Tzourio C (2016) Time orientation and 10 years risk of dementia in elderly adults: The Three-City Study. *J Alzheimers Dis* **53**, 1411-1418.
[15] Guerrero-Berroa E, Luo XD, Schmeidler J, Rapp MA, Dahlman K, Grossman HT, Haroutunian V, Beeri MS (2009) The MMSE orientation for time domain is a strong predictor of subsequent cognitive decline in the elderly. *Int J Geriatr Psychiatry* **24**, 1429-1437.
[16] Tractenberg RE, Weinstein M, Weiner MF, Aisen PS, Fuh JL, Goldman N, Chuang YL (2005) Benchmarking a test of temporal orientation with data from American and Taiwanese persons with Alzheimer's disease and American normal elderly. *Neuroepidemiology* **24**, 110-116.
[17] Fayers PM, Hjermstad MJ, Ranhoff AH, Kaasa S, Skogstad L, Klepstad P, Loge JH (2005) Which Mini-Mental State Exam items can be used to screen for delirium and cognitive impairment? *J Pain Symptom Manage* **30**, 41-50.
[18] Spector A, Davies S, Woods B, Orrell M (2000) Reality orientation for dementia: A systematic review of the evidence of effectiveness from randomized controlled trials. *Gerontologist* **40**, 206-212.
[19] Baines S, Saxby P, Ehlert K (1987) Reality orientation and reminiscence therapy - a controlled crossover study of elderly confused people. *Br J Psychiatry* **151**, 222-231.
[20] Zanetti O, Oriani M, Geroldi C, Binetti G, Frisoni GB, Di Giovanni G, De Vreese LP (2002) Predictors of cognitive improvement after reality orientation in Alzheimer's disease. *Age Ageing* **31**, 193-196.
[21] Coetzer R (2019) The potential role of relatives in designing person-centred assistive technologies (innovative practice). *Dementia (London)* **18**, 3161-3164.
[22] Tuokko H, Hadjistavropoulos T, Miller JA, Beattie BL (1992) The Clock Test: A sensitive measure to differentiate normal elderly from those with Alzheimer disease. *J Am Geriatr Soc* **40**, 579-584.
[23] Shulman KI (2000) Clock-drawing: Is it the ideal cognitive screening test? *Int J Geriatr Psychiatry* **15**, 548-561.
[24] Heinik J, Solomesh I, Berkman P (2004) Correlation between the CAMCOG, the MMSE, and three clock drawing tests in a specialized outpatient psychogeriatric service. *Arch Gerontol Geriatr* **38**, 77-84.
[25] Pinto E, Peters R (2009) Literature review of the Clock Drawing Test as a tool for cognitive screening. *Dement Geriatr Cogn Disord* **27**, 201-213.
[26] Connor DJ, Seward JD, Bauer JA, Golden KS, Salmon DP (2005) Performance of three clock scoring systems across different ranges of dementia severity. *Alzheimer Dis Assoc Disord* **19**, 119-127.
[27] Ino T, Asada T, Ito J, Kimura T, Fukuyama H (2003) Parieto-frontal networks for clock drawing revealed with fMRI. *Neurosci Res* **45**, 71-77.
[28] Leyhe T, Milian M, Muller S, Eschweiler GW, Saur R (2009) The minute hand phenomenon in the clock test of patients with early Alzheimer disease. *J Geriatr Psychiatry Neurol* **22**, 119-129.
[29] Schmidtke K, Olbrich S (2007) The Clock Reading Test: Validation of an instrument for the diagnosis of dementia and disorders of visuo-spatial cognition. *Int Psychogeriatr* **19**, 307-321.
[30] Hodges JR, Patterson K (1995) Is semantic memory consistently impaired early in the course of Alzheimer's disease? Neuroanatomical and diagnostic implications. *Neuropsychologia* **33**, 441-459.
[31] Rouleau I, Salmon DP, Butters N, Kennedy C, McGuire K (1992) Quantitative and qualitative analyses of clock drawings in Alzheimer's and Huntington's disease. *Brain Cogn* **18**, 70-87.

[32] Yamamoto S, Mogi N, Umegaki H, Suzuki Y, Ando F, Shimokata H, Iguchi A (2004) The clock drawing test as a valid screening method for mild cognitive impairment. *Dement Geriatr Cogn Disord* **18**, 172-179.

[33] Cahn DA, Salmon DP, Monsch AU, Butters N, Wiederholt WC, CoreyBloom J, BarrettConnor E (1996) Screening for dementia of the Alzheimer type in the community: The utility of the clock drawing test. *Arch Clin Neuropsychol* **11**, 529-539.

[34] Nagaratnam N, Nagaratnam K, O'Mara D (2014) Intersecting pentagon copying and clock drawing test in mild and moderate Alzheimer's disease. *J Clin Gerontol Geriatr* **5**, 47-52.

[35] de Boer C, Mattace-Raso F, van der Steen J, Pel JJM (2014) Mini-Mental State Examination subscores indicate visuomotor deficits in Alzheimer's disease patients: A cross-sectional study in a Dutch population. *Geriatri Gerontol Int* **14**, 880-885.

[36] Poeck K (1975) Neuropsychologische syndrome ohne eigenstandige bedeutung. *Aktuelle Neurol* **2**, 199-208.

[37] Ebenbichler G, Uhl F, Lang W, Lindinger G, Egkher A, Deecke L (1997) Cortical DC potential shifts accompanying the central processing of visually presented analogue and digital time displays. *Neuropsychologia* **35**, 349-357.

[38] Ilardi CR, Garofalo E, Chieffi S, Gamboz N, La Marra M, Iavarone A (2020) Daily exposure to digital displays may affect the clock-drawing test: From psychometrics to serendipity. *Neurol Sci* **41**, 3683-3690.

[39] Friedman WJ, Laycock F (1989) Children's analog and digital clock knowledge. *Child Dev* **60**, 357-371.

[40] Koreki A, Kusudo K, Suzuki H, Nozaki S, Onaya M, Bowes A, Sado M (2021) Are analogue or digital clocks friendlier for people living with dementia? *Dement Geriatr Cogn Dis Extra* **11**, 207-212.

[41] Choe YM, Lee BC, Choi IG, Suh GH, Lee DY, Kim JW (2020) MMSE subscale scores as useful predictors of AD conversion in mild cognitive impairment. *Neuropsychiatr Dis Treat* **16**, 1767-1775.

[42] Siciliano M, Santangelo G, D'Iorio A, Basile G, Piscopo F, Grossi D, Trojano L (2016) Rouleau version of the Clock Drawing Test: Age- and education-adjusted normative data from a wide Italian sample. *Clin Neuropsychol* **30**, 1501-1516.

[43] Leyhe T, Saur R, Eschweiler GW, Milian M (2009) Clock test deficits are associated with semantic memory impairment in Alzheimer disease. *J Geriatr Psychiatry Neurol* **22**, 235-245.

[44] Shibasaki H, Hallett M (2016) *The Neurologic Examination: Scientific Basis for Clinical Diagnosis*, Oxford University Press.

[45] Ska B, Poissant A, Joanette Y (1990) Line orientation judgment in normal elderly and subjects with dementia of Alzheimer's type. *J Clin Exp Neuropsychol* **12**, 695-702.