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Online Tool (Brain Assessment) for the Detection of Cognitive Function Changes during Aging

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Keywords
Cognitive decline · Dementia · Brain assessment · Cognitive score

Abstract
Introduction: It is well-known that cognitive function declines with age. In order to detect changes in cognitive function, cognitive tests should be performed repeatedly. Currently existing cognitive tests come in only a single version, so the subject is likely to remember the contents with repeated testing. And, under the outbreak of coronavirus disease 2019 (COVID-19), in-person assessment should be avoided. This study was performed to develop a new cognitive test (brain assessment, BA) that has 5 versions and can be performed on a personal computer (PC) through the Internet. ***Materials and Methods:*** Five thousand subjects performed the online BA, which consisted of 5 subtests: number memory, word memory, mental rotation test, N-back test, and judgment test. We standardized the raw scores (cognitive scores, CSs) using mean and standard deviation, which were 50 and 10, respectively. Then, we calculated the mean CS for each sex and age, plotted the relationships between ages and mean CSs on figures, and calculated the formula of cognitive changes during normal aging. ***Results:*** The CSs of all subtests decreased with aging. The regression coefficient was from −0.31 to −0.45. It is noteworthy that in most subtests, the CSs started to increase at 85 years of age. ***Discussion:*** Our BA has 5 versions and can be done on a PC using the Internet. We tested the BA in a large number of subjects, and the standard values of CSs were measured in individuals up to 89 years of age. By performing this test repeatedly, subjects can evaluate the degree of their cognitive decline. If the rate of cognitive decline is greater than that predicted using the normalized formula, the subjects can undertake strategies to improve their control of lifestyle-related diseases or other habits of daily living. ***Conclusion:*** The BA can be easily taken online using a PC, and its scores linearly declined with normal aging. The BA will be useful for detecting longitudinal cognitive changes and comparing them to the pattern seen in normal aging.

Introduction

Recent studies have demonstrated that through adequate intervention, including the control of lifestyle parameters, such as those related to hypertension or physical exercise, the occurrence of dementia can be prevented to some degree. However, the control of disease-related lifestyle risks has been very poor. For example, adequate

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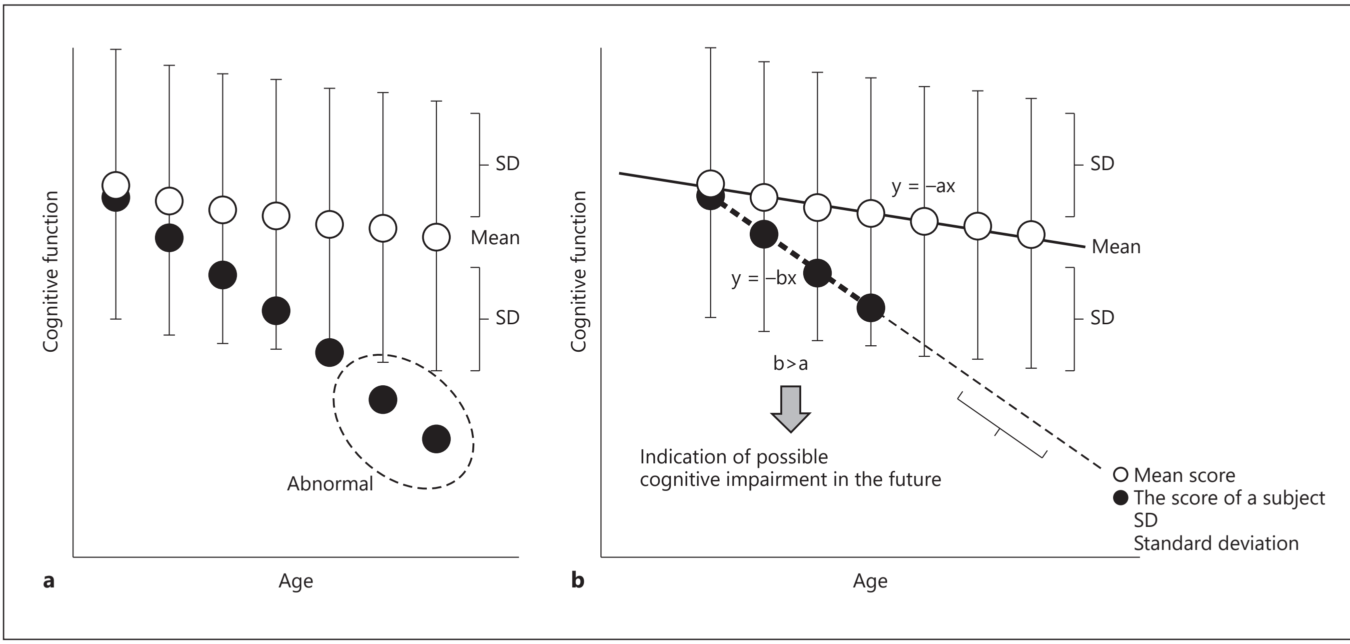

Fig. 1. Examples of cognitive tests. **a** Most cognitive tests judge whether the present cognitive function of the subject is within a normal range. If the score of the test is below the SD at the corresponding age, the subject is regarded as abnormal. **b** Generally speaking, cognitive function decreases with age. If we can identify the formula for the change of test scores across the age, the formula for each subject (based on scores from several tests) can be compared with the average population's formula. If the slope of the inclination is steeper than normal, it is possible that the cognitive function of the subject will become abnormal in the future. SD, standard deviation.

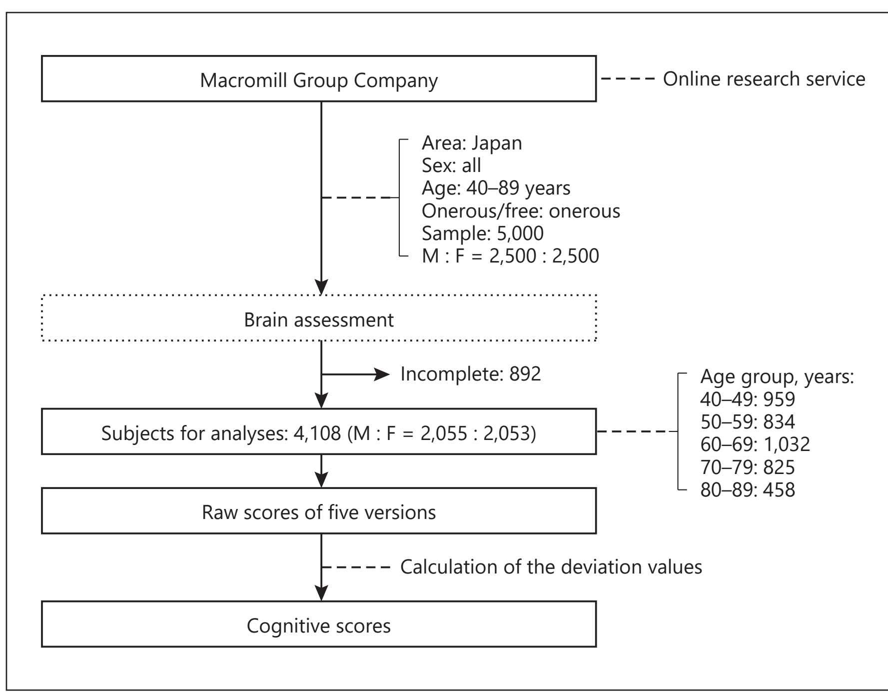

Fig. 2. Flow diagram of this study.

Table 1. Performance time for each test

Subtest	Mean (sec) ±SD
Memory of numbers	295±32
Memory of words	296±30
MRT	260±61
N-back test	286±40
Judgment	279±53

SD, standard deviation; MRT, mental rotation test.

control of hypertension is seen in only 28% of patients [1]. Similarly, for diabetes mellitus (DM), in only 1 of 4 DM patients, it is well-controlled [2]. While patients may recognize the importance of controlling their diseases, they often ignore the control measures they should be taking due to their hectic life schedules. We thus need to find opportunities that provide them with the strong motivation they need to immediately and enthusiastically address the problem and to begin to improve their lifestyles accordingly.

There are various tests in order to assess the subjects' cognitive function. For example, we developed Necker cube drawing-based assessment battery useful for detecting mild constructional apraxia which is one of the early symptoms of Alzheimer's disease [3]. We also reported that the missing fundamental phenomenon was impaired in individuals with Alzheimer's disease, and suggested its impairment represents a manifestation of the degeneration of auditory-related brain regions [4]. But the current tests, including ours mentioned previously, have several limitations. First, these tests set mean scores and standard values. If the subject's score is below the standard value of the corresponding age-group, the cognitive function of the subject is considered abnormal (Fig. 1a). On the contrary, cognitive function of a subject is not considered abnormal if the score is within normal limits. We hypothesize that if people became aware that their cognitive function is decreasing more rapidly than the norm (Fig. 1b), they will be more likely to take underlying problems seriously. Therefore, it will be useful if we can know not only the present cognitive function but also whether the speed of cognitive decline due to aging is within the normal limit or not. Second, most of the existing cognitive tests have only one version. This enables the subject to become accustomed to the contents of the test through repeated testing, so several versions are necessary to prevent this habituation because this habituation may allow the subject achieve a higher score surpassing the actual abilities that is not truly reflective of performance. And third, due to the ongoing outbreak of the coronavirus disease 2019 (COVID-19), in-person assessment is difficult. Thus, an online test is desired.

Here, we have developed an online test to detect abnormal cognitive decline. The cognitive domains assessed include memory, visuospatial abilities, working memory, and judgment. We collected the online test results from 5,000 subjects and calculated the mean score and standard deviation (SD) for each age. From this we determined the formula for cognitive decline due to normal aging.

Materials and Methods

Subjects

The subjects were gathered voluntarily by the use of Internet flyers for participation, provided by an Internet research service Macromill Group Company. The total number of subjects was 5,000, consisting of an equal number of males and females, with ages ranging from 40 to 89 years (Fig. 2). The same number of men and women was recruited in the order of arrival of participation requests. Subjects performed one version of our cognitive test (brain assessment, BA) online, details of which are explained later. The version of what was assigned to the subject was randomly assigned. The subjects were ordered to complete the test within 5 min. The mean performance time of each subtest is shown in Table 1. In the mental rotation test (MRT) and the judgment test, the majority of the subjects were able to complete the test; therefore, their performance times were relatively short. We excluded those subjects whose performance time was short over 2 SDs since we assumed the subjects might have abandoned the tests halfway through. Thus, the data from a total of 4,108 subjects were utilized for statistical analyses. The number of subjects from each age range is shown in Figure 2. We cannot completely exclude the possibility that patients with mild cognitive impairment were included in the subjects. But because of the following reason, the subjects with dementia are thought to have been excluded even in its early stage. In Japan, the old persons who can make free use of the Internet are relatively small. According to the data of White Paper Information and Communication in 2018 by the Ministry of Internal Affairs and Communications, only half of the elderly from 70 to 79 years can use the Internet. As for the persons older than 80 years, the rate decreases to almost 20%. So, only by the fact that he/she could operate the novel device and apply the participation through the Internet, we may say that they preserved the ability of novelty-seeking, willingness, and dealing with the inexperienced situation. Therefore, we can reasonably conclude that the cognitive function of the old participants to this study was relatively preserved.

Brain Assessment

The cognitive tests consisted of 5 subtests: number and word memory, mental rotation task, N-back task, and judgment (Table 2). All the tests could be performed online by clicking an answer on the screen. We named the combined package of these tests the "BA." The BA has 5 versions, and feedback regarding correct/wrong answers to the questions was not provided to the subjects.

Table 2. Contents of the test (BA)

Cognitive domain	Subtest	How-to
Memory	Numbers	The subject must memorize numbers from 3 to 9 digits, and repeat them using the numeric keypad in ascending and descending order
	Words	Memorize 5 target words. After a short distracting task, 10 words in which half of them belong to the target words are presented in order. The subject replies whether each word was included among the target words
Visuospatial	MRT	A 3-dimensional target block figure is presented. Four rotated alternatives, one of which is different from the target, are then presented. The subject selects which alternative is different
Working memory	N-back test	A series of numbers is presented. The subject must perform addition of the present and several antecedent numbers
General intellect	Judgment	The subject must find the regularity in the presented figures

BA, brain assessment; MRT, mental rotation test.

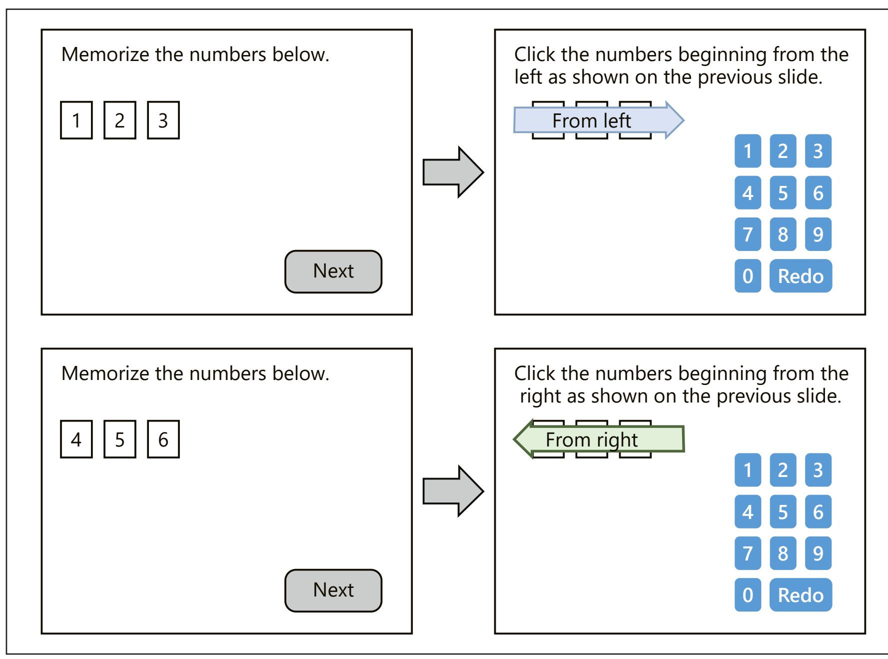

Fig. 3. Example of the number memory subtest. Two kinds of tasks were carried out: type the presented numbers from the left (upper) or from the right side (lower). The number of digits in each presented sequence ranged from 3 to 9.

The subtest for number memory was performed as follows (Fig. 3). Numbers ranging from 3 to 9 digits were presented, and the subjects were asked to memorize these numbers. On the next slide, the subjects performed 2 kinds of tasks. Using the numeric keypad on the screen, the subjects entered the numbers from the left or from the right side (ascending or descending, respectively). The time spent on each slide was determined by the subjects, and they were required to click the "next" button on the slide when they finished answering. The subjects performed as many tasks as possible over 5 min, and one point was given when both the number and its numerical position were correct.

For the word memory subtest, 6 words were presented on the first slide (Fig. 4). Three to 5 distracting slides then followed; these consisted of 6 numbers, and the subjects were asked to click the fourth biggest one, for example. Then, on the following slides, a word was shown, and the subjects were asked whether the word was included among the words on the first slide by clicking a yes or a no button. Ten words were shown, among which half were included on the first slide. The time spent on each slide was determined by the subjects, and they were required to click the "next" button on the slide when they finished answering. The subjects answered as many questions as possible over 5 min. One point was given for each correct answer.

The third subtest was an MRT. The MRT was first described by Shepard and Metzler in 1971 [5]. The stimuli consisted of 2-dimensional drawings of the 3-dimensional objects (Fig. 5). The tar-

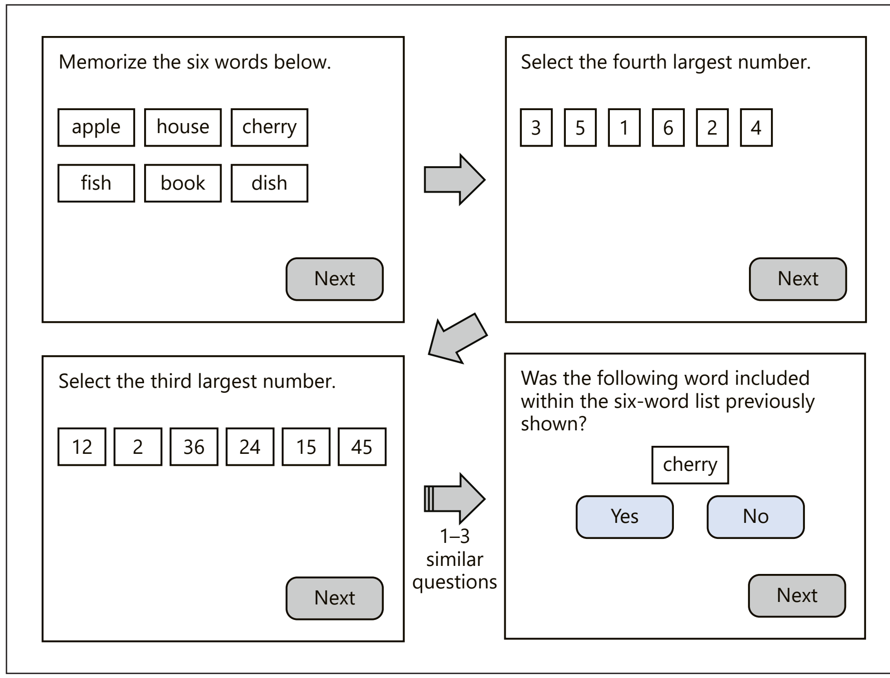

Fig. 4. Six words were presented, and the subjects were asked to memorize them. Then, 3 to 5 distracting slides were shown. These consisted of 6 numbers, and the subjects were asked to click the fourth biggest one, for example, on the next slides, a word was presented, and subjects were asked whether the word was included among the 6 words on the first slide.

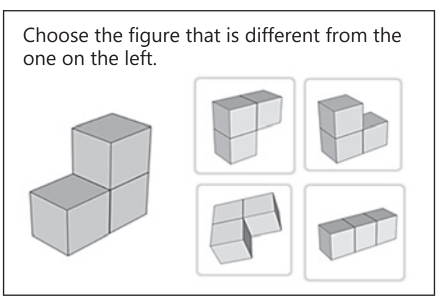

Fig. 5. Target 3-dimensional figure was presented on the left side of the slide. Four alternatives, of which 3 were rotated versions of the target, were presented on the right side of the slide. The subjects were asked to pick which figure was different from the target by clicking on it.

get figure was presented on the left side of the slide, and 4 alternatives, among which 3 of them were rotated figures of the target, were shown on the right. The subjects were asked to click the figure that was different from the target. The subjects performed as many tasks as possible over 5 min. One point was given for each correct answer.

The fourth subtest was the N-back test. The subjects were asked to memorize the presented number. In the case of the 1-back test (Fig. 6), the subjects added the number to that on the first slide and answered by clicking one of several choices. At the same time, the subjects had to memorize the number of the second slide and add it to the number on the third slide. The same process was repeated. In the 2-back test (Fig. 7), the subjects memorized 2 numbers which were presented on the first and the second slide, then were asked to add the first number to that on the third slide, and memorize the number on it. The subjects performed these tasks up to the 3-back test. The timing spent on each slide was determined by the subjects, and they were required to click the "next" button on the slide when they were finished answering. The subjects performed as many tasks as possible over 5 min. One point was given for each correct answer.

The final subtest was for judgment and speculation (Fig. 8). Several figures and operations were shown. Using operations A and B, some changes appeared to the original figures. The subject had to decide which operation had changed the original figure, by clicking the correct answer from among 4 alternatives. One point was given for each correct answer. Eighteen tasks were performed, and the total score was out of 18.

The number and word memory tests might be based on the functional activity of the medial temporal lobes, which include the hippocampus. It was reported that during the mental rotation task, activation was observed in the parietal, frontal, and occipital lobes, which represent Brodmann's areas 7, 8, and 19, respectively [6]. The N-back task has a relationship with the activity of frontoparietal regions [7, 8]. A meta-analysis of 27 experiments showed that the relational reasoning task activated the rostrolateral prefrontal cortex [9]. So, it seems reasonable to suppose that the BA reflects the function of frontal, temporal, parietal, and occipital lobes, namely, the entire cerebrum. Now, the BA is used for research purposes, and it will be opened to public at a fee when this manuscript is published.

Calculation of Cognitive Score

We controlled the difference of the 5 versions of the BA by using the following equation to standardize the raw scores as the mean score became 50, where the SD became 10. Such standard-

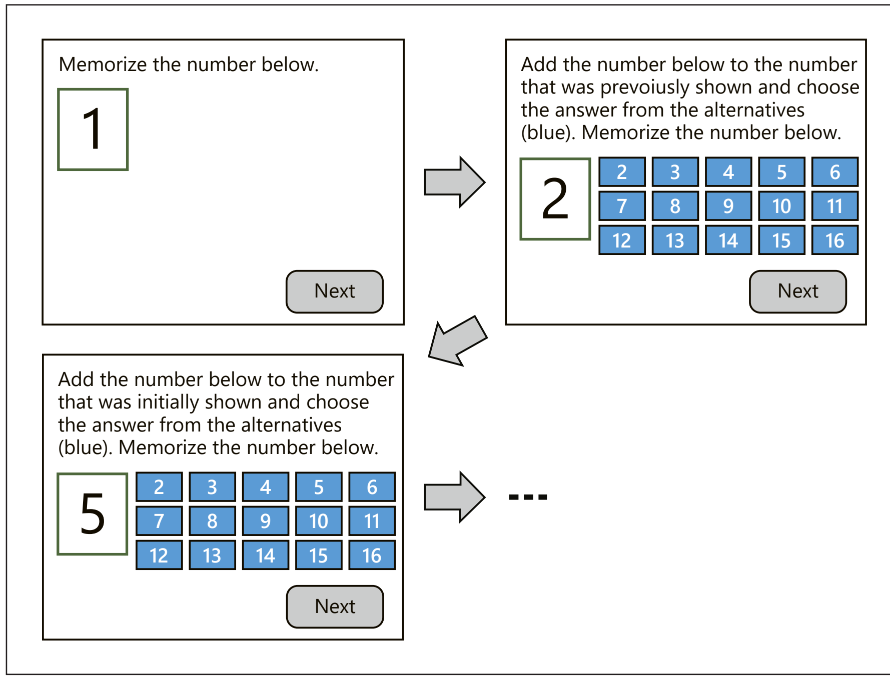

Fig. 6. 1-back test. The subjects were asked to memorize the presented number, and on the second slide, to add the number to that on the first slide. The subject answered by clicking one of several choices, and at the same time, they had to memorize the number of the second slide and add it to the number on the third slide. The same process was repeated.

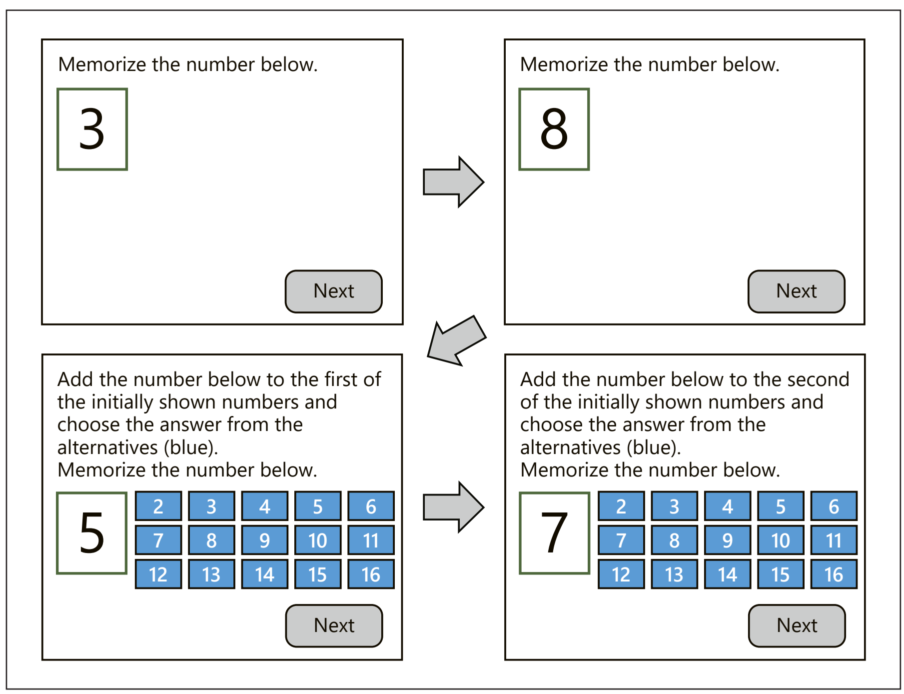

Fig. 7. 2-back test. The subjects memorized 2 numbers shown on the first and the second slide. On the third slide, a number was presented, and the subjects were asked to add the number to the number on the first slide and to click on the answer from the alternatives. On the fourth slide, another number was shown, and the subjects were asked to add it to the second one.

ized scores were termed the "cognitive score (CS)." The CS can be calculated using the following formula:

CS = ([raw score] – [mean of raw scores]) / [SD of raw scores] × 10 + 50

We then calculated the mean CS for each sex and age, plotted the relationships between ages and mean CSs on figures, and calculated the formula of cognitive changes by normal aging. We performed regression analysis and got the coefficient of determination (R^2), using IBM SPSS Statistics 23 software.

We used online not personal computer (PC) software because of the following 3 reasons: the biggest most important reason was its affordability. Because PC software needs to be downloaded, available PCs are limited. We assume that the BA can be used in health checks, for example, at companies and municipal corporations. These subjects will utilize the BA for many years. By using

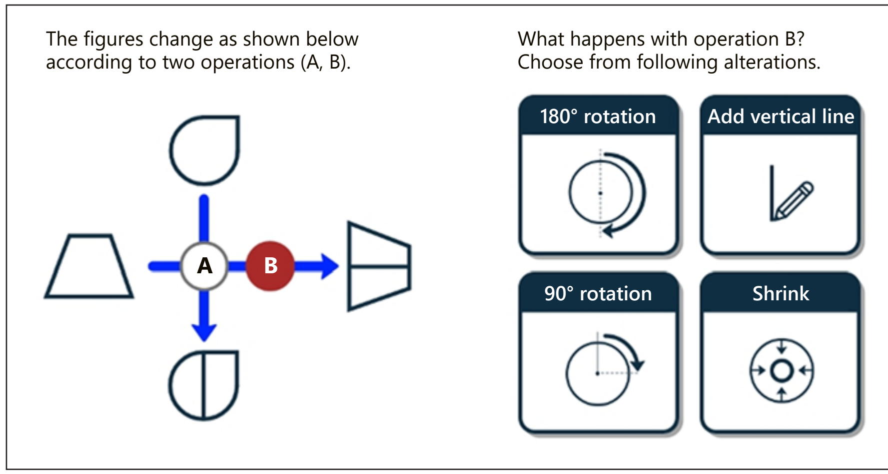

Fig. 8. Subtest of judgment. Some changes were made to 2 original figures by operation A or B. The subjects were asked which figure had changed the presented figure, by selecting the answer from 4 alternatives.

online software, it is easy to preserve data, and the subjects can access them anytime and anywhere; the second reason is economic efficiency. There are multiple operating systems in the world, and in the case of PC software, we must revise the program as soon as the version or its content is upgraded. In online software, the frequency of such revisions will be much less than PC software, so the cost will be smaller; the third reason is easy maintenance. In PC software, the subjects must upgrade the BA when it is version-upped. In online software, the subjects can perform the BA only by accessing the Internet. Based on the reasons mentioned previously, we suppose online software is more suitable to the BA, rather than the PC one.

Results

In order to complete the BA, the subjects needed to be online for approximately 25 min (see the Table 1). The mean raw scores of 5 versions of the subtests are age-stratified by 5 years for each sex (Table 3). To resolve the differences in the levels of difficulties between the 5 versions of subtests, we standardized the raw scores and calculated the mean CSs for each age (see online suppl. material; see www.karger.com/doi/10.1159/000516564 for all online suppl. material) and by 5-year increments of age (Table 4) of each sex. Figure 9 shows the relationship between the age and mean CSs for each subtest. It is obvious that CSs of all subtests decreased with aging. This suggests that cognitive function starts to gradually decrease in the 40s. We calculated the formula of regression lines for each subtest in each sex. The regression coefficient was from −0.31 to −0.45. It is noteworthy that in most of the subtests, the CSs consistently decreased until 80 years of age, but turned upward at 85 years of age.

Discussion

The present study can be summarized by the following 7 main points: (i) we described the “BA” which consists of multifaceted cognitive domains; (ii) the BA has 5 versions and can be completed on the Internet within 30 min; (iii) data for a large number of subjects whose age ranged from 40 to 89 years were collected; (iv) to resolve the differences in the levels of difficulties between the 5 versions, we standardized the raw scores and calculated mean CSs for each age-group stratified by 5 years; (v) the CS of most subtests decreased linearly with age until age 80 years; (vi) we drew the lines of the best fit and calculated the formulas of cognitive decline by normal aging; finally, (vii) at 85 years of age, the CS trended toward an improvement.

Our “BA” has 3 key characteristics. First, the BA can be done on a PC using the Internet, and its scoring is automated, without the need for specialists. Anyone can easily access the test at any time, alleviating the risk of infection through in-person contact. Second, it can encompass a large number of subjects. In Japan, there are 3 standardized intellectual tests which assess general cognitive function: the Japanese version of the Wechsler Adult Intelligence Scale-Third Edition (WAIS-III) [10], Raven’s Colored Progressive Matrices (RCPM) [11], and the Mini-Mental State Examination-Japanese (MMSE-J) [12]. The total number of subjects used for the standardization of normal values was about 1,400, 300, and 330 for the WAIS-III, RCPM, and MMSE-J, respectively. In contrast, the BA obtained data from over 4,000 subjects. Third, standard values of CSs are provided for a wider range of ages in the BA. The age range for the standard

Table 3. Mean raw scores for each subtest by age (years) and sex

Version	1		2		3		4		5	
age, years	male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD
Memory of numbers										
40~	117.2±28.6	109.7±33.5	111.4±21.8	112.7±29.7	115.4±30.7	104.9±27.7	122.1±26.5	111.7±24.7	108.6±26.5	105.5±26.1
45~	112.2±26.3	107.1±25.8	120.6±25.1	106.3±29.4	114.6±29.3	101.2±20.7	110.0±24.1	104.2±23.8	114.6±24.4	99.2±26.1
50~	107.2±29.5	91.0±28.7	101.5±24.4	94.2±27.1	105.7±25.6	96.1±23.6	110.0±25.2	97.6±27.7	106.0±30.0	96.6±25.9
55~	96.6±20.0	92.8±19.7	103.5±26.8	101.2±25.9	93.3±25.1	92.3±22.6	96.6±27.2	92.0±23.1	97.8±32.4	89.1±26.9
60~	94.5±26.4	85.2±19.4	90.1±22.9	81.3±23.2	93.8±23.9	84.3±22.0	94.8±25.1	88.7±19.4	91.9±23.2	83.9±26.6
65~	85.5±18.0	82.9±27.2	85.0±20.0	78.5±21.9	82.4±26.4	79.4±26.1	87.5±26.2	78.7±22.7	88.2±23.5	78.2±22.1
70~	76.6±21.9	75.6±25.7	73.5±23.1	72.4±24.5	71.6±23.8	70.9±23.7	77.4±25.3	74.4±23.0	77.5±27.9	72.8±23.9
75~	65.9±20.3	69.4±21.5	69.6±22.6	72.9±20.7	72.8±19.0	68.2±21.5	71.6±20.4	65.7±25.9	72.7±18.5	68.2±28.0
80~	61.3±20.1	67.7±28.5	60.6±21.7	64.0±31.2	62.2±23.3	65.2±27.1	63.0±17.2	64.4±31.8	55.7±18.9	60.8±20.4
85~	62.0±18.1	78.3±36.3	64.4±12.1	81.4±31.3	80.7±30.0	77.3±21.0	62.8±19.3	78.3±37.9	61.5±13.1	63.8±21.5
Memory of words										
40~	45.0±9.4	42.8±11.6	44.0±10.4	43.6±8.4	42.4±12.3	44.7±9.4	44.8±8.0	42.7±8.9	42.9±9.3	43.5±8.8
45~	41.3±10.2	41.8±8.0	45.3±7.5	40.7±9.6	43.5±8.3	42.3±7.9	41.4±8.9	41.9±6.9	41.8±10.2	41.7±8.7
50~	37.5±11.7	38.7±8.1	41.3±6.8	38.4±9.2	40.8±9.4	40.9±6.9	41.3±7.7	41.6±7.9	41.3±8.5	41.3±7.3
55~	39.7±8.1	37.1±8.2	39.9±8.9	40.8±7.6	38.6±8.2	39.0±6.4	38.4±8.7	37.6±5.5	38.9±12.7	37.0±7.9
60~	36.4±7.9	36.2±6.5	35.5±6.9	38.3±6.4	37.1±8.0	38.4±8.3	38.8±8.0	37.8±6.9	37.7±8.6	38.4±8.2
65~	34.4±7.8	35.5±8.2	34.8±8.8	35.9±8.9	34.0±8.9	35.3±7.4	34.9±7.0	34.6±8.9	36.0±8.3	37.4±6.8
70~	30.4±8.2	33.9±8.5	31.9±8.2	33.7±7.0	30.7±8.1	33.4±7.4	32.5±8.8	33.7±8.1	32.0±9.4	32.4±7.7
75~	26.3±5.5	30.1±8.5	29.9±9.4	33.5±11.1	28.0±5.8	30.8±8.2	31.0±7.1	28.7±7.9	29.4±8.0	30.6±8.6
80~	24.3±8.2	30.0±9.7	26.8±7.7	28.9±8.2	25.4±9.5	30.0±9.3	28.8±7.5	32.3±9.7	25.0±6.8	30.8±8.3
85~	26.6±7.4	32.6±13.0	26.8±6.2	35.1±9.4	25.0±8.3	30.5±7.2	29.1±6.6	33.0±9.4	23.7±8.4	27.5±9.2
Visuospatial										
40~	12.1±3.5	9.9±1.9	11.4±2.5	9.5±2.4	11.6±2.8	10.1±2.0	12.3±2.4	11.0±2.2	11.8±2.5	10.4±2.2
45~	11.7±2.6	10.0±2.1	11.7±2.2	9.5±1.9	11.7±2.5	9.3±2.3	13.0±2.4	9.9±2.4	11.9±2.6	10.1±2.2
50~	10.8±2.6	8.5±1.8	11.0±2.8	9.1±2.2	11.7±2.2	9.9±2.0	12.9±2.2	10.0±2.4	11.1±2.3	9.9±1.8
55~	10.6±2.3	8.5±1.9	10.0±2.7	9.3±2.0	10.8±2.1	9.2±2.0	11.3±2.5	9.8±2.2	10.7±3.1	9.1±1.8
60~	9.3±2.1	8.3±1.9	9.5±1.9	8.2±1.9	10.0±2.3	8.9±2.2	10.8±2.2	9.4±2.2	10.0±2.1	9.0±2.0
65~	9.2±2.2	7.7±1.8	8.8±2.3	7.9±1.9	9.2±2.5	8.8±2.0	10.2±1.8	8.5±2.3	9.1±1.6	8.4±1.9
70~	8.2±1.9	7.9±2.1	8.0±1.9	7.4±1.8	9.0±1.7	7.3±1.7	9.1±2.2	8.2±1.9	8.8±1.9	8.0±1.9
75~	7.7±1.6	7.3±2.1	7.3±2.1	6.8±2.1	8.2±1.6	7.5±2.1	8.1±2.1	7.4±1.6	9.0±1.9	7.8±1.8
80~	7.2±1.5	7.6±2.3	7.2±2.0	7.5±2.7	7.8±2.1	7.5±2.4	8.7±1.9	9.3±3.0	7.8±1.9	8.6±2.6
85~	8.3±2.4	7.5±1.4	7.6±1.8	9.6±2.3	7.4±2.2	8.8±2.8	8.9±2.2	8.4±2.0	8.3±1.7	9.1±2.7
Working memory										
40~	36.2±10.3	34.4±11.1	34.1±9.9	34.4±10.4	34.5±11.7	30.5±10.5	33.7±11.0	33.3±8.9	31.0±13.0	32.1±7.8
45~	32.4±10.4	33.0±10.5	35.0±9.7	33.2±8.7	32.2±11.4	28.9±9.2	33.3±11.0	32.2±9.8	34.5±10.2	29.9±10.0
50~	28.3±11.9	28.5±9.5	29.3±11.8	29.4±11.0	32.4±10.4	28.5±9.4	29.4±11.0	30.4±9.4	30.2±11.3	30.8±9.0
55~	28.9±10.1	25.2±10.4	30.8±11.5	30.0±9.0	31.4±10.2	29.1±8.8	30.3±10.1	27.2±9.3	28.9±12.6	25.0±9.9
60~	28.6±8.5	27.2±10.3	27.3±9.0	26.6±8.5	28.6±9.3	26.7±10.6	26.9±9.8	27.3±10.0	27.6±8.8	26.8±9.0
65~	27.9±10.7	25.5±8.7	26.5±8.8	24.5±10.2	24.7±10.2	23.1±11.2	25.4±8.8	24.1±10.2	25.9±9.3	24.7±7.8
70~	22.6±10.2	22.3±11.4	23.5±10.1	21.1±9.8	21.8±8.9	21.1±8.4	23.7±11.2	21.3±7.9	24.0±9.0	19.8±9.7
75~	21.1±10.5	18.0±9.6	22.5±10.3	18.3±10.3	20.1±7.0	18.2±10.8	19.1±7.4	15.7±7.3	19.6±7.2	18.8±10.5
80~	17.2±8.9	18.4±11.4	16.6±8.7	16.6±13.3	15.0±9.1	16.8±10.2	19.1±7.5	16.7±11.9	13.9±7.8	16.5±10.1
85~	16.6±5.7	25.3±13.6	17.1±10.5	21.4±14.4	23.1±13.1	21.7±11.0	16.0±6.3	26.1±11.5	9.8±6.8	13.5±5.8
General intellect										
40~	12.7±3.4	11.4±3.0	12.7±3.1	11.1±3.4	11.4±4.4	10.6±3.8	11.2±3.3	10.1±2.8	11.4±3.4	10.4±3.2
45~	11.8±3.9	10.4±3.7	12.2±3.2	10.8±3.0	11.7±4.3	9.0±4.0	11.2±3.2	8.6±2.9	12.0±3.1	10.2±3.1
50~	11.0±3.1	8.7±2.9	10.4±3.8	9.5±3.5	10.7±3.8	9.0±3.8	11.6±3.2	8.6±2.5	10.9±2.5	9.6±3.1
55~	11.1±2.8	9.4±2.9	10.4±3.2	9.1±3.4	10.3±4.1	8.7±3.2	10.4±3.1	8.7±3.0	10.1±3.5	9.2±2.8
60~	10.2±2.7	9.5±2.3	9.8±2.7	7.9±2.8	9.7±3.1	7.6±2.9	9.7±3.7	7.9±2.7	9.6±3.0	8.3±3.0
65~	8.9±3.1	7.8±2.7	9.0±2.8	7.6±2.7	7.8±3.4	6.7±3.5	8.0±2.8	7.1±3.3	8.1±2.8	6.8±2.4
70~	8.0±2.5	7.1±2.5	7.5±2.5	6.4±2.5	6.6±2.9	5.3±2.2	7.4±2.8	5.7±1.9	7.7±3.1	5.9±2.3
75~	6.8±2.3	6.0±2.1	6.6±2.4	6.2±2.7	5.7±2.0	4.6±2.4	6.7±2.0	5.3±2.2	6.3±2.4	6.2±2.8
80~	6.5±2.7	6.7±3.3	5.7±1.9	5.5±4.0	4.5±2.4	4.6±2.6	5.6±2.5	6.4±3.0	5.5±2.1	6.0±3.2
85~	5.3±3.4	9.3±4.5	4.3±1.1	8.1±2.8	7.0±4.3	7.2±3.4	6.5±2.6	8.1±2.7	5.5±1.3	6.0±2.1

SD, standard deviation.

Table 4. Mean CSs by age in 5-year increments

Age, years	Subject numbers male/female	Memory of numbers		Memory of words		Visuospatial		Working memory		General intellect		Total	
		Male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD	male mean ± SD	female mean ± SD
40~	214/240	58.6±9.2	56.7±9.6	56.6±9.9	56.3±9.4	59.5±10.7	53.2±8.3	56.7±9.8	56.1±8.4	59.0±9.9	55.9±9.0	58.1±7.2	55.6±6.3
45~	295/267	58.4±8.8	54.8±8.5	55.5±9.0	54.6±8.1	60.2±9.6	51.7±8.6	56.5±9.1	54.7±8.4	58.9±9.8	53.4±9.4	57.9±6.5	53.8±5.9
50~	225/249	55.7±9.2	52.0±8.9	53.3±8.9	53.2±7.7	58.0±9.6	50.6±8.1	53.4±9.8	53.1±8.3	56.4±9.0	51.4±8.9	55.4±6.7	52.1±5.8
55~	213/207	52.7±8.9	51.5±8.0	52.0±9.1	51.2±7.1	55.1±10.0	49.3±7.8	53.6±9.3	51.2±8.3	55.3±9.2	51.2±8.5	53.7±6.7	50.9±5.7
60~	311/312	51.3±8.2	48.5±7.5	50.1±7.8	50.8±7.2	52.2±8.2	47.7±7.9	51.6±7.9	50.9±8.3	53.4±8.4	49.1±7.8	51.7±5.6	49.4±5.3
65~	240/255	48.9±7.8	46.8±8.1	47.9±8.0	48.8±8.0	49.8±8.3	45.6±7.9	50.2±8.2	48.7±8.3	49.4±8.2	46.3±8.2	49.2±5.7	47.2±5.7
70~	291/360	45.3±8.2	44.7±8.1	44.7±8.4	46.5±7.6	47.1±7.6	43.8±7.4	47.6±8.6	45.9±8.2	46.9±7.6	43.1±6.5	46.3±5.8	44.8±5.2
75~	105/103	43.8±6.9	43.2±8.0	42.2±7.4	43.9±8.7	45.1±7.5	42.4±7.6	45.4±7.4	43.2±8.5	44.1±6.4	42.0±6.9	44.1±4.7	42.9±5.8
80~	243/146	40.3±6.9	41.7±9.4	39.3±7.8	43.8±9.0	43.7±7.3	45.1±10.2	41.8±7.3	42.5±9.6	41.6±6.6	42.5±8.9	41.3±4.9	43.1±7.8
85~	43/51	42.0±6.9	45.8±10.3	39.8±7.3	45.3±9.7	45.3±2	47.9±9.6	42.0±8.1	46.4±10.7	41.9±8.4	47.9±9.4	42.2±5.6	46.6±7.8

SD, standard deviation; CSs, cognitive scores.

values of the WAIS-III is below 75 years, although there are many patients with dementia who are older than 80 years. In contrast, the BA provides standard values up to 89 years of age.

The BA can reveal not only the levels but also the longitudinal changes in cognitive function. The WAIS-III, RCPM, and MMSE-J can determine cognitive function at the time of testing, and if their results are within normal limits, the subjects will be considered normal. The results of the BA can be described as abnormal if the longitudinal change is worse than the normal rate of change, even if the score itself is within the normal range. By repeating this test for several years, subjects can determine the degree of their cognitive decline. As described in Introduction, about 70% of hypertension and three-fourths of DM patients do not adequately control their disease. For the prevention of dementia, the control of these lifestyle-related diseases is very important, especially beginning in middle age. The results of the BA may motivate the subjects to improve their lifestyles and thus reduce the risk of related diseases.

Notably, in most of the subtests, CSs consistently decreased until age 80 years (i.e., the group that consists of subjects aged 80–84 years), but started increasing at age 85 years (i.e., the group consisting of subjects aged 85–89 years). This increase may be caused by biological selection bias. The mean life span of Japanese individuals is about 81 years for male and 87 years for female individuals. This means that someone who can complete the BA on a PC at the age of 85 years or older may be in excellent cognitive and physical condition compared with the standard elderly persons. Therefore, we speculate that this is the reason for improved results of cognitive tests in the 85 age-group.

The present study has several limitations that should be noted. First, information pertaining to the educational history was not accounted for. However, given the large number of subjects for the standardization, we believe this would negate any differences. Second, correlations between the BA and WAIS-III, RCPM, or MMSE-J were not performed. We understand the importance of these analyses and will undertake these comparisons in the near future. Third, the possibility that patients with mild cognitive impairment were included among elderly subjects could not be completely excluded. But the fact that they could deal with the novel device suggested that their cognitive function was relatively preserved. Last, longitudinal changes in the BA scores for the same subjects are yet to be assessed. Continuous follow-up of the subjects will enable us to ascertain individual rates of cognitive changes based on the results over

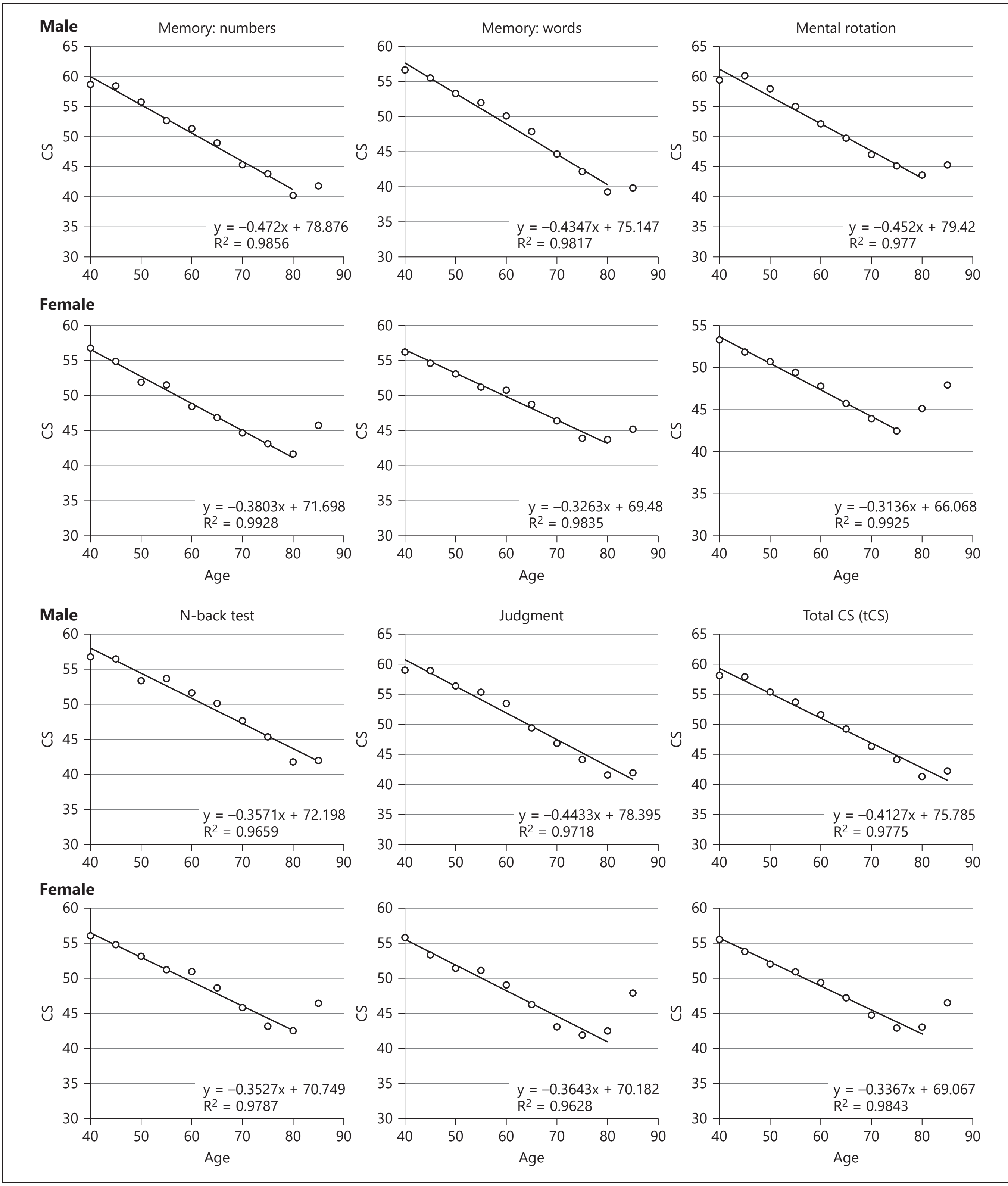

Fig. 9. Mean CSs according to age. There is a clear negative correlation between the CSs and age for all subtests. It is noteworthy that in most subtests, the CSs consistently decreased until 80 years of age, but started to increase at 85 years of age. CSs, cognitive scores.

several years, which will be nearly the same as the trends detected in the present study. Despite these limitations, we expect the BA to be useful for detecting longitudinal cognitive changes compared to the pattern seen in normal aging, and we believe that it will be able to provide the motivation for subjects to improve their lifestyles.

Conclusion

We developed a new cognitive function test, named the BA, which comprises various cognitive domains. The BA can be easily performed on a PC online, and the standardization was carried out using the data from over 4,000 subjects ranging from 40 to 89 years old. We observed that cognitive function linearly declines with normal aging. By performing the BA every year, subjects will be able to detect any abnormal rates of the cognitive decline even if the results themselves are within normal limits. This awareness may bring forth the motivation to improve aspects of their lifestyles which are critical for dementia prevention.

Statement of Ethics

This study received approval from the Advanced Institute of Industrial Technology Research Ethics Committee [Approval No.: 19009] and was conducted in accordance with the Helsinki Declaration of 1975. All of the processes of the subject recruitment and data collection were performed through the Internet, so all the participants provided informed consent by clicking the button of the Internet site of the Macromill Group Company.

Conflicts of Interest Statement

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Author Contributions

Masayuki Satoh: design of this study, interpretation of data, and writing the manuscript. Ken-ichi Tabei: interpretation of data and revision for important intellectual content. Saiko Fujita: analyses of data. Yoshinori Ota: design of this study and the acquisition of data.

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