

Japan's super-aging society and the need for the dementia prevention

-CKPT to detect decline before dementia onset and its application-

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Background: The total world population was about 7.8 billion in 2020, but is expected to exceed 10.1 billion in 2060. The population of people aged 65 and over is also expected to rapidly increase from about 700 million to about 1.8 billion. This clearly indicates that the number of dementia patients, the biggest risk factor for which is aging, is rapidly increasing, and this is a challenge for humanity. In Japan, which has the world's highest aging rate, the number of dementia patients is estimated to be about 6.3 million in 2020 and reach 11.54 million in 2060, and the burden on the public in relation to dementia care is a problem. For this reason, the government established the Dementia Policy Promotion Guidelines in 2019, and is promoting policies based on two pillars: coexistence with people with dementia and prevention of dementia.

Objective: To detect subtle changes before the onset of dementia without using expensive equipment or invasive methods in order to prevent dementia.

Methods: To achieve this goal, we devised a neuropsychological test called CKPT (Color Kanji Pick-out Test) and established evidence for it. We then established diagnostic criteria using large-scale data and are moving towards practical use.

Results: It has been about a year since we started dementia prevention activities using CKPT, and we will introduce how it works in annual CKPT Reports. Since the CKPT can be easily translated into other languages, we have been preparing an English version. We have prepared the test questions and the explanatory Power Point presentation to be used when administering the test.

Conclusion: I hope that someone will be interested in an English version of CKPT.

**Background around Dementia
Aging Society**

As the aging society is the background of dementia, the problem to solve by humanity is clearly pointed out using Table 1. (United Nations, 2024) Toward 2060, the world's population will increase as life expectancy increases thanks to advances in public health and medical technology. The total world population was about 7.8 billion in 2020, but is expected to exceed 10.1 billion in 2060. This clearly indicates that the number of dementia patients is rapidly increasing because the biggest risk factor is aging. This is one of the major problems facing humanity that needs to be solved. The population of people aged 65 and over is also expected to rapidly increase

from about 600 million to about 1.8 billion. I would like to add another comment using the population over 65. In recent years, there has not been a big difference between the populations of developed and developing Regions, but the population of developing Regions is predicted to increase dramatically towards 2060. This means that dementia issues in developing countries will become an international issue. Next, let's look at the percentage of the population over 65. As aging is the biggest risk factor for dementia, so from this perspective, we can see that even in 2060, the risk of dementia will be still higher in developed countries than in developing countries.

Table 1: The trend of population and percentage of population over 65 years' old.

	1950 year	In 2015	2060 *Median projection
Total Population	2,536 Million	7,380 Million	10,152 Million
Population over 65 years old			
Total	129 Million	608 Million	1,810 Million
Developed Regions	63 Million	221 Million	357 Million
Developing Regions	66 Million	387 Million	1,453 Million
Percentage of population over 65 years old			
Total	5.1 %	8.2 %	17.8 %
Developed Regions	7.7 %	17.6 %	28.2 %
Developing Regions	3.8 %	6.3 %	16.4 %
Life Expectancy			
Male	45.49 years	68.53 years	76.29 years
Female	48.49 years	73.31 years	80.64 years
Reference: UN, World Population Prospects: The 2019 Revision			
Developed regions include Europe, Northern America, Japan, Australia, and New Zealand. Developing regions include Africa, Asia (excluding Japan), Latin America, Melanesia, Micronesia and Polynesia.			

Next, let's look at the trends in presentation of population over 65, in each country on Fig.1. (United Nations, 2024) The graph on the left shows the trends in Europa and USA, with Japan's trends shown for reference. Japan's high rate stands out. The graph on the right shows the trends in Asian countries. Notable are the rapid changes in China, Singapore, South Korea, and Thailand. South Korea in particular is predicted to overtake Japan and becomes the world's largest aging country, by 2050.

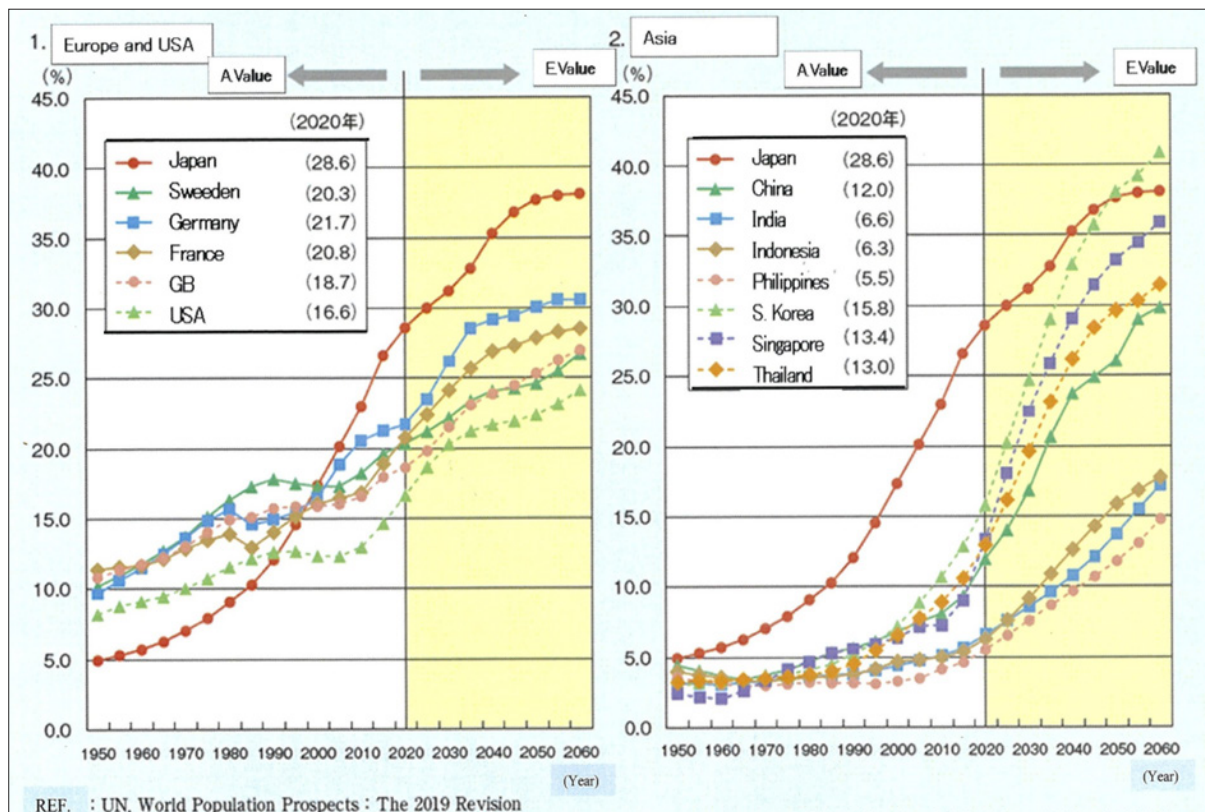


Figure 1: Changes in the world's aging rate in Actual value and Estimated value.

The progression of dementia and the target of this research

The progression of dementia is shown in Fig.2. (Shimura, 2023) Dementia progresses from Healthy to Preclinical Stage of Dementia, Mild Cognitive Impairment (MCI) and Dementia. At Healthy and Preclinical Stage of Dementia, there are no symptoms, and symptoms only appear when the causative agents are deposited to a point of near saturation during 15-20 years. The border between MCI and Dementia is when cognitive impairment progresses to the point where it interferes with daily life and the condition is called dementia. There are three types of prevention in dementia care, and today's target is healthy people and those in Preclinical Stage of Dementia, which is strictly speaking called primary prevention, but when we talk about prevention in this paper, we are referring to primary prevention and it is the target of our research.

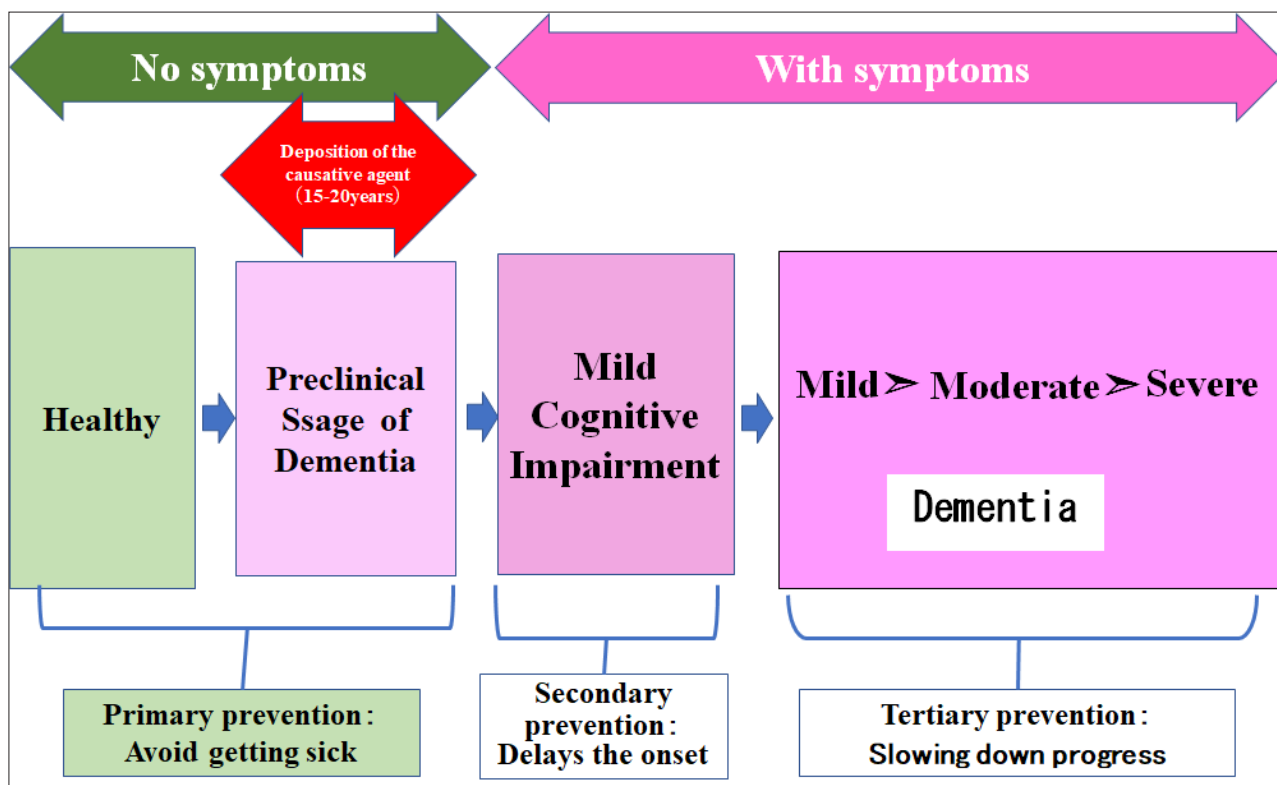


Figure 2: Progression of Dementia and Its Prevention

Japanese Government Dementia Policy

The trends in the number of people with MCI and dementia in Japan (Fig.3) (Japan Ministry of Health, Labor and Welfare [JMHLW], 2024) which has the highest aging rate in the world is show in Fig.2. The number of people with Dementia has been steadily increasing every year until 2060, when the aging rate will peak. The number of people with MCI has been also increasing every year until 2055, but it is predicted that the tendency changes in 2060. This means that the number of people with dementia has peaked at that point. In light of this situation, the Japanese government established “Five-Year Plan for Promoting Dementia Measures (Orange Plan) (Japan Ministry of Health, Labor and Welfare [JMHLW], 2024)” on 2013, “Advanced Five-Year Plan for Promoting Dementia Measures (New Orange Plan) (Japan Ministry of Health, Labor and Welfare [JMHLW], 2024)” on 2015, “Dementia Measures Promotion Principal (Japan Ministry of Health, Labor and Welfare [JMHLW], 2024)” in 2019 and enacted” the Basic Act on Dementia 2023 (Japan Ministry of Health, Labor and Welfare [JMHLW], 2023)”. Challenges have just started.

1. How the more than 10 million people with cognitive symptoms and people without dementia live together?
2. How to get the 3.5 million elderly people without cognitive symptoms to adopt good lifestyle habits tha reduce the risk of dementia and promote dementia prevention?

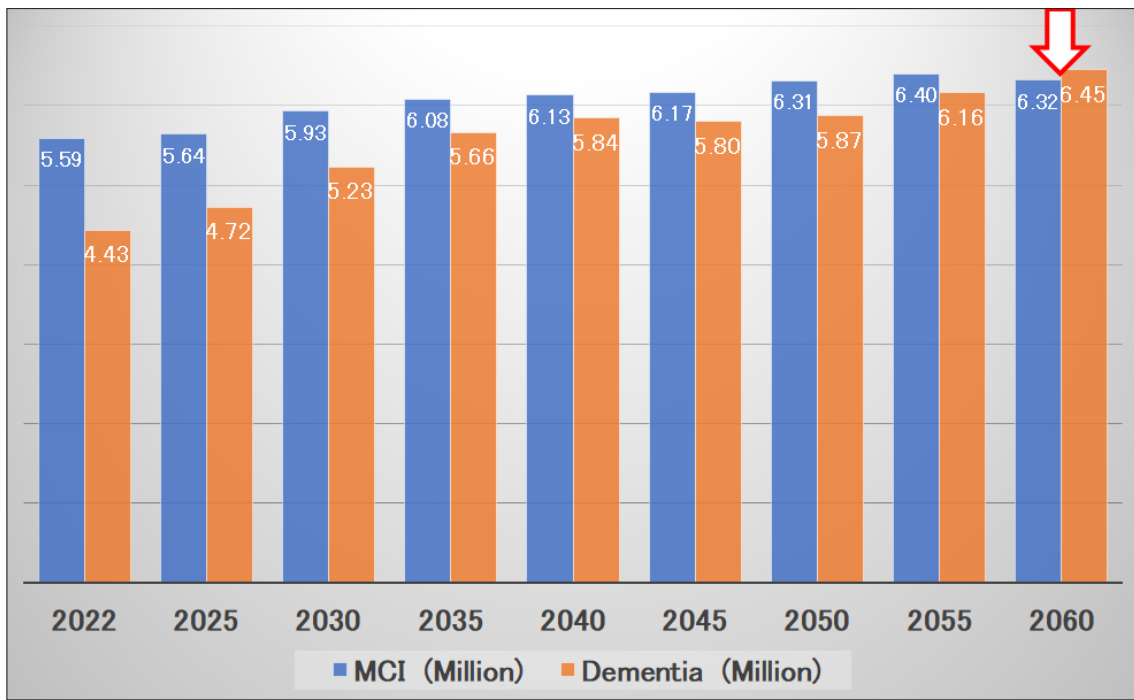


Figure 3: Japanese population with MCI and Dementia

WHO's suggestion on Dementia Prevention

Risk Factors for Dementia were suggested by WHO. Since 2019 (World Health Organization, 2019) when WHO first published guidelines on reducing the risk of dementia from the Lancet, it has been updated in 2020 (Livingston, et al., 2020) and 2024 (Livingston, et al., 2024) Fig.4 shows the latest one. It says that risk factors exist in three stages: Young, Middle, and Old, and that the total risk factor is 45%. The table on the right is a clear transcription of the circles representing risks in the chart on the right. WHO's risk reduction guidelines have provided researchers not only in Japan but also all around the world with a foothold in dementia prevention.

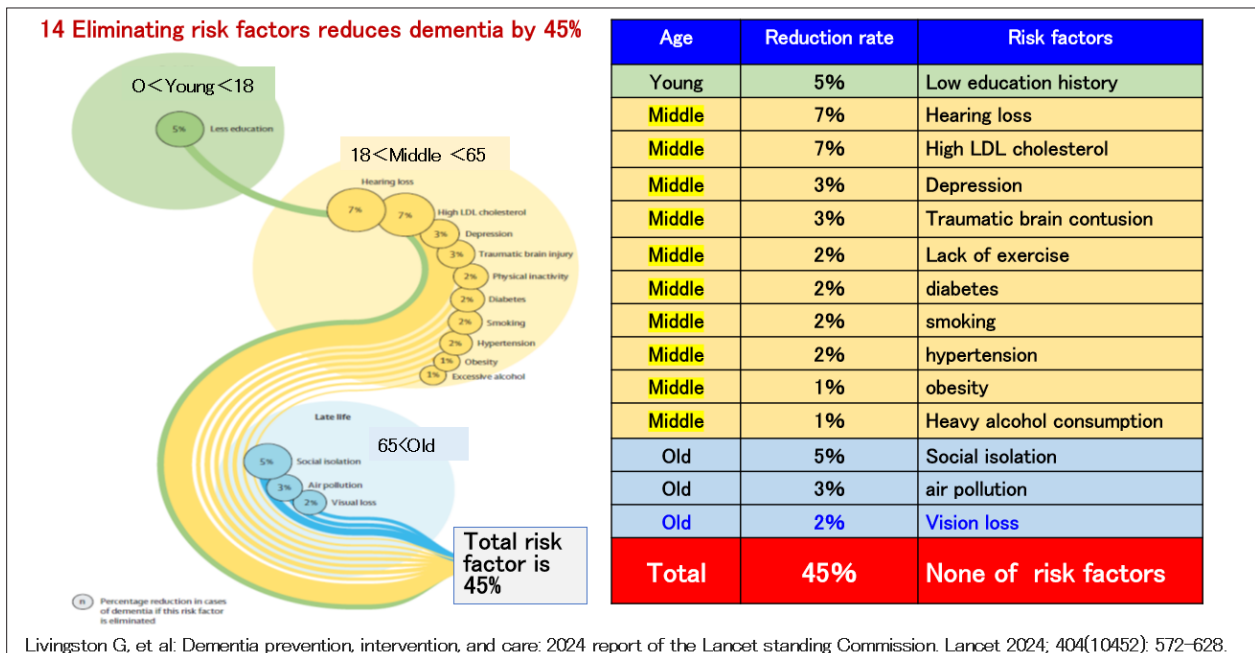


Figure 4: Risk factors for Dementia by WHO.

Two indispensable technologies for Dementia Prevention

There are two technologies that are indispensable for dementia prevention. One is the technology to detect slight declines in cognitive function before the onset of dementia. The other is the implementation of lifestyle habits to avoid the risk of developing dementia, as suggested by WHO, and attempts at brain rehabilitation. In this paper, I will introduce a method that we have been researching for many years to detect slight changes in cognitive function.

How to detect slight disorder before onset of MCI

Fig.5 is the well-known famous Alzheimer's disease diagnostic guideline presented by (Sperling et al., 2023) As I pointed out in the figure, the purpose of our research is to classify the level of disorder without using expensive instruments such as PET or invasive instrument such as CSF. To achieve this goal, we turned to neuropsychological testing.

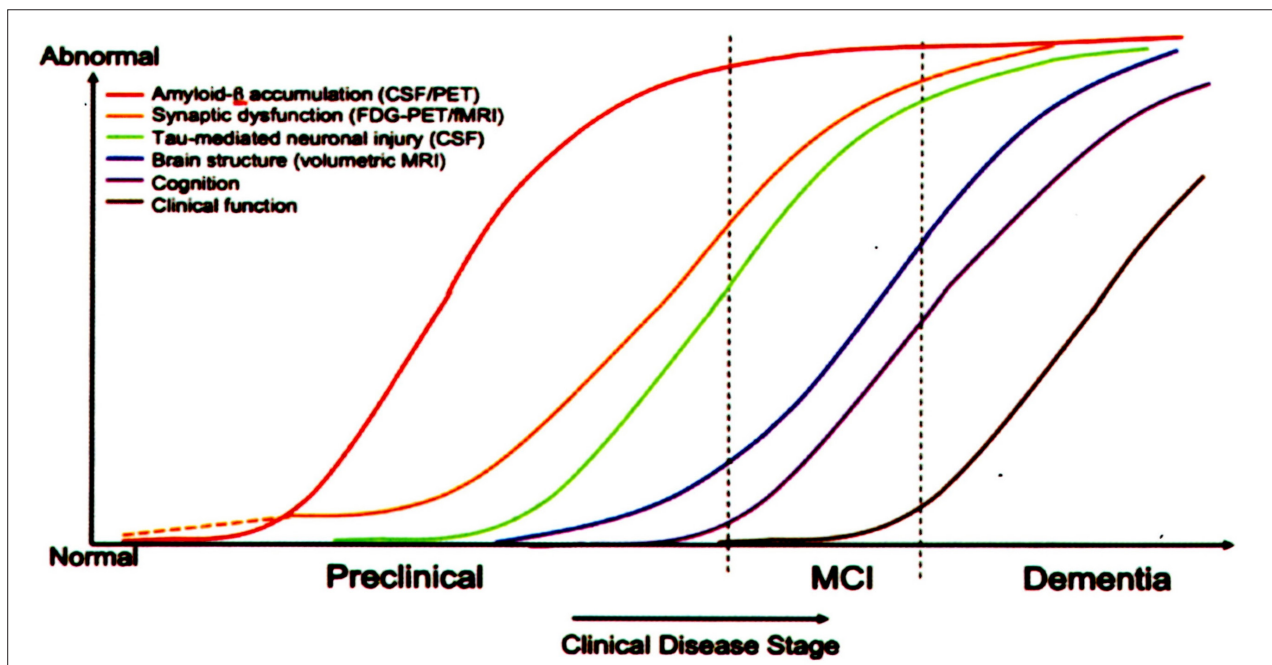


Figure 5: Alzheimer's disease diagnostic guideline.

A neuropsychological test named Color Kanji Pick-out Test (CKPT)

After the idea applied to Patents (Shimura et al., 2003; Shimura et al., 2004; Shimura et al., 2020; Shimura et al., 2020; Shimura et al., 2020) it takes quite long periods to make it a practical application. The idea is based on the hypothesis that the slight disorder of cognitive function caused by slight disorder of every part of brain is detected as a slight disorder of the prefrontal cortex functions. The reason is that the prefrontal cortex is the command tower when humans take action (Sari & Erbas, 2022). Therefore CKPT is composed of a precautionary distribution ability and working memory ability.

To examine them, two tasks were devised, which were Story and Questions. The story shown Fig.6 is the example presented to the subjects and is a translation of the Japanese story. As the test subjects read the story, when they come across a color word that describes a color, they must judge whether the meaning of the word matches the printed color or not, marking it with a circle if it matches or an X if it does not match. This is an application of Stroop Effect (Stroop, 1992) In Questions of Fig.7, subjects should answer the questions without seeing the Story. In the actual CKPT, there are 25 color words and 12 questions and the score Index1 is calculated by the products of the number of correctly judged color words and the rate of correctly answered the questions.

Natsuko grabbed her small pink bag and went to the sea to swim. Beyond the brown hills ,there was a long, gray sandy beach, where red, blue, and green parasols were lined up like flowers.

Figure 6: A sample of Story.

Enclose the answer that you think is correct in circles.

(1) What color was Natsuko's back?

(red, pink, green, forgot)

(2) What did Natsuko go to do?

(Shopping, swimming, sightseeing, forgot)

Figure 7: A sample of Questions.

Evidences of CKPT

First presentation of the results was done internationally in 2018 (Shimura et al., 2018) The following items were investigated and confirmed to establish evidence. (Shimura et al., 2019).

1. To determine whether the CKPT is a test that activates the prefrontal cortex, we used near-infrared spectroscopy to compare the CKPT with four-number reverse chants, Kawashima calculation drills, and other methods, and confirmed that the CKPT activates the prefrontal cortex the most (Shimura, 2009).
2. As for criterion-related validity, the correlation between the Honma Checklist (Ryan et al., 1990), WCST (Berman et al., 1915) MMSE (Folstein et al., 1975) and FAB (Dubois et al., 2000) was examined, and a superior correlation was found between the WCST (correct answers) and WCST (error answers).
3. As for Sensitivity and Specificity, we found that Sensitivity=1 and Specificity=0.96 when the cutoff for CKPT was taken as the average-1.5 SD, under the standard cutoff of 28 points for MCI on MMSE.

Feature of CKPT

Fig.8 explains the difference between CKPT and conventional neuropsychological tests such as MMSE, FAB, CDR (Hughes et al., 1982) etc. In the figure, histograms of the two tests, MMSE as a conventional test and CKPT are shown when applied to healthy and preclinical subjects, in which MMSE is biased towards high scores, making classification difficult, but CKPT shows a normal distribution, so classification is easy using the mean and standard deviation.

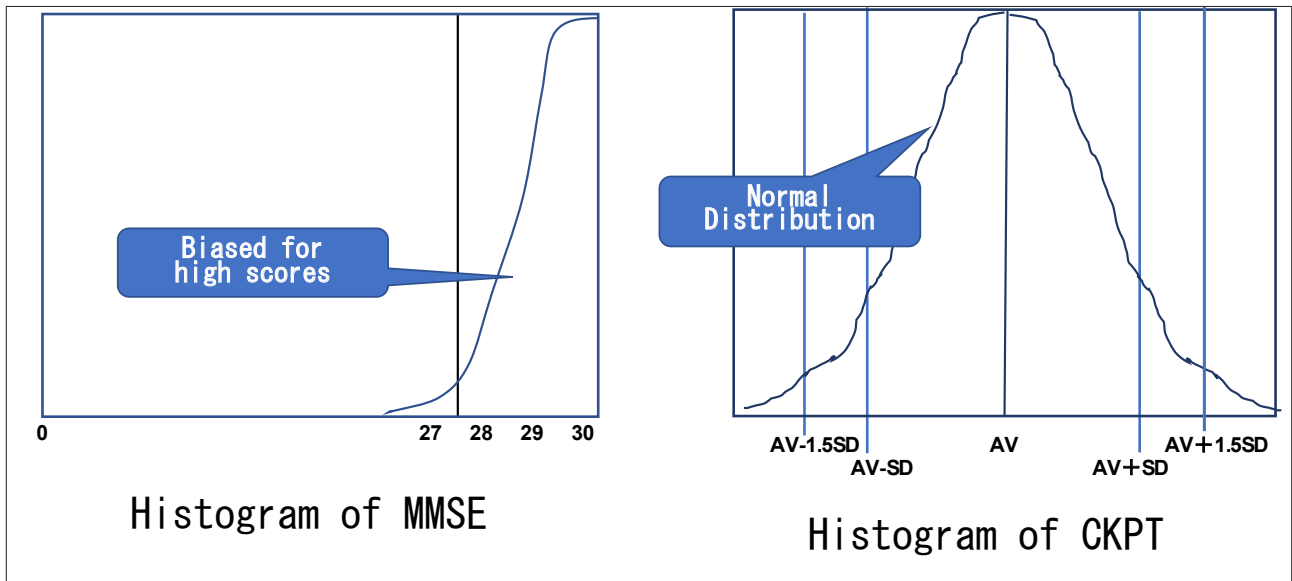


Figure 8: Comparison of Histograms Between MMSE and CKPT.

4 Distribution Parameter of CKPT obtained by healthy and preclinical subjects

This results were first presented internationally in 2019 (Shimura, et al., 2019). Table.2 shows distribution parameter of CKPT obtained by healthy and preclinical subjects (Shimura, 2020) These values are used as diagnostic criteria. In our screening, a subject whose value is below average-1.5SD. is advised to receive some treatments by Medica Doctor.

Table 2: Distribution parameter of CKPT using 1367 subjects.
Average-1.5SD or less: 0.067, Average-SD or less: 0.159.

Male	Average - 1.5SD	Average - SD	Average	Average + SD	Average + 1.5SD
Sixties	5.1	7.3	11.7	16.1	18.3
Seventies	5.1	7.0	10.7	14.4	16.2
Eighties	3.0	4.9	8.6	12.3	14.2

Female	Average - 1.5SD	Average - SD	Average	Average + SD	Average + 1.5SD
Sixties	5.9	7.9	11.9	15.9	17.9
Seventies	4.6	6.6	10.6	14.6	16.5
Eighties	2.3	4.5	8.8	13.1	15.3

Application of CKPT to Brain health checkup

We have started a dementia prevention service using CKPT to the people who would not fall in dementia. It is a brain health checkup that is examined every year and not found in conventional medical examinations, mainly blood tests.

A Japanese sample of the CKPT report used in the service is shown in Fig.9. The column below shows the annual trend in Index 1. The vertical axis shows the CKPT score Index 1, and the horizontal axis shows the age at which the test was taken. Since tests are taken every year, the trends are shown in a line graph like this. The last point is the latest score. This report also includes a column for comments on dementia prevention.

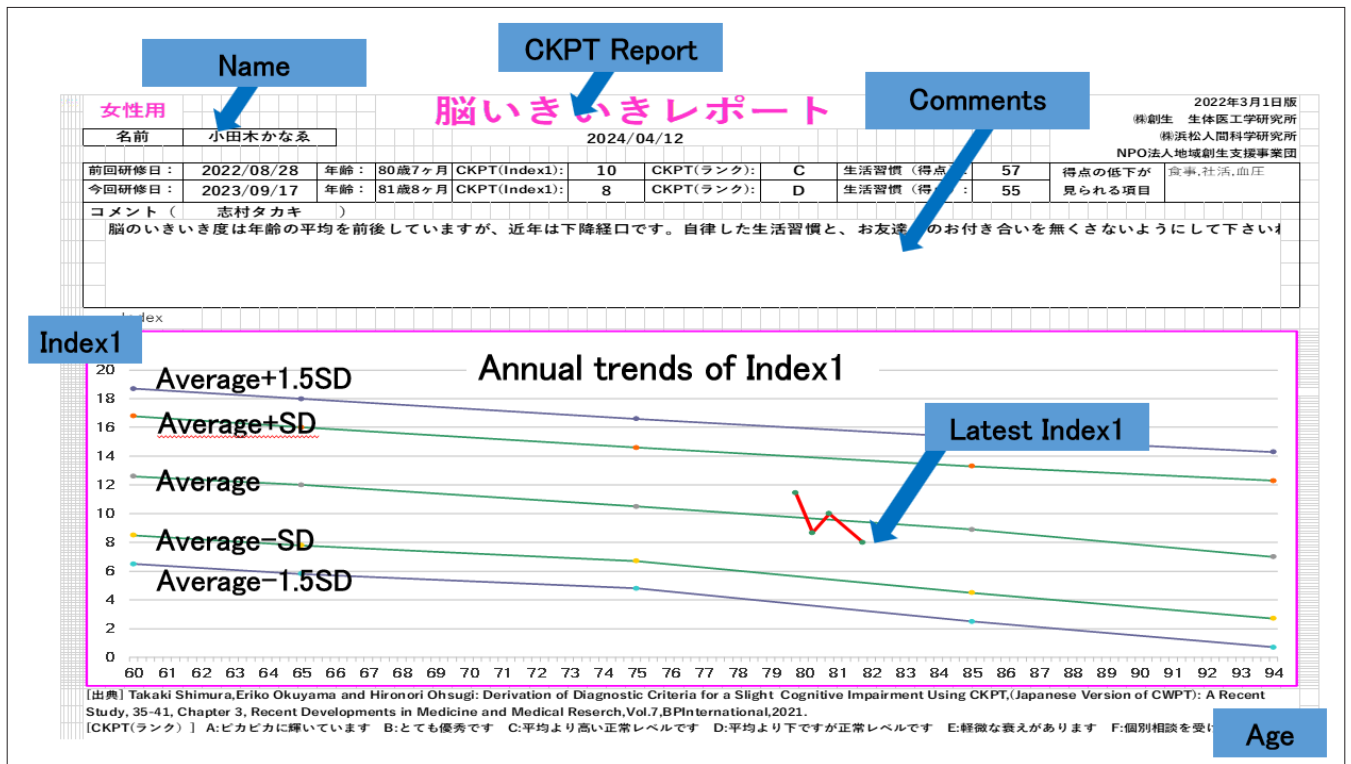


Figure 9: A Japanese sample of the CKPT report

Summary

1. The trends in the world's population and aging rate are introduced, then I pointed out that humanity faces the threat of dementia.
2. Two main measures put forwards by Japanese government are "coexistence" and "prevention."
3. I introduced a neuropsychological test called the CKPT, which we are conducting to detect slight decline in cognitive function before the onset of cognitive impairment, and Brain Checkup measures using CKPT is introduced which has just started as an application.
4. Finally I would like to say that we are recruiting collaborative researchers because we have already prepared the English Version of CKPT (Shimura, et al., 2019) and the researchers are easy to challenge it.

Acknowledgment

The content of this paper was revised based on what was announced as a keynote speaker at the 2nd International Conference on Clinical Case Reports, and I am grateful to the board members who have given the opportunity to make the presentation.

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