ORIGINAL

Usefulness of a novel higher brain dysfunction screening test for evaluating higher brain function in healthy persons

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Abstract : To accurately and rapidly screen for higher brain dysfunction, we developed a screening test named the "higher brain dysfunction screening test" (HIBRID-ST). Previous studies have reported a decrease in higher brain function with age. However, whether HIBRID-ST can detect a decrease in higher brain function in healthy persons remains unclear. We aimed to assess the usefulness of HIBRID-ST for evaluating higher brain function in healthy persons. We recruited 60 persons without physiological abnormalities and divided them into six equal groups based on their age (20s–70s). HIBRID-ST addresses orientation, short-term memory, word recall, situational awareness, visual short-term memory, and graphic replication and includes the Trail Making and Kana-hiroi tests. There was a significant negative correlation between the participants' age and their total HIBRID-ST score ($\rho = -0.68$, $p < 0.01$). The total HIBRID-ST score of participants in their 70s was significantly lower than that of participants in their 20s–60s ; the total HIBRID-ST score of participants in their 60s was significantly lower than that of participants in their 20s–50s. Our findings show that HIBRID-ST accurately detects an age-related decline in higher brain function. Further studies are needed to examine the usefulness of HIBRID-ST in patients with higher brain dysfunction. J. Med. Invest. 64 : 280-285, August, 2017

Keywords **:** *higher brain dysfunction, screening test, HIBRID-ST*

INTRODUCTION

Advances in medical technology have improved the survival rate of patients with cerebrovascular disease or traumatic brain injury ; however, the number of patients with higher brain dysfunction resulting from these diseases is increasing.

In 2001, the Japanese Ministry of Health, Labour and Welfare initiated a higher brain dysfunction support project. It promulgated diagnostic criteria and a standard training program that addressed social reintegration as well as activities of daily living and nursing care support for patients with higher brain dysfunction. Higher brain dysfunction is diagnosed based on the existence of cognitive symptoms that negatively affect the activities of daily living as well as social adaptation due to memory, executive function, and social behavior disorders and attention disturbances. Organic brain lesions that elicit cognitive symptoms can be identified using magnetic resonance imaging, computed tomography, and electroencephalography. However, because symptoms of higher brain dysfunction are not always accurately detected using widely available clinical assessments, diagnosis can be challenging. Consequently, affected patients may not receive the social security benefits for which they are eligible (1).

Because symptoms of higher brain dysfunction are obscure, several assessments are required for its diagnosis. The neuropsychological tests for the diagnosis of higher brain dysfunction include the Wechsler adult intelligence scale, Wechsler memory scale, and behavioral assessment of the dysexecutive syndrome, but these tests require several hours to complete (2). Thus, in the clinical setting, the mini-mental state examination (MMSE) (3) and the revised version of Hasegawa's dementia scale (HDS-R) (4), which are used to screen for dementia, have been used as screening tests for higher brain dysfunction. However, these tests do not include any items that evaluate executive function, social behavior disorder, and attention disturbances. To accurately and rapidly screen for higher brain dysfunction, we developed a screening test named the "higher brain dysfunction screening test" (HIBRID-ST).

Studies have reported that aging leads to a decrease in higher brain function (5-9). However, whether HIBRID-ST can detect a decrease in higher brain function in healthy persons remains unclear. The purpose of this study was to assess the usefulness of HIBRID-ST for evaluating higher brain function in healthy persons.

MATERIALS AND METHODS

Participants

We enrolled 60 healthy volunteers (30 men, 30 women) from June 2014 to July 2014 and divided them into six equal groups based on their age (20s–70s). The mean age of the cohort was 48.6 ± 18.7 years. All participants were recruited using advertisements. Potential participants who had neurological disorders were excluded. All participants provided informed consent for inclusion in this study and for the publication of the study results. The current study protocol was approved by the Ethics Committee of Tokushima University.

Study design

In this investigative study, we used a cross-sectional design.

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Assessment using HIBRID-ST

HIBRID-ST addresses eight factors : the participant's orientation, short-term memory, word recall, situational awareness, visual short-term memory, and graphic replication and includes the Trail Making and Kana-hiroi tests. As shown in Table 1, it includes 21 items : items 1–9 are orientation factors, 10–15 are short-term memory factors, 16 is a word recall factor, 17 a situational awareness factor (Fig. 1), 18 a visual short-term memory factor (Fig. 2), 19 a graphic replication factor, 20 a Trail Making factor (TMT-A and TMT-B) (Fig.3, 4) (10), and 21 is the Kana-hiroi test. The scores of TMT-A and TMT-B are adjusted by reference time required of in the 20s–60s. The scores of the Kana-hiroi test are adjusted by references which number of correct answers in the 20s–70s.

Each correct response to items 1–15 and item 18 received a score of 1. The tasks and the scores assigned to correct responses to the other items are listed in Table 1. The highest possible HIBRID-ST score is 50. To determine the reliability of HIBRID-ST, we additionally recruited six healthy volunteers (mean age, 47.0 ± 5.6 years) and compared their results for the same tests completed after a 1-week interval. We also recorded the time required for completion of HIBRID-ST.

Table 1. Check sheet for the higher brain dysfunction screening test (HIBRID-ST)

Higher brain dysfunction screening test (HIBRID-ST)

	Examination question/task		Score	
			Incorrect (0)	Correct (1-8)
1	What year is it?		0	1
2	What month is it?		0	1
3	What is the date?		0	1
4	What day of the week is it?		0	1
5	Approximately what is the time?		0	1
6	What season is it?		0	1
7	Where are you?		0	1
8	Where are you from?		0	1
9	What is your address?		0	1
10	Repeat these numbers : 5-8-2		0	1
11	Repeat these numbers : 7-2-8-6		0	1
12	Repeat these numbers : 7-5-8-3-6		0	1
13	Count backward from 5 to 7		0	1
14	Repeat the numbers 4-1-5 in backward order		0	1
15	Repeat the numbers 4-9-6-8 in backward order		0	1
16[1]	Name as many vegetables as you can Name more than 12 vegetables in 60 seconds		0	1 2 3 4 5 6
17[2]	Interpret this picture		0	1 2 3 4 5 6
18[3]	Call out the items in this picture Memorize the items in this picture		0	1 2 3 4 5 6 7 8
19[4]	Graphic replication	Cube	0	2
		Flower	0	2
20[5]	Trail making tests	Trail making test A	0	1 2 3 4
		Trail making test B	0	1 2 3 4
21[6]	Kana-Hiroi test		0	1 2 3

Total score () / 50

Scores assigned for items 16 - 21 :

[1]Item 16
The participant is asked to name as many vegetables as possible within one minute.
For 7 vegetables named the score is 1, for each additional vegetable a score of 1 is assigned (maximum score = 6). When fewer than 7 vegetables are named, the score is 0.

[2]Item 17 (Fig. 1)
The participant is asked to interpret the situation depicted in the picture (maximum score = 6).
Examples of correct answers are :
The picture is about a snack (or doughnut).
One child (or the girl in the center) is angry.
One child (or the girl in the center) is angry because she does not have a doughnut (snack).
One child (or the girl on the right) is surprised/confused.
One child (or the girl on the right) says she didn't take the doughnut.
One child (or the boy) is eating the girl's doughnut.
etc. Each acceptable interpretation receives a score of 1.

[3]Item 18 (Fig. 2)
The participant names the displayed items (no score is assigned for this task).
The picture is removed and the participant is asked to recall as many items as possible.
Each correctly memorized item receives a score of 1 (maximum score = 8).

[4]Item 19
The participant is shown a cube or a flower and is asked to replicate “cube” and “flower” for the shown item. Each correctly replicated item receives a score of 2 (maximum score = 4).

[5]Item 20 (Fig. 3, 4)
The participant first performs practice trail making tests. In test A, the numbers from 1 to 25 must be connected. In test B, the presented numbers and Japanese characters must be connected. When the time required by the participant for the completion of each test is less than the mean + one standard deviation (SD), between the mean + 1 SD and the mean + 2 SD, or longer than the mean + 2 SD of the mean value recorded for his/her age group, a score of 4, 3, or 2, respectively, is assigned. A score of 0 is recorded when the participant does not complete the test (maximum score = 8).

[6]Item 21
In the Kana-Hiroi test, the participant must eliminate Japanese characters with vowel sounds (a,e,i,o,u). When the number of correct responses is below the mean minus one standard deviation (SD), between the mean -1 SD and the mean -2 SD, or above the mean -2 SD of the mean value recorded for his/her age group, a score of 3, 2, or 1, respectively, is assigned. A score of 0 is recorded when the participant does not complete the test (maximum score = 3).

Fig. 1 Illustration used for the situational awareness test

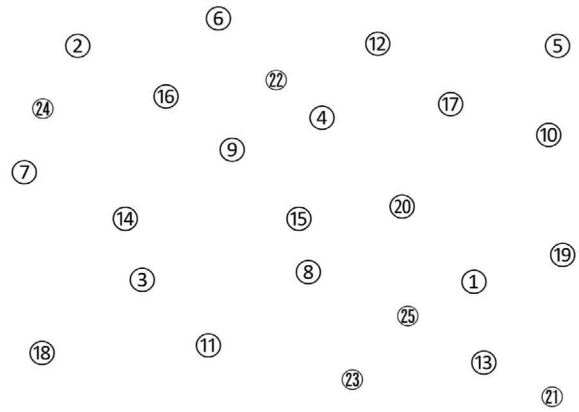

Fig. 3 Digits to be connected in the Trail Making test (part A) -item 20

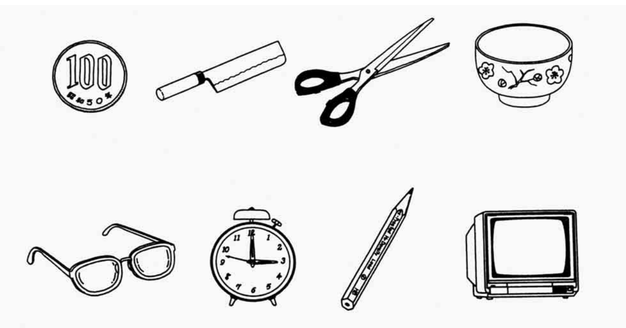

Fig. 2 Drawings of objects used for the visual short-term memory test

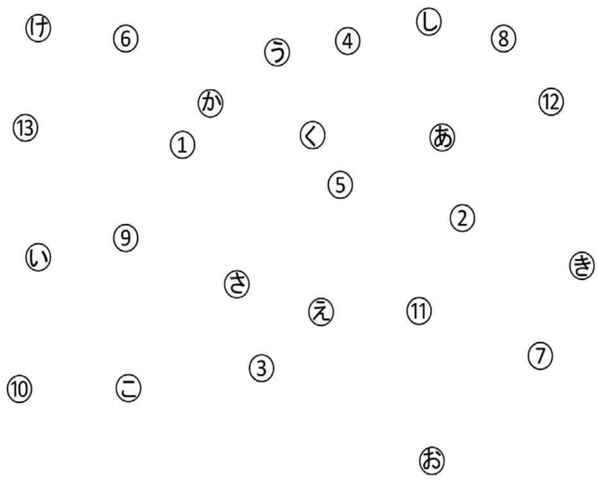

Fig. 4 Hiragana (Japanese characters) and digits for the Trail Making Test (part B) -item 20

Statistical analysis

Statistical analyses were performed using SPSS version 21 (IBM SPSS Japan, Tokyo, Japan). Normally distributed variables were identified using Shapiro-Wilk test. We used Spearman's correlation test to assess the correlation between the participants' age and their total HIBRID-ST score. The Mann–Whitney U test was performed to reveal differences in the total HIBRID-ST scores in men and women based on the sex. The total HIBRID-ST score and the median scores assigned to the eight factors for each age group were compared using Kruskal–Wallis test. The significance of specific inter-group differences was determined using Bonferroni test. To examine the reliability of HIBRID-ST, we calculated the Spearman's rank correlation coefficient and intra-class correlation coefficients [ICCs (1.1)]. P values of < 0.05 were considered significant.

RESULTS

HIBRID-ST detects an age-related decline in higher brain function

The median total HIBRID-ST score of the 60 participants was 46.0 ; there was a significant negative correlation between the total HIBRID-ST score and the age in total participants (correlation coefficient = –0.68, $p < 0.01$; Fig. 5). The median total HIBRID-ST scores for men and women were 45.0 and 46.5, respectively. No significant differences were observed in the total HIBRID-ST scores based on the sex.

The median score of the six age groups for the eight factors and the total HIBRID-ST scores are shown in Table 2. The total HIBRID-ST median score of participants in their 70s was significantly lower than that of participants in their 20s–60s ($p < 0.01$) ; the total HIBRID-ST median score of participants in their 60s was significantly lower than that of participants in their 20s–50s ($p < 0.01$). These results indicated a possibility that HIBRID-ST detects an age-related decline in higher brain function.

HIBRID-ST showed that participants older than 60 years manifested a decline in function in their word recall, situational awareness, visual short-term memory, and graphic replication

The word recall score was significantly lower in the 70s group than in the 20s group ($p < 0.05$). The situational awareness score of participants in their 70s was also significantly lower than that of participants in their 20s–50s ($p < 0.01$) ; it was also significantly lower in participants in their 60s than in those younger than the 30s and 40s ($p < 0.05$). The visual short-term memory score was significantly lower in participants in their 70s than in participants in their 20s ($p < 0.01$), and it was lower in participants in their 60s than in participants in their 20s–40s. The graphic replication score of the oldest age group was significantly lower than that of the 20s, 30s, and 50s groups (Table 2). There was no significant inter-group difference with respect to orientation, short-term memory, and the Trail Making and Kana-hiroi test results among the six age groups.

The first and second median scores of the total HIBRID-ST were 49.5 and 50.0, respectively, and the Spearman's rank correlation coefficient and ICCs (1.1) were 0.707 (substantial) and 0.706 (substantial), respectively. The average completion time for HIBRID-ST was 15.9 ± 1.8 min.

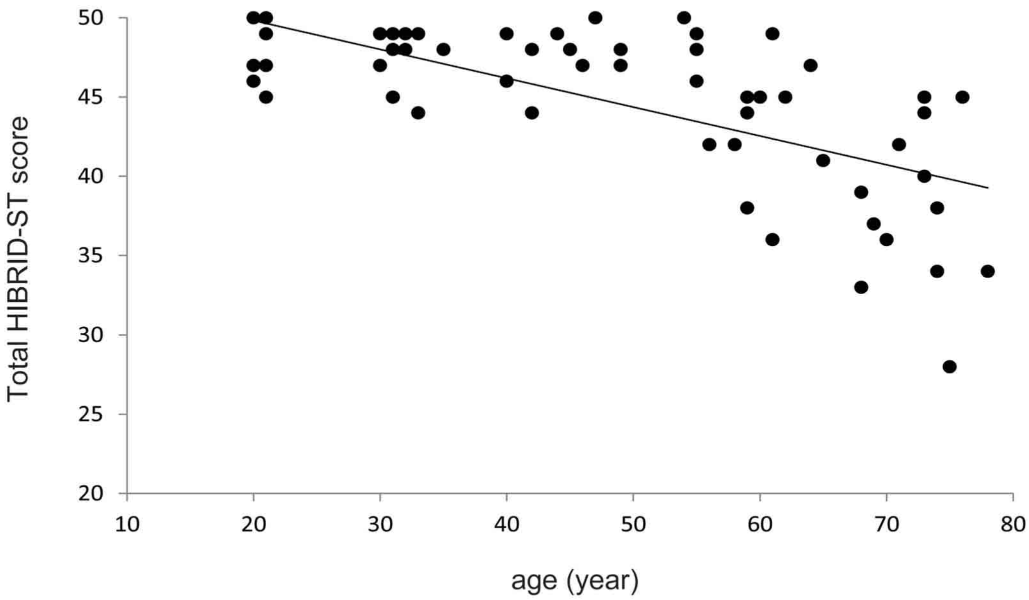

Fig. 5 Negative correlation between the total HIBRID-ST score and the test-taker's age (Spearman's correlation coefficient : –0.68, $p < 0.01$)

Table 2. Median HIBRID-ST score of participants

Factor	20s n = 10	30s n = 10	40s n = 10	50s n = 10	60s n = 10	70s n = 10
Orientation	9.0	9.0	9.0	9.0	9.0	9.0
Short-term memory	6.0	6.0	6.0	6.0	5.5	5.0
Word recall	6.0	6.0	6.0	6.0	6.0	4.5*
Situation awareness	5.0	6.0	6.0	5.0	4.5†‡	3.0**††‡‡§§
Visual short-term memory	7.5	6.5	6.5	6.0	4.0**‡	5.0**
Graphic replication	4.0	4.0	4.0	4.0	4.0	3.0*†§
Trail making tests	8.0	8.0	8.0	8.0	8.0	8.0
Kana-Hiroi test	3.0	3.0	3.0	3.0	3.0	3.0
Total HIBRID-ST score	48.0	48.0	48.0	45.5	40.0**††‡‡	39.0**††‡‡§§

Data are shown as the median
Statistical analysis by the Bonferroni test
* $p < 0.05$, ** $p < 0.01$ vs 20s
† $p < 0.05$, †† $p < 0.01$ vs 30s
‡ $p < 0.05$, ‡‡ $p < 0.01$ vs 40s
§ $p < 0.05$, §§ $p < 0.01$ vs 50s

DISCUSSION

We showed that HIBRID-ST detects an age-related decline in higher brain function. In addition, considering that there were no differences in the total HIBRID-ST scores in men and women, we think that sex does not influence the total HIBRID-ST score. This novel screening test showed that the decline in higher brain function in terms of word recall, visual short-term memory, situational awareness, and cognitive and graphic replications was more severe in elderly individuals. These findings corroborate those of earlier studies (5-9).

We found that there was no significant difference in the scores assigned for orientation, short-term memory, and the Trail Making (A and B) and Kana-hiroi tests among the six age groups ; however, earlier studies have reported a decline in short-term memory, attention, and executive functions with age (11-20). We consider that this discrepancy is attributable to the facts that the short-term memory tasks of HIBRID-ST may be easier to perform for healthy persons and scores for attention and executive function are adjusted by age. With respect to orientation, we confirmed the existence of a ceiling effect in all age groups.

The incidence of traffic accidents in the elderly with lowered cognitive function has increased and is now a social problem in Japan (21). Requiring elderly drivers to take HIBRID-ST before renewing their driver's license may help prevent such accidents because this test screens for attention dysfunction.

Our study has several limitations. First, we did not assess the HIBRID-ST scores of healthy individuals aged between 10 and 19 years and those aged > 80 years. Second, we did not take into account our participants' educational level, even though it has been shown that the educational level is related to higher brain function (22-24). Third, we have not evaluated the cognitive function of healthy volunteers using MMSE or HDS-R. Finally, we did not recruit patients with higher brain dysfunction.

In clinical settings, higher brain dysfunction with complex symptoms (25) is screened using tests such as MMSE and HDS-R. However, MMSE and HDS-R do not include tools for evaluating the executive function or social behavior disorders. Considering this problem, we developed HIBRID-ST and suggest that it may be a useful screening test for accurately and rapidly diagnosing higher brain dysfunction. Further studies on the utility of HIBRID-ST in patients with higher brain dysfunction are required.

In conclusion, HIBRID-ST accurately detects an age-related decline in higher brain function.

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CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

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