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Brain Activation in Middle-aged Healthy Adults by the Computer-based Cognitive Training Program for Elderly.

- An Activation Study Using Functional Near-infrared Spectroscopy (fNIRS) -

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Abstract

Due to the growth of aging population, cognitive training has been noted as one of the preventive approaches for cognitive decline. While there has been an accumulation of knowledge, it has not been incorporated into programs that are currently used clinically. We developed a set of tasks named "Atama-no-dojo", designed to activate multiple cognitive functions and enhance motivational incentives. The objective of our study was to examine the effects of our program on brain activation. We tested 10 middle aged subjects (49.6±8.1 years old) using functional near-infrared spectroscopy. Significant changes in oxygenated hemoglobin were demonstrated over a large portion of the brain, and obvious effects were found especially in the lateral prefrontal cortex area. The graph showed task related waveforms which appeared to indicate general concentration, task phase (thinking, answering, and waiting for the next trial), and the process of becoming accustomed to the tasks. The subjectively rated pleasantness score was correlated to the correct ratio in tasks of inhibition (r=.75, p<.01), and memory (r=.67, p<.05). These correlations suggested the possibility of a decrease in pleasantness due to the difficulty level.

Key Words

Atama-no-dojo, aging, cognitive decline, cognitive function, prefrontal cortex, PFC

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INTRODUCTION

The increase of aged population is currently a serious subject, to which we should correspond immediately, not only in Japan[1)], but also in many developed and some developing countries[2)]. One of the main problems due to aging is cognitive decline. In recent decades, many studies on age-related cognitive decline and possible preventive means have been conducted. Deterioration of cognitive function with aging has been seen in multiple domains, including memory, executive functions, reasoning, attention, inhibition, and cognitive control [3-7)]. These declining functions are mainly related to the prefrontal cortex (PFC) and cause problems in the daily lives of elderly people. Many cognitive training intervention studies have exhibited positive effects on the cognitive functions of the elderly [8-15)]. Plassman *et al*. (2010) conducted a systematic review about factors and possible prevention of cognitive decline in later life. They found clear evidence of a decreased risk of cognitive decline through cognitive training [16)]. Gates *et al*. (2010) recommended computer-based training, because it has potential to facilitate multi-modal and multi-domain training, enable unobtrusive real time monitoring of cognitive performance, and a reduction in personnel and implementation costs [17)]. Such knowledge, however, has not yet been incorporated in the programs for clinical use.

Therefore, we decided to develop a cognitive training program named “Atama-no-dojo” for the elderly according to the recommendations from the past studies. “Atama-no-dojo” is a multi-tasked program, which can be operated on a Personal Computer (PC). We considered that a useful intervention program in this area should contain an adequately high difficulty level and some incentives for participants to maintain high motivation for the tasks. A high difficulty level is important to achieve effective activation of the target function to improve this function [18-22)]. At the same time, we should be careful not to make participants feel frustration by the difficult tasks. We decided the difficulty level according to the average scores of standardized neuropsychological tests, especially tasks including attentional load. To maintain high motivation, we introduced novelty of stimuli. Buitenweg *et al*. (2012) suggested that novelty is an important factor for more lasting effects of brain training, especially in the elderly, and the inclusion of novel stimuli or tasks can motivate the elderly to invest more effort and energy into learning [23)]. Therefore, each session of our program contained different and unfamiliar items. In addition, we adopted task materials being related to seasonal events and everyday life, with amiable illustrations, to create feelings of familiarity and pleasantness for participants in the program.

Our series of studies included an activation study, followed by a 6-month intervention study [24)]. The contents of the intervention program were revised based on the results of the activation study.

In this paper, we report the characteristics of brain activation during the “Atama-no-dojo” measured by the functional near-infrared spectroscopy (fNIRS), and subjective reactions to the tasks related to the difficulty levels.

Task set “Atama-no-dojo”

“Atama-no-dojo”, means “training gym for brain” in Japanese, and was developed by using JAVA script. The characteristics of the program are shown in Table 1. The task contents and images are shown in Table 2 and Fig. 1.

Table 1. The characteristics of “Atama-no-dojo”

Play mode	Play Alone	Play in a Group
Total task number	14	9
Variation of task combination	48 (4 combinations for a month)	48 (4 combinations for a month)
Task number for a session	8	7
Scoring for each task	0-5	0-5
Method of answering	Mouse and keyboard or touch panel screen	Answering sheet
Performance recording	Log data	Answering sheet
Program operation	By the participant (instruction on the screen)	By a facilitator

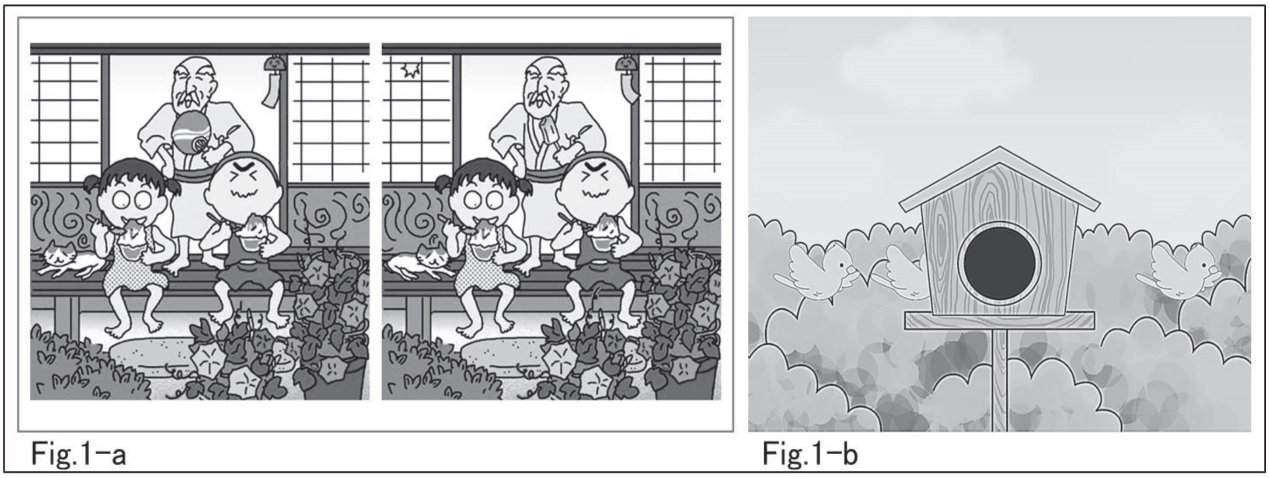


Fig. 1. The task images of Atama-no-dojo. a: Spot the 5 differences. b: Calculation (hidden number).
Each task had a different version in each session (same rules but different materials, words, and images).

Table 2. Atama-no-dojo task contents

Warm-up (Don't be deceived)	Answering quickly to the stimulus emerging on the screen one after another, with an inhibiting Stroop effect. The item categories are number, color, form vs. words, defeat rock/ paper/ scissors. In a session, 15 trials of one category are presented continuously. Stimulus duration changes from 2 sec to 1 sec as the difficulty level changes.
What's This? (Reasoning)	Reason what the item is, from the partial photo image. The difficulty level changes as the size of the part changes; smaller parts of the whole image will be more difficult to recognize, and the hint button changes the photo to an easier one.
What's This? (Puzzle)	Sort the 10 pieces of the photograph to recreate the whole image within the time limit.
Witty Words	Reason how to read words from the letter characterized by special features of form, layout, and color. 5-step hints are prepared to give letters of the name one by one from the beginning of the word.
Spot the 5 Differences	Find 5 differences in two almost identical paintings. The differences are arranged into 5 difficulty levels of noticeability according to changes in shape color, size, and the subject or background.
Catch It (Word)	Touch or click the word that suits the given rule from words that appear one after another in 2 sec of duration. The dummy words are similar in visual or phonological features.
Catch It (Moving image)	Touch or click on the moving target, but not the dummy target. The motion-speed and the number of targets change as the difficulty level changes.
Calculation (Cooking)	Calculate the quantity or price of ingredients to make a certain dish. The complexity of the calculations increases as the difficulty level increases.
Calculation (Hidden number)	Count the number of items that are going in and out of the shade, and answer the number of items remaining behind the shade at the end. The player tries the sequence 5 times. The frequency of in/out increases from 3 to 7 times as the difficulty level increases.
Remember (Breakdown)	Find 10 pairs of the same pictures from 10 closed cards by opening 2 cards at once during the time limit. This has the same rule as the card game breakdown.
Remember (Motion sequence)	Three graphic images move one after another. Participants remember and reproduce the motion order afterwards. The player tries the sequence 5 times. The frequency of motion increases from 3 to 7 as the difficulty level changes.
Remember (Word sequence)	Remember the order of the words that appear one after another, and answer the sequence number of the word indicated afterwards. The player tries the sequence 5 times. The number of words increases 3 to 7 as the difficulty level increases.
Remember (Today's tasks)	Answer 5 questions (4 questions for Group mode) about the task contents that have been carried out in the same session.
Read Aloud	Read a famous poem or sentence aloud, fluently, heartily, and comfortably, then evaluate the performance using self-rating scales.

MATERIALS AND METHODS

Subjects

Ten right-handed healthy senior volunteers (5 males and 5 females, age 49.6±8.1) participated in this study. This study was approved by the ethical review board of the Graduate School of Health Sciences, Kobe University. Written informed consent was obtained from all participants. Although our future participants for the intervention approach will be older people in their 70-80's, we selected a middle-aged group for this pilot study, because the measurement by using fNIRS was carried out. It takes approximately 30 minutes, staying still in a chair during the mechanical setting up and measurements with head lapping probes. Therefore, it might lead to too much fatigue and frustration for older participants for them concentrate on the tasks.

MEASUREMENTS

The change in oxygenated hemoglobin (Oxy-Hb) during the program was measured by the fNIRS (FOIRE-3000, Shimazu co., Tokyo, Japan). The system of the fNIRS can measure tissue absorbance of light at several wavelengths in the spectral region from 700–1000 nm, thus enabling the determination of concentration changes in Oxy-Hb, and deoxygenated hemoglobin [25-26]. The probes were set in the areas of the prefrontal (19ch), left temporal (10ch), and parietal/occipital (12ch) lobes of the participant's head (Fig. 2) following the international 10–20 electrode system [27] (ch2-F4, ch5-F3, ch28-T3, ch35-O1, ch36-O2). Participants' reactions to the tasks were recorded by using a video camera. The performance of participants was recorded by the program as log data, and then calculated into a correct ratio (%).

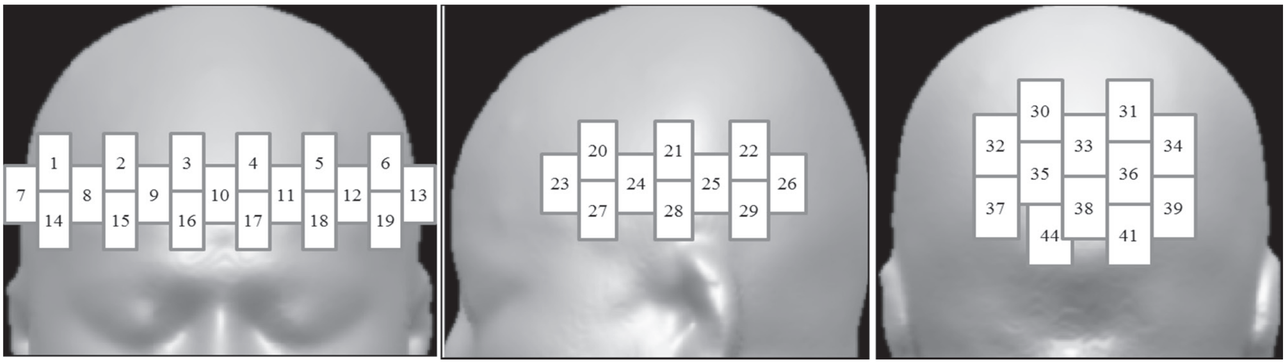


Fig. 2. The location of channels of fNIRS. The probes were set in the areas of the prefrontal (19ch), left temporal (10ch), and parietal/occipital (12ch) lobe of the participant's head

PROCEDURE

This experiment was conducted in a quiet room with a shade curtain to block the sunlight through the window. Participants were seated in a comfortable cushioned armchair with a headrest. A touch screen PC (12.1-inch, TouchSmart tx2, Hewlett-Packard co.) was placed in front of the participant with an adjustable PC stand to keep each participant in a relaxed posture without moving their head and trunk while they looked at and touched the screen.

Prior to the measurement, we gave instructions to the participants using an instruction sheet with screen images until they understood the tasks and how to operate the program. For a baseline measurement, participants gazed at a black dot centered on a white screen on the PC monitor. After a 30 sec baseline, participants began the “Play Alone” session. The session contained “Warm-up (form),” “What’s This (reasoning),” “Witty Word, Spot the 5 Differences,” “Catch It (word), Calculation (hidden number),” “Remember (today’s tasks),” and “Read Aloud”. Each session took approximately 10 minutes. After the measurement finished, participants completed the 10-point self-rating scale for pleasantness (1: “unpleasant” to 10: “pleasant”) for each task, and wrote comments in the open-ended response section.

ANALYSIS

The purpose of this activation study was to examine the brain activation occurring during a session, especially in the PFC, to which we paid a special attention in this study. We examined the brain activation during the session by checking the changes in the average of Oxy-Hb and trend graphs of each channel to know the time-dependent change occurred. The amount of Oxy-Hb change during the task period in each channel was calculated by the difference from the baseline, based on the average of 30 sec data. The difference in Oxy-Hb concentration between the baseline and the task period was tested by paired t-test (Excel statistics 2008, SSRI Co.), and the effect size was calculated (Cohen’s-d). The trend graphs in each area were analyzed to find out the characteristics of the waveform.

We also inspected the correlation between the task scores (correct ratio, %), and the subjectively rated pleasantness (Spearman’s rank correlation, Excel statistics 2008, SSRI Co.) for each task to examine the effect of difficulty levels on pleasantness, which relates to motivation.

RESULTS

The change in average of Oxy-Hb during the task period in each channel and the comparison with the baseline are shown in Fig. 3. The average of Oxy-Hb concentration increased from the baseline in all channels, and the changes were statiscally significant in almost all channels. The effect sizes were larger in the PFC, extremely in both lateral areas, and the former and upper temporal lobe areas. An example of the trend graphs for each area is shown in Fig. 4. Fig. 5 is the enlarged view of the trend graph in the left lateral PFC. Those trend graphs showed that the Oxy-Hb concentration rose from the start of the session and was higher than that of baseline throughout the session. The wave curves contained some different types of wave form pattern upon the large wave curve throughout the session; some small amplitudes in short period which changed with task phases upon bigger amplitudes which rose up at the starts of each tasks and drop down to the task ends.

Measuring area		Oxy-Hb change (mM·mm)		t-test (paired)	Effect size
Brain parts	ch	Ave.	SD.	p-valure	*Cohen's-d*
Frontal lobe	1	.029	.024	.0023**	1.50
	2	.015	.016	.011*	1.10
	3	.0083	.042	.27	.26
	4	.0089	.040	.25	.30
	5	.015	.016	.0090**	1.07
	6	.029	.022	.001**	2.25
	7	.068	.050	.00099**	1.96
	8	.025	.021	.0027**	1.46
	9	.015	.024	.045*	.87
	10	.012	.033	.15	.39
	11	.024	.022	.0039**	1.25
	12	.026	.017	.00051**	1.95
	13	.033	.047	.026*	.78
	14	.051	.035	.00061**	2.01
	15	.028	.028	.0057**	1.30
	16	.021	.030	.030*	.96
	17	.024	.025	.0077**	1.17
	18	.032	.025	.0015**	1.63
	19	.030	.043	.028*	.94
Left Temporal lobe	20	.036	.036	.0059**	1.45
	21	.030	.035	.012*	1.13
	22	.031	.037	.013*	1.07
	23	.062	.051	.0018**	1.75
	24	.040	.049	.013*	.96
	25	.028	.037	.019*	.69
	26	.038	.057	.032*	.75
	27	.058	.053	.0036**	1.57
	28	.023	.045	.068	.45
	29	.020	.034	.046*	.90
Parietal and Occipital lobe	30	.013	.020	.036*	.61
	31	.019	.018	.0051**	.35
	32	.0055	.026	.26**	.12
	33	.024	.022	.0035**	.97
	34	.026	.022	.0024**	.72
	35	.010	.020	.071	.19
	36	.023	.021	.0034**	.52
	37	.017	.027	.037*	.55
	38	.032	.045	.026*	.84
	39	.026	.028	.0086**	1.02
	40	.034	.043	.016*	1.07
	41	.029	.048	.043*	.69

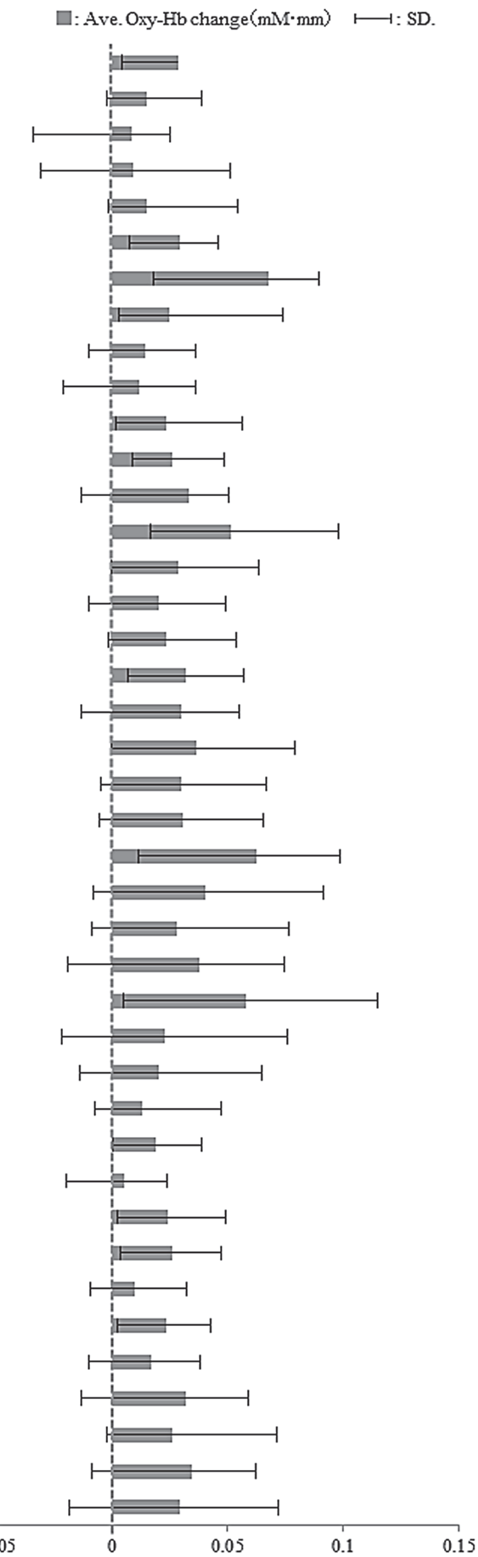


Fig. 3. Average Oxy-Hb change, result from t-test and effect sizes in each channel. All average Oxy-Hb concentration increased from the baseline, and the changes were significant in almost all channels. Many of the effect sizes were large in the PFC, especially in both lateral areas, and the former and upper temporal lobe areas.

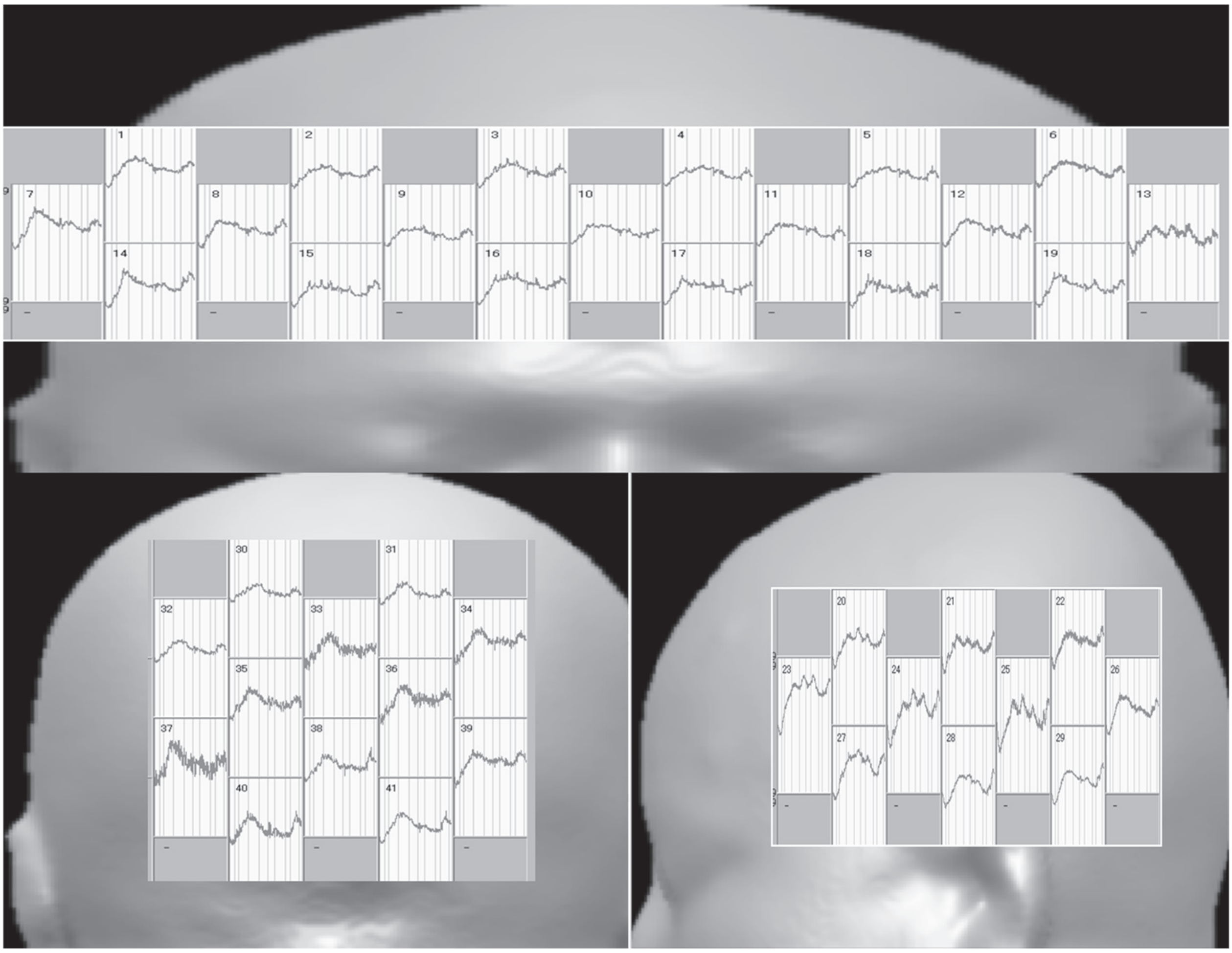


Fig. 4. An example of trend graphs in each brain area.

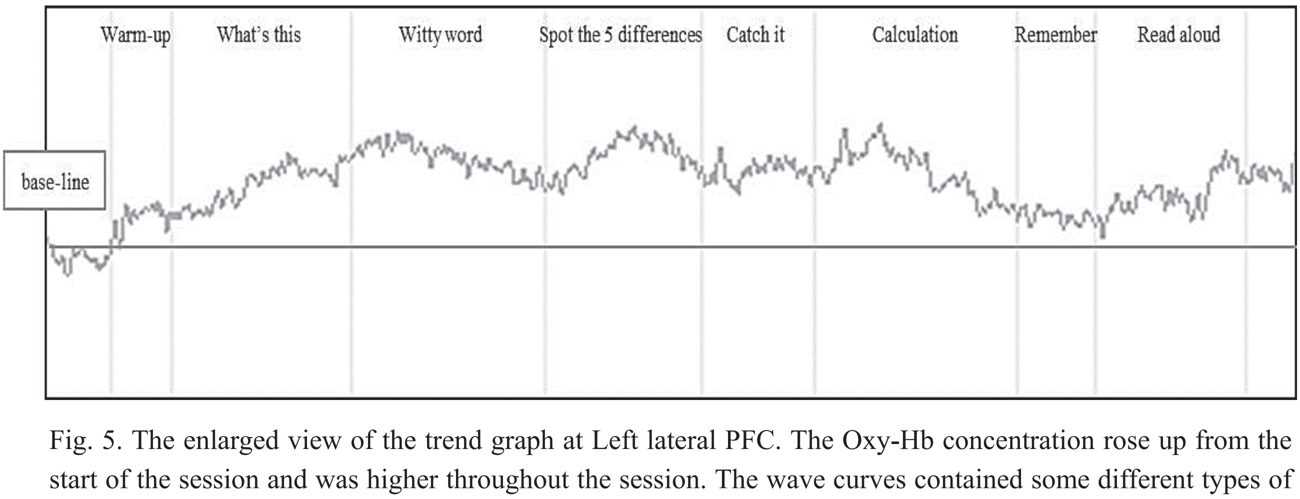
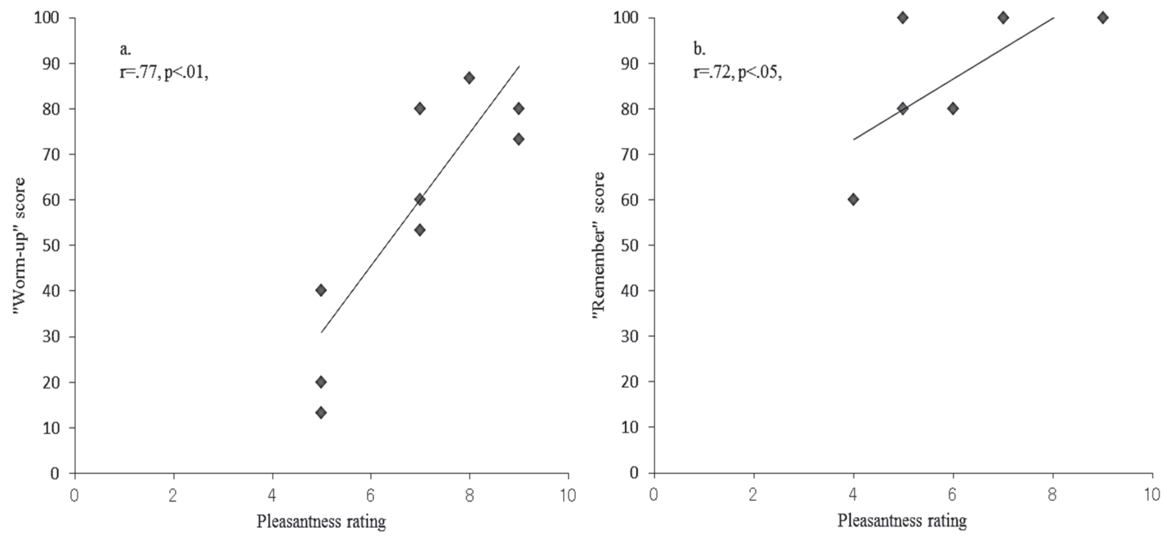


Fig. 5. The enlarged view of the trend graph at Left lateral PFC. The Oxy-Hb concentration rose up from the start of the session and was higher throughout the session. The wave curves contained some different types of wave form pattern upon the large wave curve throughout the session; some small amplitudes in short period which changed with the thinking-answering phases upon bigger amplitudes which rose up at the starts of each tasks and went down to the task ends.

The average scores for each task and results from subjective ratings of pleasantness are shown in Table 3. Some significant correlations were found between the items in “Warm-up” (r=.77, p<.01, Fig. 6-a), and in “Remember” (r=.72, p<.05, Fig. 6-b). Before the experiment, we inspected the correlation of age with these items, but we could not find any significant correlation. Several participants commented that the speed of stimulus motions and changes were too fast in “Warm-up,” “Catch It,” and “Calculation”. One participant commented, “I gave up in the middle of the task, it was too fast!”



.Fig. 6. The correlation between task score and pleasantness ratings in Warm-up (a) and Remember (b).

Table 3. Average scores of each task and subjective ratings of pleasantness.

	Warm-up	What’s this (reasoning)	Witty word	Spot the 5 differences	Catch it (word)	Calculation (hidden number)	Remember (today’s tasks)	Read aloud	Total
Correct ratio (%) Ave.(SD.)	58.67 (26.44)	48 (40.22)	44 (35.02)	76 (18.38)	85.33 (9.32)	72 (19.32)	86 (13.49)	54.67 (10.32)	65.58 (14.08)
Pleasantness (1-10) Median (QD.)	7 (1.13)	6 (1.0)	5 (1.38)	6 (.88)	6.5 (1.38)	6.5 (1.75)	5.5 (.88)	5 (.5)	5.75 (6.87)

DISCUSSION

We found high activation in many portions of the brain. It was said that the activation in the PFC, particularly in the lateral area showing a large effect, mainly represented the function of working memory, attentional control, and inhibition [28]. The medial prefrontal cortex, which is known to be related to the functional decline in Alzheimer's disease and MCI [29], also showed large effect sizes—although smaller than that of the lateral parts of the PFC. The activation of the temporal lobe area may reflect the verbal process and that of the parietal/occipital lobe area, the visual-spatial processing, respectively. However, we should be careful for estimating the functional mapping, because of the low spatial resolution of fNIRS. It is possible that the data from the left temporal lobe area, especially from the former and upper area, actually measured the activation in the inferior part of the frontal or parietal cortex. Since the structure of the head is somewhat different among each subject, it might be difficult to control the brain focal matching to the specific probe settings. Therefore, we should roughly estimate that the Oxy-Hb concentration had significantly increased throughout the PFC, left temporal, and parietal/occipital lobe area.

We presented the trend graphs from one subject as an example. Characteristics of waveforms were different in each participant, therefore, we tried to know the meaning of each waveform and the common features among participants. We considered that wave curves were related to the general concentration in the tasks throughout the session, task phase (thinking or searching, finding the answer and answering, waiting for the next trial or task), and the process of becoming accustomed to the tasks. For general concentration, we mean the readiness for the program session, and in this enlarged sample, the Oxy-Hb concentration which rose from the start of the session that kept higher amplitude than that of the baseline until the later tasks. This characteristic was common in all measured areas and was found in other participants, but had different characteristics in the size, number, and position of the peak. The task phase related trend curves were interpreted by comparing with the video data. The amplitude tended to rise with the thinking or searching phases, and tended to be downward after the answering phases. This waveform was different among the tasks, because they had different numbers of trials or answering phases. The bigger amplitudes which rose at the starts of each task and drop at the task end represented the process of becoming accustomed to each task, and the brain activity assumed to represent the understanding of efficient strategies to manage the tasks. These factors affecting the waveform were sometimes difficult to be clearly indicated, because several factors that affect brain activation might occur simultaneously.

These results from the fNIRS study reinforced the validity of this program, because the task related activation was seen over the whole brain area. This might relate to the multimodal cognitive function, especially in the PFC, which is thought to be an important area in cognitive training for preventing cognitive decline.

The analysis of the performance and subjective ratings of pleasantness pointed to some issues that we must address. The principal purpose of this study was to create an enjoyable set of tasks with effective contents to assist the elderly with the cognitive function. However, in the activation study, our tasks were rated relatively low for pleasantness. Subjective feelings of pleasantness may be influenced by the uncomfortable situation of measurement with a cramped headset. However, as to the correlations between the score and the pleasantness in “Warm-up” and “Remember (word)” it might be possible to explain the significance. The average of the correct ratio for “Warm-up” was 58.67%. This score was relatively low, but the median of the pleasantness rating score of 7.0 was relatively high. In other words, the subjects enjoyed a task that required inhibitory function to the stereotype, with a generally high difficulty level. Therefore, the correlation may indicate the frustration of making mistakes during a quick stimulus change, particularly for the participants with low performance, as demonstrated in his comments. On the other hand, in “Remember”, the average score was 86%, and 9 out of the 10 participants were over 80% for the correct ratio. However, pleasantness was rated a median of 5.0. This task required participants to answer five questions about the task items that they had just completed, and this task was possibly too easy to be enjoyable, for the middle-aged participants in this study. Therefore, the correlation suggests that the task seemed to be overly easy, and the frustration from failing is more severe than the tasks at a higher level of difficulty.

It is necessary to make a revision to address these issues, especially regarding the speed of stimulus change and motion. This is important for maintaining the right level of challenge in the tasks. In addition, the target participants of our future intervention study will be older than the current study, and they will have some amount of decline in processing speed. Even though some amount of difficulty is necessary to activate cognitive functions effectively, when participants lose motivation, nothing will be gained from the intervention.

CONCLUSION

We developed a set of tasks for a cognitive training program “Atama-no-dojo,” which is intended to prevent age-related cognitive decline. “Atama-no-dojo” includes 14 tasks for two play modes, and was created with consideration for requiring multimodal cognitive function with adequately high difficulty level and novelty of task contents for participant motivation. The activation study demonstrated that the session from “Atama-no-dojo” could activate a large area of the brain. We were able to recognize some task phase related waveforms in Oxy-Hb trend graphs. However, we also found some deficiencies in the task settings, which indicate the possibility of a decrease in pleasantness due to the difficulty level.

Declaration of interest

The authors report no conflict of interest. The authors alone are responsible for the content and writing of the paper.

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