Evaluation of Real Brain Activity Using an Ultracompact Brain Activity Sensor for the Assessment of Cognitive Function

Tatsuo Yasumitsu (sahara0808@yahoo.co.jp)
4-6-1 Hyakunin-cho, Shinjuku-ku, Tokyo, 169-0073, Japan ORCID: 0000-0001-7716-4730

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Abstract

Background: The present study purpose aims to improve cognitive function at the preclinical stage of dementia and measure real-time brain activity levels in participants wearing an ultracompact brain activity sensor called XB-01.

Methods: Four healthy people (two males and two females) aged 20–50 years involved in the dementia prevention program participated in the study. During the experiment, the participants wore XB-01, which was connected to their iPhone by Bluetooth to collect data. XB-01 data indicating the brain activity (blood flow) during the program was demonstrated by real-time color changes on the connected iPhone to evaluate the results on a 100-point scale. We examined 21 programs in total, including those reported to increase brain activity.

Results: We conducted an analysis of variance for each of the four programs in the upper and lower positions detected to compare brain activity, resulting in finding a main effect of the program, $F(7,21) = 4.35$, $p < .05$.

Conclusions: An exercise program including a dual-task with large limb movements was highly effective in increasing brain activity in the dorsolateral prefrontal cortex (DLPFC). Moreover, slightly higher speed, pace, and difficulty level of the program most suitable for participants were more effective. Brain activity increased in the DLPFC during the program and several minutes after its completion. These findings can help develop programs that prevent and improve cognitive function.

Trial Registration: The research ethics committee at PCY, Ltd. Trial Registry, approval number 20-2. Registered 04 January 2020. Retrospectively registered.

Key Points

- An exercise program including a dual-task with large limb movements was highly effective to increase brain activity in the dorsolateral prefrontal cortex (DLPFC).
- Slightly higher speed, pace, and difficulty level of the program most suitable for participants were more effective.
- Brain activity increased in the DLPFC not only during the program but also several minutes after its completion.

1 Introduction

The World Health Organization (WHO) [1] reported approximately 50 million worldwide dementia cases in September 2020, with a gradual increase of approximately 10 million new cases every year. The estimated global cost (direct and indirect financial burden on healthcare) of dementia is $818 billion, which is expected to increase to $2 trillion by 2030. Hence, WHO has declared dementia prevention and treatment a public health priority; simulation studies [2, 3] suggest that even delaying disease onset by 2 years would have substantial public health, economic, and societal benefits. Decreased cognitive function has varied adverse effects, including complications such as vascular factors and depressive disorders [4]. Multiple long-term follow-up studies have explored the connection between physical activity and dementia, including the LADIS [5] and the Rotterdam [6] studies. Asada [7] reported that the most evidenced method for preventing dementia includes exercise or an exercise habit, followed by Web-mediated cognitive training. Plassman et al. [8] analyzed and validated 172 observational studies and 22 randomized controlled trials (RCTs), evaluating the effect of exercise and cognitive training. Walking was the most used method for exercise interventions among the 22 RCTs. The Life Randomized Trial was conducted on 1,635 people at risk of cognitive impairment, however, this trial showed contradictory results [9]. Several cohort studies have reported the preventive effect of late-life physical exercise on cognitive deterioration. An 8-year-long study on elderly Taiwanese [10] examined the relationship between exercise and cognitive function and indicated that a 30-min exercise session reduced the risk of cognitive decline. Kawashima [11] studied the age-related control of cognitive functions. Age-related cognitive decline may occur due to linear decline in the prefrontal cortex function. Executive function is the core of various higher cognitive activities and requires the cooperative operation of various brain areas. As dementia and other cognitive developmental disorders may impair executive function, we hypothesized that it could be improved by introducing certain training methods demonstrated to maintain and improve the brain function (prefrontal cortex function) in healthy aged people. A study of secondary results from an RCT on the effects of exercise on memory in older adults with probable mild cognitive impairment has supported the prevailing notion that exercise can positively impact cognitive function and may represent an effective strategy to improve memory in those who have begun to experience cognitive decline [12]. In a study on brain-derived neurotrophic factor (BDNF), the interaction of estrogen, physical activity, and hippocampal BDNF was demonstrated to be important for maintaining brain health, plasticity, and general well-being, particularly in women [13]. Furthermore, physical exercise was effective in reducing proinflammatory cytokines and improving BDNF peripheral levels, with positive effects on cognition [14]. Treadmill exercise can impact the hippocampal histone acetylation profile in an age- and lysine-dependent manner [15], suggesting that prolonged exercise increases the capillary reserve. Capillary growth occurs in motor areas of the cerebral cortex as a robust adaptation to prolonged motor activity [16]. The applicability of primary functional brain imaging modalities to cognitive neuroscience has been confirmed by performing cognitive tasks on a computer and combining magnetic resonance imaging (MRI) with a method for examining performance such as key press responses [17]. However, there are issues associated with MRI such as limited movement, noise, high cost, and the requirement for specialized knowledge. Moreover, it is hard to test out the programs in real-time due to the abovementioned problems. These factors are delaying progress in brain science as well as treatment against dementia. However, the ultracompact brain function measurement device "XB-01" (hereinafter referred to as XB-01; length 80 mm, width 40 mm, thickness 13 mm, and weight 30 g), released by NeU Inc. in 2018, made it possible to measure brain activity changes in real daily life situations. By measuring changes in brain–blood flow with weak near-infrared light, this device can visualize the state of brain activity to measure brain–blood flow changes, pulse rate, and acceleration. This device uses near-infrared spectroscopy, which irradiates active brain areas with near-infrared light and detects the returning near-infrared light as a proxy for changes in hemoglobin levels in the blood circulating in the brain to assess changes in blood oxygenation and cerebral blood flow. These real-time measurements help determine the type of exercise program that can be effective in increasing brain activity and efficiently develop a working program. Most studies on brain activity using this device were performed on the memorization of numbers and calculation problems performed on the screen, but few studies focused on body exercises, whereas few neurological studies have reported real-time brain activity using XB-01. This study aimed to determine real-time brain activity levels while wearing an ultracompact brain activity sensor at the preclinical stage of dementia and verify the extent of the actual activation state during the programs reported to improve brain activity.

2 Methods

Four participants were recruited in advance: two healthy women (age: 39 ± 18.4 years) and two healthy men (age: 43 ± 12.7 years) aged 20–50 years. As the study was conducted during the coronavirus disease 2019 pandemic, it was conducted on a small number of people to prioritize the participants' safety. This participant group was not linked to dementia, but they lived near the institute and were supportive of dementia prevention program research. The program lasted from June 7 to July 4, 2020. Given the preliminary nature of the study, no control group was set; similar studies have been performed on other populations. Before the experiments, the purpose and methods of this study were fully explained to the participants, and written informed consent to participate in the experiment was obtained. Patients anxious about participating in the program were excluded. The experiment was performed with the approval of the research ethics committee at PCY, Ltd. (approval number 20 – 2). The experiment was conducted in a room available for exercise at a room temperature (20°C). During the experiment, the participants wore a precharged XB-01 with a headband a little over the left eyebrow on the forehead and connected to an iPhone using Bluetooth for data collection. The Active Brain CLUB app (hereinafter referred to as ABCa, NeU Inc., Tokyo, Japan) to the iPhone was downloaded and the function called Brain Meter was stated; then, it was paired with XB-01. XB-01 data indicate real-time brain activity (blood flow volume) during the exercise program by color changes on the screen of the connected iPhone. The color changed to red for high and to blue for low brain activity. Brain activity results on a 100-point scale were evaluated. This activity score is automatically displayed by ABCa. Data were collected over 3 days per participant, as the program was conducted for 1 hour per day. The participants were questioned about the presence of any adverse effect such as musculoskeletal pain on each exercise session. Furthermore, the instructors monitored participants for symptoms of angina and shortness of breath during the exercise classes. We examined each exercise program including one recognized to increase brain activity [7, 18], which included the following elements:

A Walking: Participants walked on a treadmill for 3 min at 6 km/h with a wide stride and strong arm swing.

B Raising the thigh: On the spot, the participants raised the thigh on each side alternatively 30 times up to waist height.

C Self-weight strength training [19]: The participants performed this exercise for approximately 2 min while watching a video. First, their hands were crossed in front of their chest with their knees and toes facing outward, and their legs spread more than twice their shoulder-width apart. Slowly, from this position, they lowered their hips and moved up and down 20 times while contracting their buttocks. Then, with their legs spread more than twice their shoulder-width apart, they lowered their hips with their elbows placed on the inside of their knees. For 10 s, they closed the knees with all their strength and then opened them, with the elbows simultaneously doing a similar movement.

D Synapsology [20]: For approximately 3 min while watching a video, the participants performed a program of movements only for the upper body. Synapsology is an original program developed by Renaissance, Inc. First, they learned three movements directed by numbers. If the instructor said 1, they placed their right hand on their head and their left hand on their waist. If 2, they placed their left hand on their head and their right hand on their waist. If 3, they placed their hands on their shoulders. Next, the numbers directed by the instructor changed to colors. Instead of 1, 2, and 3, the instructor directed them by naming colors: red, yellow, and blue. Finally, the color indicated by the instructor was changed to a visual stimulus. When the instructor showed red, yellow, and blue balls, the participants said the colors simultaneously aloud with movements.

E Brain-training exercises to prevent dementia (Web version): The participants underwent memory training for approximately 4 min while watching a computer screen. After memorizing the pictures one by one, they watched the video and got the assignment (Table 1).

Table 1
Brain-training exercises to prevent dementia (Web version the task)

What day is May 5th?
What time is it now?
Calculate 27 × 8.
Which photos did they see earlier among many photos?

F Droutability: Total 10 programs were performed with two Vision Drout program types. Droutability is derived from the “Draw out Ability” coordination exercise program devised by Dr. Yasumitsu [21]. Vision Drout is a program performed while looking at the monitor.

F 1 Program performed using a Drout cross (a cross-shaped training tool). The participants stood at a cross mark placing on the floor in front of them and performed the four programs while watching the video.

F 1–1 After a circle appeared on the screen, they moved their right foot to that position of the cross and stood there on one foot. After a triangle appeared, they moved their left foot to that position of the cross.

F 1–2 After a circle appeared on the screen, they squatted down, touched their right hand to that position on the cross, and stood there. After a triangle appeared, they did the same with their left hand.

F 1–3 At the beginning, they acted similarly to F 1–1, and in the middle, after the blue cross appeared on the screen, they performed the movement for phase F 1–2. After the second appearance of the blue cross on the screen, they performed the movement for F 1–1, thus alternating the movements for F 1–2 and F 1–1.

F 1–4 The participants performed the program as in F 1–3 with hands and feet switched: circles correspond to left foot and hand and triangles to right foot and hand.

F 2 Programs to move, stop, and up and down.

While watching the computer screen, the participants underwent a practice program, followed by both a) and b). a) While “Move” was shown on the screen, they stepped in the spot with large movements of their arms and legs. During “Stop,” they stopped and stood upright. During “Up,” they lightly jumped and clapped their hands once on their head while saying “up.” During “Down,” they squatted down; while saying “down,” they put their hands on the floor and stood up fast. The participants performed three programs at three different speeds—F 2-a-1: slow, F 2-a-2: normal, and F 2-a-3: fast. b) While “Move” was shown in green on the screen, they stepped in the spot with large movements of their arms and legs. During “Move” in red, they stopped perfectly and stood upright. During “Stop” in green, they stopped perfectly and stood upright. During “Stop” in red, they stepped in the spot with large moving their arms and legs. During “Up” in green, they jumped lightly and clapped their hands once on their head while saying “up.” During “Up" in red, they squatted down; while saying down, they placed their hands on the floor and stood up fast. During “Down” in green, they squatted down; while saying down, they placed their hands on the floor and stood up fast. During “Down” in red, they jumped lightly and clapped their hands once on their head while saying “up.” The participants performed three programs at three different speeds—F 2-b-1: slow, F 2-b-2: normal, and F 2-b-3: fast.

G Spot the Differences: We used p92–93 in “Spot the Differences to Train Your Brain” [22]. The participants were seated and performed the test for 1 min using two sheets of paper.

H Crossword: We used p20–21 of the March 2020 issue of Crossword Mate [23]. The participants were seated and performed the test for 1 min using two sheets of paper.

I Radio Exercise No. 1: The participants exercised for about 3.5 min while watching a video. “Radio exercise” is a physical exercise routine, which every Japanese person learns in their childhood.

J Kickboxing: The participants performed for 3 min including an explanation and practice interval while watching the video. They performed a middle kick with their front foot, followed with their back foot, for 60 s each.

K Tai chi: The participants performed the movements for about 3 min while watching a movie. They performed the movements of “Introductory Taijiquan,” Taijiquan for beginners.

L Boxing [24]: The participants performed for 4 min including an explanation and practice interval while watching the video. First, they performed a one–two, next to webbing, followed by a one–two webbing.

Before the start of all programs, they performed deep breathing for 15 s. Moreover, they required to remain stationary until receiving the finish signal at the end of the program. When the color of the brain activity turned blue on the iPhone screen and remained so for ≥ 5 s, we gave the signal to end the program. Statistical processing software (IBM SPSS Statistics 24) was used to test the difference in mean values among groups in each calculation item. We performed a one-way within-participants analysis of variance (ANOVA) for each of the four programs at the maximum and minimum values. We performed multiple comparisons by the Bonferroni method for items with significant F values. We set the significance level at 5%.

3 Results

In this study, we examined the brain activity levels produced by the 21 programs in the 12 categories. In Table 2, we compare the levels of brain activity among them. We performed an ANOVA for each of the four programs in the maximum and minimum levels to compare brain activity. As a result, a main effect was shown in the program ($F(7,21) = 4.35$, $p < .05$).

Table 2
Brain activity rankings and average program scores

Program	*Means*	*SD*	Rankings
A	54.00	9.27	17
B	56.50	10.88	13
C	46.25	11.27	20
D	56.00	7.87	14
E	55.00	11.20	16
F 1–1	43.75	4.03	21
F 1–2	57.25	5.91	12
F 1–3	61.75	15.17	3
F 1–4	55.25	11.59	15
F 2-a-1	61.25	9.64	4
F 2-a-2	58.00	15.30	8
F 2-a-3	59.00	13.83	5
F 2-b-1	64.50	8.51	1
F 2-b-2	57.50	19.60	11
F 2-b-3	52.25	5.97	19
G	58.00	6.27	9
H	58.25	10.28	7
I	57.75	1.50	10
J	64.25	5.32	2
K	52.75	5.19	18
L	58.50	5.51	6

4 Discussion

In this study, the exercise program using dual-tasks obtained the highest scores. Despite walking being used as an exercise intervention method in many previous studies on dementia [25], the scores of walking were intermediate in this study. We did not get high scores in exercises performed with slow movements such as strength training with body weight and tai chi. Previous studies [26] have reported that slow and relaxed movements do not activate the dorsolateral prefrontal cortex (DLPFC). We reported lower scores if exercise programs using the dual-task were too easy and higher scores if the speed and thinking pace increased. However, we observed a lower score if the difficulty level was too high or the speed too fast (Fig. 1). Kawashima [26] considered the act of thinking to be the most complex activity and to require the cooperation of many brain regions, but only using a portion of the left prefrontal cortex and that brain activity was low during meditating. Moreover, we reported the scores were higher even if participants did not perform the exercise correctly; they just needed to continue performing the program till the end. We reported higher scores when the movements during the program included large motions using limbs such as bending, stretching, and kicking but not for unconscious and familiar movements such as radio exercise. We reported lower scores if there were any negative factors such as pain in the knees or other body parts during moving or experiencing difficulty to see the letters. In the case of dementia, which often affects the middle-aged and elderly people, it is necessary to develop and introduce a program that considers these factors. Negative emotions during cognitive training interfere with the improvement of cognitive function by training [27]. In this study, we confirmed that scores increased when the participants performed the program with painless knees. Summarizing previous cognitive neuroscience studies [28] recommended aerobic exercise at an intensity ≥ 75% HRR for 30–40 min, thrice a week over 3–6 months to improve cognitive function in the elderly. Considering this study, cognitive function could be impacted by increasing the DLPFC activity even with light load short time daily exercises, which the aged can more easily perform. Event-related potentials (ERPs) are transient brain fluctuations temporally related to external or internal events, and greatly vary among individuals. In the present study, we identified various cases of blood flow changes in the DLPFC. Brain–blood flow could remain elevated for a long time although they often appear to be rising and falling. Often, we could observe increased brain activity during the program. However, we could observe the opposite, with activity increasing only after the program finished. Colcombe et al. [29] reported that it is possible to identify task-related brain activated regions and the dynamics of neural activity when observing neural activity (cerebral hemodynamics) during conducting a cognitive task by functional MRI (fMRI). In this study, by using XB-01, we could confirm the brain activity in the DLPFC and detect ERPs difficult to characterize by fMRI. There are limitations to this study, including the small number of samples, the fact that the participants were only from 20–50 years age group, and that only blood flow changes in the DLPFC were confirmed. In future, we want to increase the number of participants to improve the accuracy of the study, verify the results in participants aged ≥ 50 years, and examine the effectiveness of these exercise programs in preventing and improving dementia. One disadvantage of the verified program is that it is intended for people who can move to some extent, and it is difficult to introduce it to people with a limited range of motion or those who cannot freely move their bodies. In future, we will examine the programs with high scores and develop highly effective programs for dementia prevention implementing them at facilities for the elderly, nursing homes.

5 Conclusion

An exercise program including a dual-task with large limb movements was highly effective to increase brain activity in the DLPFC. Moreover, a slightly higher speed, pace, and difficulty level of the program most suitable for participants was reported to be more effective. Brain activity increased in the DLPFC not only during the program but also several minutes after its completion. These results show that they can contribute to the development of programs that help prevent and improve cognitive function.

Abbreviations

WHO

World Health Organization; RCTs:randomized controlled trials; BDNF:brain-derived neurotrophic factor; MRI:magnetic resonance imaging; ABCa:Active Brain CLUB app; ANOVA:analysis of variance; DLPFC:dorsolateral prefrontal cortex; ERPs:Event-related potentials; fMRI:functional MRI

Declarations

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Availability of data and materials

All data generated or analysed during this study are included in this published article.

Ethics Approval and Consent to Participate

The experiment was performed with the approval of the research ethics committee at PCY, Ltd. (approval number 20-2). Before the experiments, the purpose and methods of this study were fully explained to the participants, and written informed consent to participate in the experiment was obtained.

Consent for publication

Not applicable

Competing interests

There are no conflicts of interest to declare.

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Figures

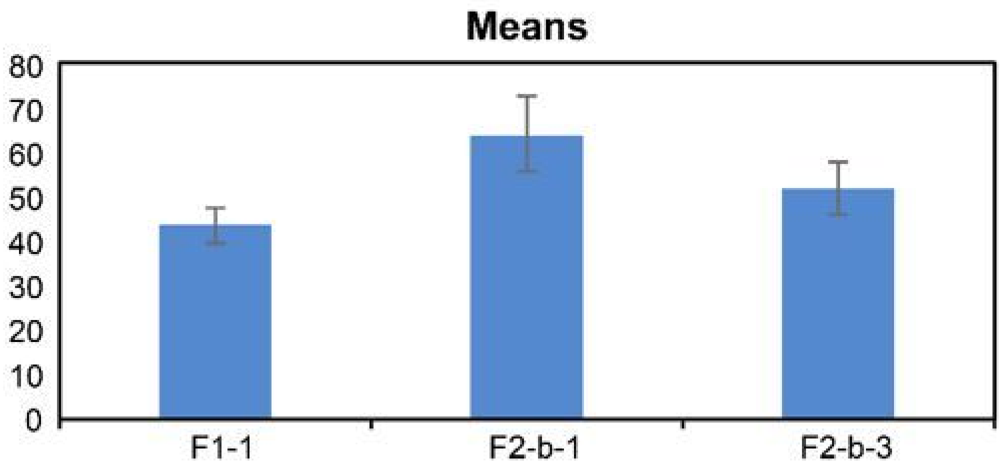

Figure 1

Score difference for each difficulty level in the dual task program. F1-1: too easy content. F2-b-1 increases the speed and thinking pace. F2-b-3: too difficult or too fast.