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Original Article

Observing brain function via functional near-infrared spectroscopy during cognitive program training (dual task) in young people

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Abstract. [Purpose] To study the brain function during a dual task (cycling exercise and cognitive training) via functional near-infrared spectroscopy in young males. [Participants and Methods] Twenty Japanese young male participants were divided into intervention and control groups by simple randomization (n=10 per group). In the intervention group, participants were given a cognitive program training and cycling exercise (dual task). The control group was given the cognitive program training (single task) only. The cognitive program training consisted of a warm up, followed by 2 minutes of rock-paper-scissors, 2 minutes of numeric memory, 2 minutes of color matching, 2 minutes of calculations, and a cool down. Brain function tests were performed individually throughout the programs by functional near-infrared spectroscopy. [Results] The oxyhemoglobin levels significantly increased in the frontal lobe of the intervention and control groups after program completion compared to before. And the oxyhemoglobin levels of the intervention group also significantly increased more than control group in the prefrontal cortex and motor area. [Conclusion] This program used by Cognibike was also effective for improving hemoglobin oxygen levels at the frontal lobe in young males.

Key words: Brain function, Cognibike, Functional Near-Infrared Spectroscopy (fNIR or fNIRS)

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INTRODUCTION

Exercise is an important part of a healthy lifestyle. It can improve physical health, mental health, brain function and reduce the risk of developing several chronic diseases (e.g., cardiovascular disease, diabetes, cancer, hypertension, obesity, depression and osteoporosis) and premature death[1–3)]. Recent evidence have shown that long-term exercise can not only lead to structural changes of the brain, but also prevent age-related cognitive decline[4)]. Short-term effect of exercise would improve brain functions by increasing cerebral blood volume and oxygen levels in the brain. Mild cycling exercise can increase oxygenation of the prefrontal cortex[5)], induced arousal system and result in improves executive function[4)].

Cognitive training is another type of exercise that focused on improving brain function. The design of brain stimulation programs must be related to the function of the brain, including stimulating; thinking process, analysis, learning, memory, using languages together with the attraction and interesting. Previous study suggested exercise with dual task has significant benefit on cognitive function compared to single task exercise. The dual task exercise such as digit backward test with a cycle ergometer exercise can improved performance changes on cognitive tests in young and elderly[6)]. However, from literature review, there are reports of physical function and cognitive function through implementation of dual tasks. But there have been no reports of dual task using Cognibike related to the effect of brain function.

To address this issue, we used a dual task exercise which is a combination of cognitive training task and cycling ergometer

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*Corresponding author. Ratri Techayusukcharoen (E-mail: Ratri_t@outlook.co.th) task for evaluate brain activity by use function near-infrared spectroscopy (fNIRS) measure oxygenation changes during and after exercise. The purpose of the study was to investigate the cerebral oxygenation changes in the prefrontal area in response to dual task exercise which is a combination of cognitive training task and cycling ergometer task in healthy young adult.

PARTICIPANTS AND METHODS

Twenty right-handed Japanese male who studied at Teikyo Heisei University aged between 20 to 25 years participated in the study (mean age 21.2 ± 0.6 years, height 172.6 ± 4.8 cm, weight 64.7 ± 6 kg). All participants were in good physical and mental health condition; they had no history of any major psychiatric disorder, neurological disorder, substance abuse, head injury, major physical illness, communication problem, or visual problems and listening problem. This study was approved by the Ethics Committee of Teikyo Heisei University (approval No. 29-115). After the information was given and the participants submitted a written consent, participant was randomly assigned into 2 groups, 10 participants in the single task group (ST) and 10 participants in dual task group (DT) by using simple random sampling.

Function Near-Infrared Spectroscopy (fNIRS) were conducted to evaluate brain function of frontal lobe. Brain activity of prefrontal cortex and premotor cortex were recorded throughout the experiment. fNIRS is measured through hemodynamic responses which associated with neuron behavior. The hemodynamic activity was monitored using a continuous wave multi-channel fNIRS (SHIMADZU Corporation, Japan) using two wavelengths of near infrared light (780 and 830 nm) which was adopted to monitor cortical hemodynamic changes. Oxygen hemoglobin (Oxy-Hb) and deoxygenated-hemoglobin (deoxy-Hb) are stronger absorbers of light. And also, readily diffuses easily through biological tissue, can be used to measure localized blood oxygenation levels of the brain to monitor where activity occurs in response to a task or stimulus. This method allowed us to calculate signals reflecting the oxy-Hb, deoxy-Hb, and total hemoglobin (total-Hb) concentration changes, calculated in units of millimolar-millimeter (mM•mm)7). The oxygen hemoglobin and the deoxygenate hemoglobin signals were analyzed and sampling rate was set at 10 Hz. The optical data from fNIRS was analyzed based on the modified Beer-Lambert law8).

The fNIRS probes covered the prefrontal cortex and premotor cortex activation. Two sets of 4 × 2 multichannel probe holders were used. These consisted of 8 illuminative and 8 detective probes arranged alternately at an inter-probe distance of 3 cm, resulting in 8 channels (CH) per set. Divide the area of the brain into 4 parts9, 10) (Fig. 1).

Both groups practiced cognitive task from cognitive training program of Cognibike but only DT practiced cognitive during cycling ergometer. The Cognibike is an innovation of new workout that can exercise with cyclic ergometer and practice cognitive training in the same time as presented in Fig. 2. Cognibike exercise was based on the concept of “cognicise” that promote by the national center of Geriatrics and Gerotorgy as an exercise program to prevent dementia. Procedure of experimental design was shown in Fig. 3 (A). Participants in ST group received cognitive program training while sitting on Cognibike following step of warm up with touch screen practice 2 minutes, cognitive program training 8 minutes and cool down with relax sitting 5 minutes. DT group received series of exercise including; 5 minutes warm up with riding ergometer at 50 rpm speed with load, without load and with touch screen practice respectively, 8 minutes of cognitive training with ride bicycle with load 30 watt in the same time and 5 minutes cool down with riding ergometer at 50 rpm speed without load. The cognitive training tasks which used in this study consisted of Rock-paper-scissors, Numeric memory, Color matching and Calculation. Each program takes 2 minutes from easy to difficult respectively (Fig. 3B). Brain activities of both groups were measured by fNIRS continuously throughout the experiment.

After data extraction to a personal computer with Microsoft excel, analysis was conducted at eight different time points: before programs, warm up, each program, cool down, and after programs. The average data used is oxygen hemoglobin only.

Statistical analysis was performed using SPSS v.22 for Windows. Data are expressed as mean values with standard deviations. Variable data for ST and DT were compared using the independent t-test. Within-group change in oxygen hemoglobin level between pre-intervention and each program, was evaluated using One-way ANOVA test. $P<0.05$ was considered statistically significant.

RESULTS

Characteristics of the participants in Table 1 shows the characteristics of the DT group (n=10) and the ST group (n=10). There were no significant differences observed between two groups in age, gender, and BMI.

Oxy-hemoglobin in prefrontal cortex in two groups were shown in Table 2. There were no significant differences between before cognitive training for the ST and DT group. Oxy-hemoglobin in prefrontal lobe and left premotor cortex showed significant increase in DT group than ST group in calculation task and after used cognitive training ($p<0.05$). Whereas, oxy-hemoglobin in right premotor cortex were not significantly different between groups.

DT group showed more increase of oxy-hemoglobin in supplement motor area during numeric memory task than ST group ($p=0.03$) which was significant.

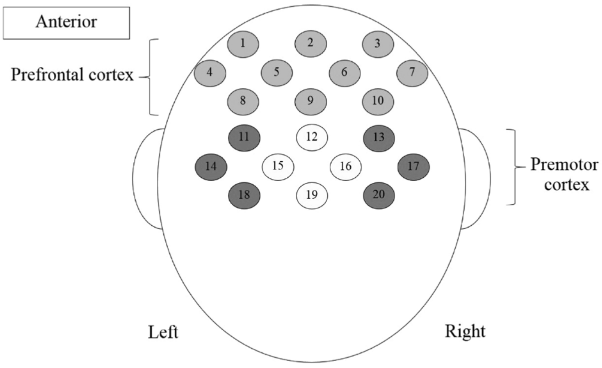

Fig. 1. Measurement area at the frontal lobe. Chanel 1–10: Prefrontal cortex, Chanel 11–20: Premotor cortex divided into 3 subdivisions, including Chanel 11, 14, 18: Left premotor cortex, Chanel 12, 15, 16, 19: Supplementary motor area, and Chanel 13, 17, 20: Right premotor cortex.

Fig. 2. Cognibike. Retrieved from: Start of functional training to prevent dementia at TSUKUI Day Service[43].

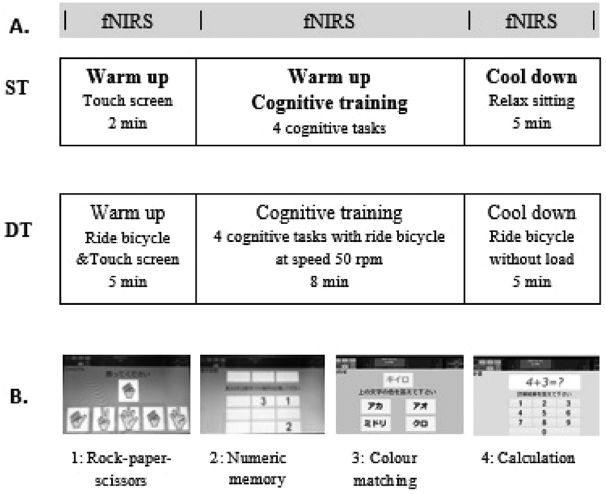

Fig. 3. (A) Experimental design, consisting of the single task (ST) and dual task (DT) conditions. Frontal lobe hemodynamic changes were continuing monitored with functional near-infrared spectroscopy (fNIRS) throughout the experiment. (B) Illustration of cognitive training including of 4 tasks; 1) Rock-paper-scissors is a memory, thinking and resolving task, 2) Numeric memory is a short-term memory task, 3) Color matching is an analytical thinking, long term memory and thinking task, and 4) Calculation is thinking task.

Table 1. Characteristics at baseline measurements in both intervention and control groups

	Intervention group N=10	Control group N=10	p value
Age (years)	21 ± 0.5	21.4 ± 0.7	0.06
Gender (Female/male)	0/10	0/10	N
BMI (kg/m^2)	21.8 ± 2.1	21.3 ± 1.7	0.35

Data are expressed as mean ± SD.

Table 2. Comparison of oxy-hemoglobin in frontal lobe between dual and single task groups

Task	Prefrontal cortex				Left Premotor cortex				Right Premotor cortex				Supplementary motor area			
	DT	ST	F	p	DT	ST	F	p	DT	ST	F	p	DT	ST	F	p
Before (Touch screen)	0	0.02 ± 0.02	0.84	0.37	0 ± 0.03	0.02 ± 0.01	0.84	0.37	0.01 ± 0.02	0 ± 0.04	0.14	0.71	0 ± 0.01	0.01 ± 0.04	0.58	0.46
Rock paper scissors	0.02 ± 0.01	0.01 ± 0.02	0.03	0.86	0.01 ± 0.03	0.02 ± 0.02	0.03	0.86	0 ± 0.02	0.01 ± 0.04	1.31	0.27	0 ± 0.01	0.01 ± 0.03	2.09	0.17
Numeric memory	0.02 ± 0.02	0.02 ± 0.02	2.68	0.12	0.02 ± 0.04	0.02 ± 0.02	2.68	0.12	0.01 ± 0.03	0.01 ± 0.04	0.44	0.52	0 ± 0.03	0.01 ± 0.03	5.25	0.03*
Color matching	0.06 ± 0.06	0.04 ± 0.04	1.58	0.23	0.06 ± 0.05	0.04 ± 0.04	1.58	0.23	0.02 ± 0.03	0.01 ± 0.06	0.03	0.88	0 ± 0.03	0.01 ± 0.03	3.84	0.07
Calculation	0.06 ± 0.06	0.03 ± 0.02	5.56	0.03*	0.06 ± 0.04	0.03 ± 0.02	5.66	0.03*	0.02 ± 0.03	0.02 ± 0.05	0.07	0.80	0 ± 0.03	0.02 ± 0.03	2.47	0.13
Cool down	0.10 ± 0.09	0.04 ± 0.01	3.37	0.08	0.09 ± 0.04	0.04 ± 0.01	3.37	0.08	0.03 ± 0.03	0.02 ± 0.04	0.55	0.47	0.01 ± 0.03	0.02 ± 0.04	2.62	0.12
After training	0.07 ± 0.07	0.04 ± 0.01	5.88	0.03*	0.07 ± 0.04	0.042 ± 0.01	5.88	0.03*	0.03 ± 0.03	0.02 ± 0.04	1.90	0.19	0.01 ± 0.03	0.01 ± 0.04	2.40	0.14

Data are expressed as mean ± SD. DT: dual task group (n=10), ST: single task group (n=10) *Significance was set at p<0.05.

DISCUSSION

This study examined effect of cognitive training (single task and dual task) on frontal lobe activation by measuring changes in the concentration of oxy-hemoglobin levels in the frontal lobe using fNIRS during a cognitive program. The results have been confirmed effectiveness of cognitive program training (single task and dual task) for increased brain activity in healthy male young people. Both single and dual task training with Cognibike induced oxy-hemoglobin improvement in frontal lobe, but dual task has more significant improvement in difficulty task and at the end of exercises.

Increased oxy-hemoglobin levels at frontal lobe are associated with cognitive program training, which affects to increase executive brain function. Previous studies related to the four programs, such as Pock-Paper-Scissors task can increase in the frontal region, especially the lateral prefrontal area[11]. NIRS study using the 'to lose' Rock-Paper-Scissors task increase to oxy-Hb in the laterally dominant prefrontal cortex in adults[12]. The study about the arithmetic network. Showing dorsolateral prefrontal cortex (DLPFC) and ventrolateral prefrontal cortex (VLPFC) were related to the calculation mechanism etc[13]. Which reviewed several areas of research suggesting a close neural link between, and substantial co-activation of the cerebellum, critical for complex and coordinated movement, and DLPFC, critical for executive function. Showing that the cerebellum seems to be important for complex cognitive functions as well as complex motor functions; likewise, the DLPFC seems to be important for complex motor functions as well as complex cognitive functions[14]. And also, the neuroimaging studies have revealed that the DLPFC plays a significant role in the performance of a working memory task[15, 16].

The pattern of the cognitive program training should have a direct effect on the brain's function. From the previous research of Brondmann's area 10 observed increased recruitment of the rostral parts of Brondmann's area 10 in multi-tasking conditions compared to a control task[17, 18], consistent with the present and previous research in young adults. Finding of prefrontal cortex activation during multitasking confirms the relationship between dual tasking and prefrontal lobe function[19]. Moreover, our findings show that oxygen hemoglobin levels were different during ST and DT. ST apparently do elicit a large increase in blood oxygenation in the frontal area as this could be considered a relatively simple motor task, as least in healthy male young people. Conversely, oxygen hemoglobin levels were much higher when the DT. Consistent with the previous research in young adults. Findings show that oxygen hemoglobin levels were not different during quiet standing and usual-walking. Usual-walking apparently does not elicit a large increase in blood oxygenation in the frontal area as this could be considered a relatively simple motor task, as least in healthy young adults. Conversely, oxygen hemoglobin levels were much higher when the walking task was paired with either simple counting or a more complex DT[19]. So, increasing the oxygen hemoglobin at frontal lobe. It has a direct effect on the increasing work of working memory and executive brain function. However, the direction of increasing oxygen hemoglobin between ST and DT was also observations as well as the study Doi et al.[20], although the younger participants showed slightly higher baseline levels of activation than the patients with mild cognitive impairment. Thus, it is likely that oxygenation levels in response to a DT may be affected by age and disease, decreasing the initial activation level and limiting the hemodynamic response and the ability of the brain to adapt to complex situations. This is consistent with the hypotheses explaining possible mechanisms of diminished DT performance in older adults[21, 22].

The pattern of the cognitive program training consists of 4 successive programs. It can help stimulate brain function in the frontal lobe. This is similar to their assumption that Hiroyuki Suzuki said the frequent use of brain neural network strengthens its connections and helps to prevent possible morbid invasions[23]. Which the programs focuses on repeated training to brain thinking and learning. But this study was not conducted in the same way as the elderly. Therefore, it is not possible to summarize the relationship with age and experience. Because as age increases, it correlates with the experience and degeneration of various systems in the body.

In addition, exercise and cognitive program training (DT) both increase cerebral blood flow (CBF). From the previous research found that exercise-induced cognitive improvements is that increased CBF makes more oxygen and glucose available for metabolic functions and improves the clearance of metabolic waste[24, 25)]. And facilitating neurogenesis, synaptogenesis and neurotrophins[26–31)]. Especially, Brain-derived neurotrophic factor (BDNF). BDNF is a protein that promotes neuroplasticity: the growth and survival of neurons, regulation of axonal and dendritic branching, and synaptic transmission. Which improve memory and cognitive functions[32–35)]. Moreover, increases of the volume of hippocampus of >2% together with plasma concentration of brain-derived neurotrophic factor (BDNF) were also observed in older healthy participants and in individuals with AD following one year of moderately intense aerobic exercise (3 days per week, 40 min per session)[36, 37)]. However, aerobic exercise on serum BDNF levels has generated complex findings. In young adults have documented significant transient increases of circulating BDNF with short-term aerobic exercise[38–41)]. Thus, 5 weeks of chronic aerobic exercise in young adults was associated with increased levels of circulating BDNF[42)]. Although, this study found that the increase in oxygen hemoglobin may be the effect to BDNF. But, on this study is not directly measured BDNF level. So, in the future research, should study more about the effect of BDNF level by cognitive program training (Dual task) for young people.

This study has three limitations. First, this research is conducted in male young people. The brain is in full development phase, so it may need to be studied at other ages and in female. Second, the program used to stimulate the brain of all four programs to stimulate the brain function continuously for only a short time. Therefore, it may not be possible to conclude that this program can provide long-term brain function stimulation. Third, the application of the program to stimulate the brain function. It is necessary to use all four programs continuously. Therefore, application of one or two programs may not only stimulate frontal activity as described above.

The young male people participated in the cognitive program training achieved significant improvement in oxygen hemoglobin at frontal lobe. Especially, prefrontal cortex, left premotor cortex and supplementary motor area. Clearly showing the beneficial effects of cognitive program training (Dual task) can stimulate oxy-hemoglobin at frontal lobe more than cognitive program training (Single task). However, using the program together with exercise can stimulate the brain rather than using the program alone. Future research should be applied to the elderly or elderly people with mild cognitive impairment. To see the clear results. Application of basic principles related to basic functions of the frontal lobe using Cognibike is convenient, safe and stimulating or promote the brain working. Also, it can prevent Dementia for elderly in the future.

Conflict of interest

None.

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REFERENCES

1) Rezab S: Exercise and cognition in young adults. Psychological Sciences Undergraduate Publications, 2015.
2) Dishman RK, Berthoud HR, Booth FW, et al.: Neurobiology of exercise. Obesity (Silver Spring), 2006, 14: 345–356. [Medline] [CrossRef]
3) Warburton DE, Nicol CW, Bredin SS: Health benefits of physical activity: the evidence. CMAJ, 2006, 174: 801–809 [CrossRef]. [Medline]
4) Byun K, Hyodo K, Suwabe K, et al.: Positive effect of acute mild exercise on executive function via arousal-related prefrontal activations: an fNIRS study. Neuroimage, 2014, 98: 336–345. [Medline] [CrossRef]
5) Timinkul A, Kato M, Omori T, et al.: Enhancing effect of cerebral blood volume by mild exercise in healthy young men: a near-infrared spectroscopy study. Neurosci Res, 2008, 61: 242–248. [Medline] [CrossRef]
6) Moraes H, Deslandes A, Silveira H, et al.: Effects of motor and cognitive dual-task performance in depressive elderly, healthy older adults, and healthy young individuals. Dement Neuropsychol, 2011, 5: 198–202. [Medline] [CrossRef]
7) Maki A, Yamashita Y, Ito Y, et al.: Spatial and temporal analysis of human motor activity using noninvasive NIR topography. Med Phys, 1995, 22: 1997–2005. [Medline] [CrossRef]
8) Cope M, Delpy DT, Reynolds EO, et al.: Methods of quantitating cerebral near infrared spectroscopy data. Adv Exp Med Biol, 1988, 222: 183–189. [Medline] [CrossRef]
9) Shimadzu Corporation: Functional Near-Infrared Spectroscopy System for Research (LABNIRS). https://www.shimadzu.com/an/lifescience/imaging/nirs/nirs_top.html. (Accessed 2013)
10) Carrión JL, Domínguez UL: Functional Near-Infrared Spectroscopy (fNIRS): principles and neuroscientific applications. Neuroimaging −Methods, 2012, 47–66.

11) Ishii S, Kaga Y, Tando T, et al.: Disinhibition in children with attention-deficit/hyperactivity disorder: changes in [oxy-Hb] on near-infrared spectroscopy during "rock, paper, scissors" task. Brain Dev, 2017, 39: 395–402. [Medline] [CrossRef]

12) Kikuchi S, Iwata K, Onishi Y, et al.: Prefrontal cerebral activity during a simple "rock, paper, scissors" task measured by the noninvasive near-infrared spectroscopy method. Psychiatry Res, 2007, 156: 199–208. [Medline] [CrossRef]

13) Peters L, De Smedt B: Arithmetic in the developing brain: a review of brain imaging studies. Dev Cogn Neurosci, 2018, 30: 265–279. [Medline] [CrossRef]

14) Diamond A: Close interrelation of motor development and cognitive development and of the cerebellum and prefrontal cortex. Child Dev, 2000, 71: 44–56. [Medline] [CrossRef]

15) Owen AM, Herrod NJ, Menon DK, et al.: Redefining the functional organization of working memory processes within human lateral prefrontal cortex. Eur J Neurosci, 1999, 11: 567–574. [Medline] [CrossRef]

16) Ungerleider LG, Courtney SM, Haxby JV: A neural system for human visual working memory. Proc Natl Acad Sci USA, 1998, 95: 883–890. [Medline] [CrossRef]

17) Dumontheil I, Gilbert SJ, Frith CD, et al.: Recruitment of lateral rostral prefrontal cortex in spontaneous and task-related thoughts. Q J Exp Psychol Hove, 2010, 63: 1740–1756. [Medline] [CrossRef]

18) Okuda J, Fujii T, Ohtake H, et al.: Differential involvement of regions of rostral prefrontal cortex (Brodmann area 10) in time- and event-based prospective memory. Int J Psychophysiol, 2007, 64: 233–246. [Medline] [CrossRef]

19) Mirelman A, Maidan I, Bernad-Elazari H, et al.: Increased frontal brain activation during walking while dual tasking: an fNIRS study in healthy young adults. J Neuroeng Rehabil, 2014, 11: 85. [Medline] [CrossRef]

20) Doi T, Makizako H, Shimada H, et al.: Brain activation during dual-task walking and executive function among older adults with mild cognitive impairment: a fNIRS study. Aging Clin Exp Res, 2013, 25: 539–544. [Medline] [CrossRef]

21) Ruthruff E, Pashler HE, Klaassen A: Processing bottlenecks in dual-task performance: structural limitation or strategic postponement? Psychon Bull Rev, 2001, 8: 73–80. [Medline] [CrossRef]

22) Tombu M, Jolicoeur P: A central capacity sharing model of dual-task performance. J Exp Psychol Hum Percept Perform, 2003, 29: 3–18. [Medline] [CrossRef]

23) Suzuki H, Kuraoka M, Yasunaka M, et al.: Cognitive intervention through a training program for picture book reading in community-dwelling older adults: a randomized controlled trial. BMC Geriatrics, 2014, 14: 122.

24) Popa-Wagner A, Buga AM, Popescu B, et al.: Vascular cognitive impairment, dementia, aging and energy demand. A vicious cycle. J Neural Transm (Vienna), 2015, 122: S47–S54. [Medline] [CrossRef]

25) Ide K, Secher NH: Cerebral blood flow and metabolism during exercise. Prog Neurobiol, 2000, 61: 397–414. [Medline] [CrossRef]

26) Archer T: Physical exercise alleviates debilities of normal aging and Alzheimer's disease. Acta Neurol Scand, 2011, 123: 221–238. [Medline] [CrossRef]

27) Yu F, Kolanowski AM, Strumpf NE, et al.: Improving cognition and function through exercise intervention in Alzheimer's disease. J Nurs Scholarsh, 2006, 38: 358–365. [Medline] [CrossRef]

28) Pereira AC, Huddleston DE, Brickman AM, et al.: An in vivo correlate of exercise-induced neurogenesis in the adult dentate gyrus. Proc Natl Acad Sci USA, 2007, 104: 5638–5643. [Medline] [CrossRef]

29) Lange-Asschenfeldt C, Kojda G: Alzheimer's disease, cerebrovascular dysfunction and the benefits of exercise: from vessels to neurons. Exp Gerontol, 2008, 43: 499–504. [Medline] [CrossRef]

30) Radak Z, Hart N, Sarga L, et al.: Exercise plays a preventive role against Alzheimer's disease. J Alzheimers Dis, 2010, 20: 777–783. [Medline] [CrossRef]

31) Pérez CA, Cancela Carral JM: Benefits of physical exercise for older adults with Alzheimer's disease. Geriatr Nurs, 2008, 29: 384–391. [Medline] [CrossRef]

32) Hwang J, Brothers RM, Castelli DM, et al.: Acute high-intensity exercise-induced cognitive enhancement and brain-derived neurotrophic factor in young, healthy adults. Neurosci Lett, 2016, 630: 247–253. [Medline] [CrossRef]

33) Calabrese F, Rossetti AC, Racagni G, et al.: Brain-derived neurotrophic factor: a bridge between inflammation and neuroplasticity. Front Cell Neurosci, 2014, 8: 430. [Medline] [CrossRef]

34) Etnier JL, Wideman L, Labban JD, et al.: The effects of acute exercise on memory and brain-derived neurotrophic factor (BDNF). J Sport Exerc Psychol, 2016, 38: 331–340. [Medline] [CrossRef]

35) Vaynman S, Ying Z, Gomez-Pinilla F: Hippocampal BDNF mediates the efficacy of exercise on synaptic plasticity and cognition. Eur J Neurosci, 2004, 20: 2580–2590. [Medline] [CrossRef]

36) Erickson KI, Voss MW, Prakash RS, et al.: Exercise training increases size of hippocampus and improves memory. Proc Natl Acad Sci USA, 2011, 108: 3017–3022. [Medline] [CrossRef]

37) Coelho FG, Vital TM, Stein AM, et al.: Acute aerobic exercise increases brain-derived neurotrophic factor levels in elderly with Alzheimer's disease. J Alzheimers Dis, 2014, 39: 401–408. [Medline] [CrossRef]

38) Gold SM, Schulz KH, Hartmann S, et al.: Basal serum levels and reactivity of nerve growth factor and brain-derived neurotrophic factor to standardized acute exercise in multiple sclerosis and controls. J Neuroimmunol, 2003, 138: 99–105. [Medline] [CrossRef]

39) Ferris LT, Williams JS, Shen CL: The effect of acute exercise on serum brain-derived neurotrophic factor levels and cognitive function. Med Sci Sports Exerc, 2007, 39: 728–734. [Medline] [CrossRef]

40) Tang SW, Chu E, Hui T, et al.: Influence of exercise on serum brain-derived neurotrophic factor concentrations in healthy human subjects. Neurosci Lett, 2008, 431: 62–65. [Medline] [CrossRef]

41) Rojas Vega S, Strüder HK, Vera Wahrmann B, et al.: Acute BDNF and cortisol response to low intensity exercise and following ramp incremental exercise to exhaustion in humans. Brain Res, 2006, 1121: 59–65. [Medline] [CrossRef]

42) Zoladz JA, Pilc A, Majerczak J, et al.: Endurance training increases plasma brain-derived neurotrophic factor concentration in young healthy men. J Physiol Pharmacol, 2008, 59: 119–132. [Medline]

43) Tsukui Corporation: Start of Functional training to prevent dementia at TSUKUI Day Service: new introduction of "cognibike" ergometer based on the concept of "cognicise". 2015.