Original

Comparison of Cerebral Blood Volume during Cold and Warm Stimulation in Elderly and Young Subjects

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ABSTRACT

Background: Dementia involves a neuronal loss in the primary somatosensory cortex of the parietal lobe, causing dementia patients to perceive pain stimuli hardly. The function of temperature sensation declines. Studies measuring brain blood volume using near-infrared light have reported that patients suffering from dementia have less activation than healthy elderly people. However, the majority of these studies used tests related to cognitive function and the frontal lobe, and few have examined thermal sensation.

Objective: The present study aimed to investigate the effect of cold and warm stimulation on cerebral blood volume in elderly and young subjects.

Material and Methods: This observational study measured changes in oxygenated hemoglobin concentrations in the frontal cortex during cold and warm stimulation in elderly and young subjects using a near-infrared light device. The mean and standard deviation of the change in oxygenated hemoglobin concentration before and after cold and warm stimulation, as well as the center-of-gravity values, were compared between the young and the elderly.

Results: During warm stimulation, the younger subjects showed an increase in blood oxygenated hemoglobin levels; however, the difference was not significant. For the elderly, no change was observed during the task. The center of gravity values was lower in the young compared to the elderly which was similar to the reaction threshold. No significant changes were observed during cold stimulation.

Conclusion: Thermal sensation thresholds were impaired in the elderly compared to the young; however, cerebral blood volume changes were unclear.

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Keywords

Cold Stimuli; Cerebral Blood Volume; Elderly; Mini-Mental State Examination; Spectroscopy, Near-Infrared; Thermal Sensation; Warm Stimuli; Mental Status and Dementia Tests

Introduction

Brain function measurement using near-infrared light is studied in various fields, and devices ranging from large to portable devices are developed. Near-infrared spectroscopy is approved as a diagnostic aid for depression [1] for the elderly and dementia patients in the future for examinations and treatments.

Based on the studies, dementia is associated with brain atrophy and functional decline, particularly in the frontal and temporal lobes the frontal lobe plays a role in decision-making, executive control [2], and

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memory [3]; the temporal lobe includes areas involved in auditory, olfactory, vestibular and visual functions, and spoken as well as written language perception [4]. In addition to these areas where the brain is atrophied due to dementia (frontal and temporal lobes), patients mostly experience a loss of neurons in the primary somatosensory cortex of the parietal lobe, causing dementia patients to perceive pain stimuli hardly [5]. The somatosensory system is a sensory system that consciously recognizes the sensations of touch, pressure, pain, temperature, position, movement, and vibration [6]. In dementia patients and elderly individuals with lower cognitive function, the function of temperature sensation declines. The thermal sensory system not only detects the temperature information of external objects but also plays a role in the reception of thermal factors in the internal environment of the body, which is an extremely important function.

Studies of cerebral blood volume measurement using near-infrared light reported that dementia patients and elderly people with lower cognitive function have less activation of cerebral blood volume compared to healthy elderly people [7-9]. However, these studies have mostly used tests related to cognitive function and the frontal lobe, rather than thermal sensation. In addition, in our previous report, the magnitude (amount of change) of the response was evaluated during the category fluency task [10], but the center-of-gravity value was also evaluated as a diagnostic aid for depression.

This study focused on cold as well as warm stimulation and measured changes in oxygenated hemoglobin concentration in the frontal cortex during cold and warm stimulation in elderly and young subjects using a device using near-infrared light. In the current study, the Mini-Mental State Examination (MMSE), a cognitive function test for the elderly, was conducted and also examined the relationship between the MMSE score and cerebral blood volume. Finally, the effectiveness of cerebral blood volume and thermal sensation measurements was examined in estimating cognitive function.

Material and Methods

In this observational study, three elderly individuals (two males and one female; age, 77.7±8.4 years) and nine young individuals (five males and four females; age, 20.8±0.4 years) were included without any motor disabilities and abnormalities in hand movements. The change in oxygenated hemoglobin concentration was measured during cold and warm stimulation using the Wearable Optical Topography (WOT-HS) system manufactured by Hitachi High-Technologies Corporation and Hitachi Kokusai Yagi Solutions. The cold and warm temperatures were stimulated on the opposite side of the dominant arm using a Peltier element in two types of stimuli: cold and warm. The measurement protocol for the cold stimulation involved a 1 min rest, 1 min cold stimulation, and another 1 min rest. Similarly, the measurement protocol for the warm stimulation involved a 1 min rest, 1 min warm stimulation, and another 1 min rest. The maximum number of measurement channels of the WOT-HS is 34 since the Fp1 (left front polar) and Fp2 (right-front polar) regions (frontal lobe) were selected as the regions of interest, and 10-25 channels were used. The signals of each channel were transformed into Z-scores [11-13]. The mean, standard deviation, and center-of-gravity values were calculated from the averaged values of 10-16 CH (Fp2 region) and 19-25 CH (Fp1 region). The center-of-gravity value was the timing of the response during the task (Figure 1), and the center-of-gravity value was calculated during cold and warm stimuli. In this study, the center-of-gravity value calculated was the point, at which the area (integral volume) was halved in the positive direction (above 0) [14].

The statistical analyses were done using SPSS statistics (version 27.0). Mann-Whitney's U test was used to determine the differ-

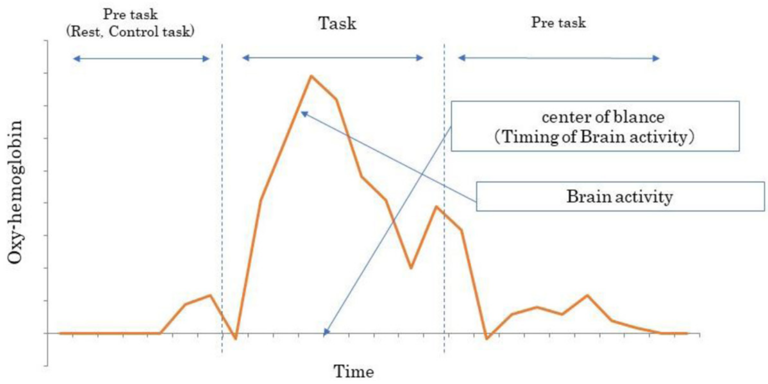

Figure 1: Near-infrared spectroscopy signal

ence in stimulus-response threshold and oxygenated hemoglobin concentration between the groups. Pearson's correlation coefficient was calculated to determine the correlation between the time of temperature change and the concentration of oxygenated hemoglobin.

Wearable optical topography system (WOT-HS)

WOT-HS used near-infrared light to measure the concentration of oxygenated hemoglobin (NIRS: near-infrared spectroscopy) that indirectly measured neural activity in the surface layers of the brain based on changes in hemoglobin concentration according to the neurovascular coupling theory and the modified Beer-Lambert law. In the psychiatric field, optical topography was approved as an auxiliary diagnostic test for treatment-resistant depression [1]. Near-infrared light was harmless to live organisms as its wavelength was close to that of visible light, and the device using near-infrared light is not invasive in measurement. The WOT-HS used in this study was a wearable device measuring the frontal and temporal areas. However, skin blood was a problem for NIRS measurement [15], WOT-HS device used a multi-distance method to reduce biological noise, such as skin blood flow.

Cold and warm stimuli using the Peltier element

The Peltier device is a semiconductor that can cool, heat, and control temperature freely using a direct current (DC); Figure 2 shows thermal stimulation.

Temperature stimulation was performed on the contralateral side of the dominant arm. On the opposite side of the dominant hand, a switch was prepared to evaluate the time when the temperature changed, and the participants were trained to press the switch when felt the temperature change [16]. For cold and warm sensations, the amount of time until the switch was pressed for cold stimulation was calculated as the cold response threshold, and the amount of time before the switch was pressed for warm stimulation was calculated as the warm response threshold. At the same time, the ambient air temperature and skin temperature of the subject's palm were measured at 100 Hz intervals using a thermistor thermometer

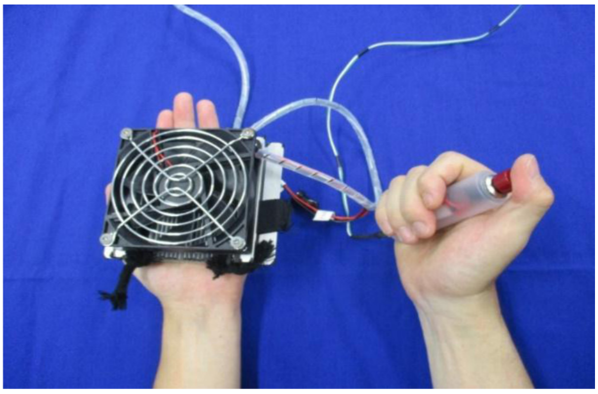

Figure 2: Overview of the cold and warm stimuli

attached to a Peltier device. The measurement protocol used in this study was as follows: rest for 1 min, cold or warm stimulation for 1 min, and rest again for 1 min. In the resting period, the Peltier device was set to 25 °C; in the cold stimulation period, the temperature was set to 20 °C for 1 min. In the warm stimulation period, the temperature was set to 35 °C for 1 min, and the temperature in the room was set to 25 °C using an air conditioner.

Results

The participants' demographics are shown separately for the young (n=9) and the elderly (n=3) groups (Table 1).

The young and elderly groups had the following demographics: mean age (young 20.8±0.4 years vs. elderly 77.7±8.4 years), sex (young 5 males/4 females vs. elderly 2 males/1 female), mean warm response threshold (young 25.5±26.1 s vs. elderly 56.2±6.6 s), and mean cold response threshold (young 6.9±5.1 s vs. elderly 12.3±13.6 s). For the warm stimuli, no individual noticed the temperature change; however, two young individuals and one elderly individual noticed the temperature change for the cooling stimulus. No significant difference was in the cold and warm response thresholds between the elderly and young individuals. The mean MMSE score for the cognitive function was 21.3±4.0 for the elderly individuals.

Table 1: Subject demographics and temperature response threshold

	Young subjects	Elderly subjects
Age (year)	20.8±0.4	77.7±8.4
Sex (M/F)	5/4	2/1
Cold response threshold (sec)	6.9±5.1	12.3±13.6
Warm response threshold (sec)	25.5±26.1	56.2±6.6

Changes in oxygenated hemoglobin concentration are shown in Figures 3-6.

During the cold stimulation, no significant changes in oxygenated hemoglobin levels were observed during the task in both young and elderly subjects; during the warm stimulation, the younger individuals showed an increase in oxygenated hemoglobin levels after the start of the task, but the difference was not significant. In the elderly, no change was observed during the task. The oxygenated hemoglobin concentrations and center-of-gravity values are shown in Table 2.

The oxygenated hemoglobin concentration during the task was calculated separately for the first half of the task, 60-90 s, and the second half, 90-120 s. In terms of the center-of-gravity values, the difference was considered between the young and the elderly individuals that were not significant.

Discussion

In this study, changes were measured in oxygenated hemoglobin concentration

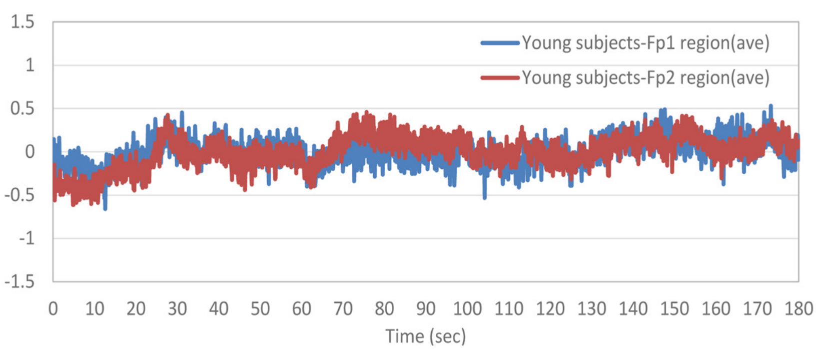

Figure 3: Change in oxygenated hemoglobin levels during cold stimulation in young subjects

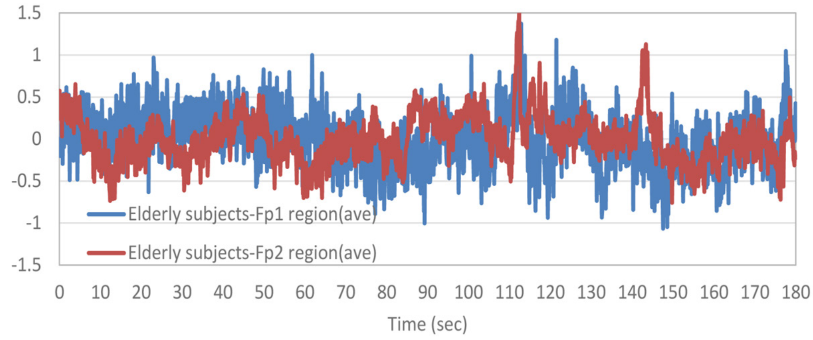

Figure 4: Change in oxygenated hemoglobin levels during cold stimulation in elderly subjects

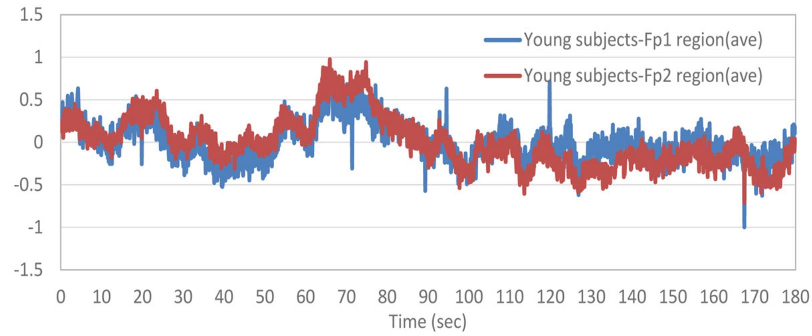

Figure 5: Change in oxygenated hemoglobin levels during warm stimulation in young subjects

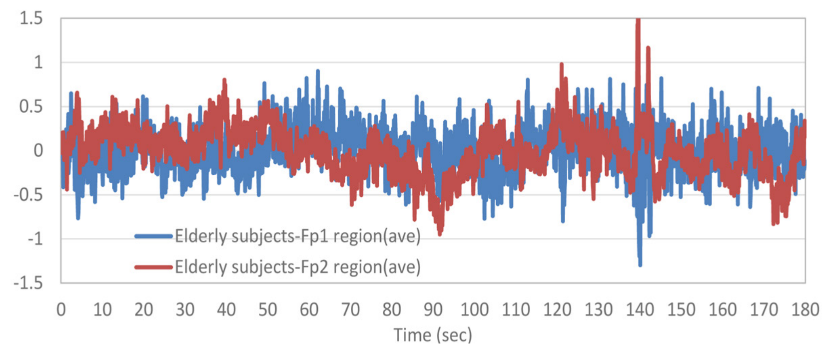

Figure 6: Change in oxygenated hemoglobin levels during warm stimulation in elderly subjects

during cold and warm stimulation in elderly and young individuals using a device that uses near-infrared light. The results indicated that thermal sensation thresholds were impaired in the elderly individuals compared to the young individuals. However, the relationship between thermal stimulation and cerebral blood volume was unclear in the frontal lobe. Since cold and warm stimuli are strongly related to the primary somatosensory cortex, measuring both the frontal and parietal lobes is necessary for future studies. The results also indicate that the cold and warm response thresholds were lower in the young individuals, and the warm and cold sensations were superior, while the values were higher in the elderly. The results showed that the cold and warm response thresholds were lower in the young individuals compared to the elderly individuals, showing that the thermal sensitivity of the young

Table 2: Changes in oxygenated hemoglobin levels and center-of-gravity values

	Fp1 regions at rest with young subjects	Fp1 regions at task (60-90 sec) with young subjects	Fp1 regions at task (90-120 sec) with young subjects	Fp1 regions at rest with young subjects	Fp1 regions center-of-gravity value	Fp2 regions at rest with young subjects	Fp2 regions at task (60-90 sec) with young subjects	Fp2 regions at task (90-120 sec) with young subjects	Fp2 regions at rest with young subjects	Fp2 regions center-of-gravity value
Young subjects in cold stimuli	-0.0810±0.3743	-0.1592±0.4141	-0.0234±0.4483	0.1724±0.3995	92.3±17.7	-0.1325±0.5399	0.0871±0.3776	0.0348±0.5530	0.0718±0.5109	91.2±17.2
Elderly subjects in cold stimuli	0.1562±0.1742	-0.1531±0.1758	0.0192±0.1499	-0.0895±0.2411	99.5±8.5	-0.0338±0.2556	-0.0711±0.0591	0.2279±0.1503	-0.0445±0.1877	100.7±9.9
Young subjects in warm stimuli	0.0167±0.3117	0.2610±0.5169	-0.0746±0.3474	-0.1099±0.2396	80.0±12.8	0.1160±0.5522	0.3950±0.4785	-0.1406±0.4917	-0.2434±0.4885	79.4±13.1
Elderly subjects in warm stimuli	-0.0197±0.0913	0.0914±0.1755	-0.0327±0.024	-0.0096±0.1728	86.7±8.7	0.1627±0.2704	-0.1422±0.2131	-0.1192±0.1141	-0.0323±0.3219	93.1±16.1

subjects was superior to that of the elderly participants. Further, the mean MMSE score of the elderly was 21.3 (Normal cognition: ≥24), indicating a decline in cognitive function. Similar to the reaction threshold, the center-of-gravity values were lower in the young and higher in the elderly.

Furthermore, the threshold for cold stimuli was shorter than that for warm stimuli in both age groups. Similarly, cold receptors were about 10 times more than warm receptors in the skin [17-18]. The responses to both cold and warm stimuli were lower in the elderly compared to the young individuals. Further, the mean MMSE score of the elderly indicated a decline in cognitive function. The response thresholds for cooling and heating were lowered in dementia patients, and neuronal loss in the primary somatosensory cortex of the parietal lobe leads to less-perceptible pain stimuli in dementia [5]. Therefore, the function of thermal sensation may also be impaired as a result of neuronal loss in this area.

As for the oxygenated hemoglobin concentration, an increase was after the start of the thermal stimulation in the younger individuals, but not in the older subjects. Previous studies have shown that the oxygenated hemoglobin concentration decreased in the elderly compared to that in the young. In the present study, young individuals also showed higher values; however, no significant increase in young subjects was at rest and during the task compared to the elderly subjects. In the report and other studies, a significant increase was in oxygenated hemoglobin concentration at rest, during the control condition task and the task [19-20]; however, the task used was one in which the frontal lobe was activated. On the other hand, the task conducted in this study required sensory functions and judgmental abilities as the switch was pressed with warm or cold stimuli. It has been reported that in a dual-task, competition for processing resources was considered between two simultaneous tasks, further degrading task performance [21]. Since the task used the parietal lobe to detect and analyze the temperature, the parietal lobe possibly experienced an increase in blood flow that was not present in the frontal lobe. Therefore, the results did not indicate a significant increase in blood flow. Future studies should measure cerebral blood flow in the parietal lobe and fully clarify these results.

Regarding the center-of-gravity values, the values were lower in the young individuals compared to the elderly individuals, and higher in the elderly subjects compared to the young subjects. This was similar to the reaction threshold, and the oxygenated hemoglobin concentration increased with a temperature change. The timing of the increase in oxygenated hemoglobin concentration in normal subjects and depressed patients using the verbal fluency task was earlier in normal individuals and later in depressed patients [14]. Based on the center-of-gravity values, the same results are obtained without the frontal lobe task.

In the current study, several limitations were as follows: 1) the number of individuals was small, and 2) a statistical analysis could not be sufficiently performed. Therefore, the number of participants has to increase in a future study. In addition, the temperature settings were 25 °C to 20 °C for the cold stimuli and 25 °C to 35 °C for the warm stimuli. Since NIRS was used as an aid in the differential diagnosis of psychiatric disorders, more detailed studies were needed to discriminate between the elderly and dementia patients. In addition, the present study was conducted among elderly individuals. Finally, a frontal lobe-only measurement system was selected due to easy use, which was needed as our experiment was performed on elderly people.

Conclusion

In this study, changes were measured in oxygenated hemoglobin concentration during cold and warm stimulation in elderly and young individuals using a near-infrared light device. The results indicated that thermal sensation thresholds were impaired in the elderly individuals compared with those of the young individuals. However, the relationship between thermal stimulation and cerebral blood volume in the frontal lobe was unclear. Since cold and warm stimuli are strongly related to the primary somatosensory cortex, future studies should investigate both the frontal and parietal lobes to fully understand this phenomenon.

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Authors' Contribution

Sh. Takahashi, D. Takahashi, H. Matsuo, and N. Kodama were involved in the study design. Sh. Takahashi, D. Takahashi, and T. Tamura were involved in the data measurement and analysis. Sh. Takahashi and N. Kodama were involved in the data interpretation. All authors critically revised the manuscript, commented on the drafts, and approved the final manuscript.

Ethical Approval

This study was conducted with the approval of the Research Ethics Committee of the Takasaki University of Health and welfare (approval No. 3063).

Informed consent

Informed consent was obtained from all subjects involved in the study.

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Conflict of Interest

None

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