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Hemodynamic Changes in the Prefrontal Cortex during Digit Span Task: A Near-Infrared Spectroscopy Study

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Key Words

Near-infrared spectroscopy · Prefrontal cortex activation · Digit span · Hemoglobin

Abstract

Background/Aims: In this study, we examined changes in the concentrations of oxygenated and deoxygenated hemoglobin (oxy- and deoxy-Hb, respectively) in the prefrontal cortex (PFC) during the digit span task by using near-infrared spectroscopy (NIRS). ***Methods:*** The digit span task consists of the digit span forward and backward tasks. The tasks were performed by 22 healthy undergraduate students who participated in this study. Differences in the mean concentrations of oxy-Hb and deoxy-Hb between the baseline and task intervals were evaluated. ***Results:*** In digit span backward, oxy-Hb was significantly higher during the task interval than during the baseline. Further, deoxy-Hb was significantly lower during the task interval than during the baseline in both digit span forward and digit span backward. Digit span forward performance was significantly higher for the right-PFC-dominant group than for the left-PFC-dominant group. ***Conclusion:*** These results suggest that the digit span backward task is more demanding and requires greater activation of the prefrontal cortex than the digit span forward task. Our NIRS findings suggest that the digit span backward task involves executive functioning.

Introduction

The digit span task has been widely used in neuropsychological research and as a part of the clinical evaluations belonging to Wechsler's intelligence scale. This task consists of 2 components – the forward and backward components. Digit span forward requires repeating a digit sequence in the order that the digits are recited, while digit span backward requires repeating digits in the reverse order of the recited sequence. These tasks are used to assess phonological short-term memory. Several studies have revealed that patients with psychiatric disorders such as schizophrenia [1, 2], Parkinson's disease [3], and Alzheimer's disease [4] score lower than healthy people in these tests.

However, the functional relationship between digit span forward and digit span backward has not yet been fully investigated. The digit span task is often conceptu-

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alized in terms of working memory, which consists of 4 components: central executive, phonological loop, visuospatial sketchpad, and episodic buffer [5]. Digit span forward is considered to provide a measure of the capacity of the phonological loop, which involves retention of the auditory stimulus and articulatory rehearsal. On the other hand, digit span backward requires transformation to reorder the input digits in a reversed sequence after retention of the digits; this is considered to be part of the execution process [6]. Therefore, digit span backward is considered to be a more demanding task than digit span forward.

Near-infrared spectroscopy (NIRS) uses infrared light to measure the changes in the concentrations of oxygenated and deoxygenated hemoglobin (oxy-Hb and deoxy-Hb, respectively). It is possible to use NIRS measurements to assess brain activation in the human cortex during cognitive tasks [7–13]. NIRS is a noninvasive technique with high time resolution. It also has fewer restrictions than functional magnetic resonance imaging (fMRI) or positron emission tomography (PET). Although NIRS cannot measure the activation of deep brain structures and has a relatively low spatial resolution, it is advantageous over fMRI or PET in terms of the ease of measurement and low cost.

To the best of our knowledge, only one study has assessed brain activation during the digit span task by using NIRS [14], although several studies have assessed brain activation during this task by using PET [15, 16] or fMRI [17]. Hoshi et al. [14] conducted an NIRS study and reported that activation of the right dorsolateral prefrontal cortex (DLPFC) is related to performance in the digit span backward task. A previous repetitive transcranial magnetic stimulation study has suggested that the right DLPFC plays a crucial role in the performance of the digit span task [18]. Nevertheless, it has not yet been clearly established whether the right DLPFC plays a crucial role during the performance of this task. A previous study demonstrated greater activation of the left prefrontal cortex (PFC) during digit span backward than during digit span forward [17]. Hoshi et al. [14] studied activation of regions of the DLPFC and observed that half of the subjects in their study exhibited greater activation of the right DLPFC whereas the other half exhibited greater activation of the left DLPFC. In the study of Aleman and Wout [18], the left DLPFC was not examined; this suggests that it may be involved in the digit span task. Furthermore, the sample size of the latter two studies was very small; therefore, further studies are required to clarify the involvement of the DLPFC in the digit span task.

The aim of this study was to examine the changes in the concentrations of oxy-Hb and deoxy-Hb during the digit span task by using NIRS. We hypothesized that PFC activation would be greater in digit span backward than in digit span forward. We also investigated whether the activation of the right PFC is related to digit span performance.

Methods

Subjects

For this study, we recruited 26 healthy undergraduate students. Of these, 4 participants were excluded from this study due to an error in the NIRS measurements. Of the remaining 22 participants (18 female and 4 male students; mean age ± SD: 18.45 ± 0.60), 20 were right-handed and 2 were left-handed, as assessed by the Edinburgh Handedness Inventory [19].

The participants were asked to complete several cognitive tasks, including the digit span task. The tests were spread over 2 days to ensure that the participants did not get tired. The experiments allotted for each day could be completed in approximately 90 min. In this paper, we document the results of the digit span task. This task was conducted as the first experiment on the second day.

Written informed consent was obtained from the subjects after the study objectives were clearly explained to them. This study was approved by the Ethics Committee of the Graduate School of Medicine, Nagoya University, Japan. The participants received JPY 5,000 (approximately USD 45) as a reward for their participation in the study for 2 days.

Procedure

The digit span forward and backward tasks were conducted. The participants were first asked to relax with their eyes open, during the rest time. The duration of this rest time was 120 s. Thereafter, they were asked to repeat the vowels /a/, /i/, /u/, /e/, and /o/ as a baseline. The baseline time was 60 s, following which we conducted the task. The digit span forward is a test used in the Japanese version of the Wechsler Adult Intelligence Scale-Revised. Digit span forward began with a sequence of 3 digits. If the participants could respond correctly, a longer sequence was given. Each sequence consisted of 2 assignments, and the test was stopped when the participants incorrectly repeated both assignments. After digit span forward, the participants were instructed to rest, which was followed by the baseline period; both the rest and baseline periods lasted for 60 s each. Next, digit span backward was conducted. The digits for the task had been previously recorded and played to the participants on a MiniDisc player (Sony, Japan).

Near-Infrared Spectroscopy

We used the NIRO-200 (Hamamatsu, Japan), which is a dual-channel system, to measure the changes in oxy-Hb and deoxy-Hb concentrations. Three wavelengths of near-infrared light (775, 810, and 850 nm) were used. The differences in the oxy-Hb and deoxy-Hb absorption were used to calculate the concentration changes by using the Beer-Lambert law. The distance between the emitter and detector was 4.0 cm. Probes were placed between Fp1/F3 and Fp2/F4 according to the international 10/20 system.

The sampling time was 0.5 s. The estimated path length factor was 24 cm. The units of concentration change of oxy-Hb and deoxy-Hb were μm/l = $10e^{-6}$ mol/l. The data were transferred from the NIRO-200 instrument to a PC via an RS232C interface.

Data Analysis and Statistics

The difference between the score of the digit span forward and backward tasks was analyzed by the paired t test. The average concentrations for the last 30 s during baseline were calculated as the baseline interval concentrations. Similarly, the average concentrations during the last 30 s of the task were calculated as task interval concentrations. Differences between the average concentrations during the baseline interval and task interval were evaluated using Wilcoxon's signed-rank test. Furthermore, we conducted additional analysis by directly comparing the average oxy-Hb and deoxy-Hb concentrations between the digit span forward and backward tasks by using Wilcoxon's signed-rank test.

In order to investigate asymmetrical activation of the PFC, we first calculated a laterality index (right – left)/(right + left) [20]. However, 6 subjects (27%) showed deactivation in both hemispheres. Consequently, we divided the subjects into groups according to the relative increment from the baseline interval to the task interval observed for each hemisphere. Subjects with a greater increment in the right PFC than in the left PFC were assigned to a right-PFC-dominant group. Differences in the digit span forward and backward scores between the right and left dominant PFC activity groups were analyzed using Wilcoxon's signed-rank test.

Results

Digit Span Test

The mean scores of the digit span forward and digit span backward tasks were 9.55 ± 2.11 (SD) and 9.27 ± 2.10, respectively. There were no significant differences between the scores of the digit span forward and backward tasks ($t_{21} = 0.69$; n.s.).

Near-Infrared Spectroscopy

The typical time courses of changes in oxy-Hb and deoxy-Hb during the digit span task are shown in figure 1. Table 1 shows the mean concentrations of oxy-Hb and deoxy-Hb during the digit span task. In digit span forward, the deoxy-Hb concentration was significantly lower during the task interval than during the rest interval (left frontal: $z = -3.56$, $p < 0.001$; right frontal: $z = -3.72$, $p < 0.001$). There were no significant differences in the oxy-Hb concentration between the rest interval and task interval (left frontal: $z = -1.61$; right frontal: $z = -0.80$; both n.s.).

In digit span backward, the concentration of oxy-Hb was significantly higher during the task interval than during the rest interval (left frontal: $z = -2.19$, $p < 0.05$; right frontal: $z = -1.90$, $p < 0.10$). In addition, the concentration of deoxy-Hb was significantly lower during the task interval than during the rest interval (left frontal: $z = -2.22$, $p < 0.05$; right frontal: $z = -2.68$, $p < 0.01$).

The direct comparison revealed that in the left frontal cortex, the concentrations of both oxy-Hb and deoxy-Hb were significantly lower (borderline) in the digit span backward task than the digit span forward task ($z = -1.77$, $p < 0.10$ for both). In the right frontal cortex, these concentrations did not differ significantly between the digit span forward and backward tasks ($z = -1.22$, n.s. for oxy-Hb and $z = -0.80$, n.s. for deoxy-Hb).

Of the 22 participants in this study, 6 exhibited deactivation in both hemispheres. Of the 16 remaining participants, 10 exhibited right-PFC-dominant activity during the digit span forward task. The digit span forward scores of the group exhibiting right PFC dominance (mean score = 10.30) were significantly higher than those of the group exhibiting left PFC dominance (mean score = 8.50; $z = -1.75$, $p < 0.10$). Digit span backward scores did not differ significantly between these groups ($z = -0.22$, n.s.).

Discussion

In the present study, we demonstrated that the oxy-Hb concentrations in the subjects performing digit span backward were higher during the task interval than during the rest interval. Further, in the subjects performing this task, the deoxy-Hb concentration during the task interval was lower than that during the baseline interval. However, in digit span forward, the oxy-Hb concentration did not significantly differ across the task and baseline intervals, although the deoxy-Hb concentration was lower during the task interval than during the baseline interval. When using NIRS measurements, neural activation is typically expressed as an increase in oxy-Hb and a decrease in deoxy-Hb concentrations [7, 21–25]. Our results indicate that the digit span backward task requires greater PFC activation than digit span forward. The findings of the present study, obtained with the relatively new noninvasive NIRS technique, replicate those of earlier studies in which other imaging methods were used [16]. Our findings are thus consistent with NIRS being a reliable alternative to more invasive imaging methods.

Digit span backward requires transformation to reorder the input digits in a reversed sequence before generating the output; this involves the executive process heavily.

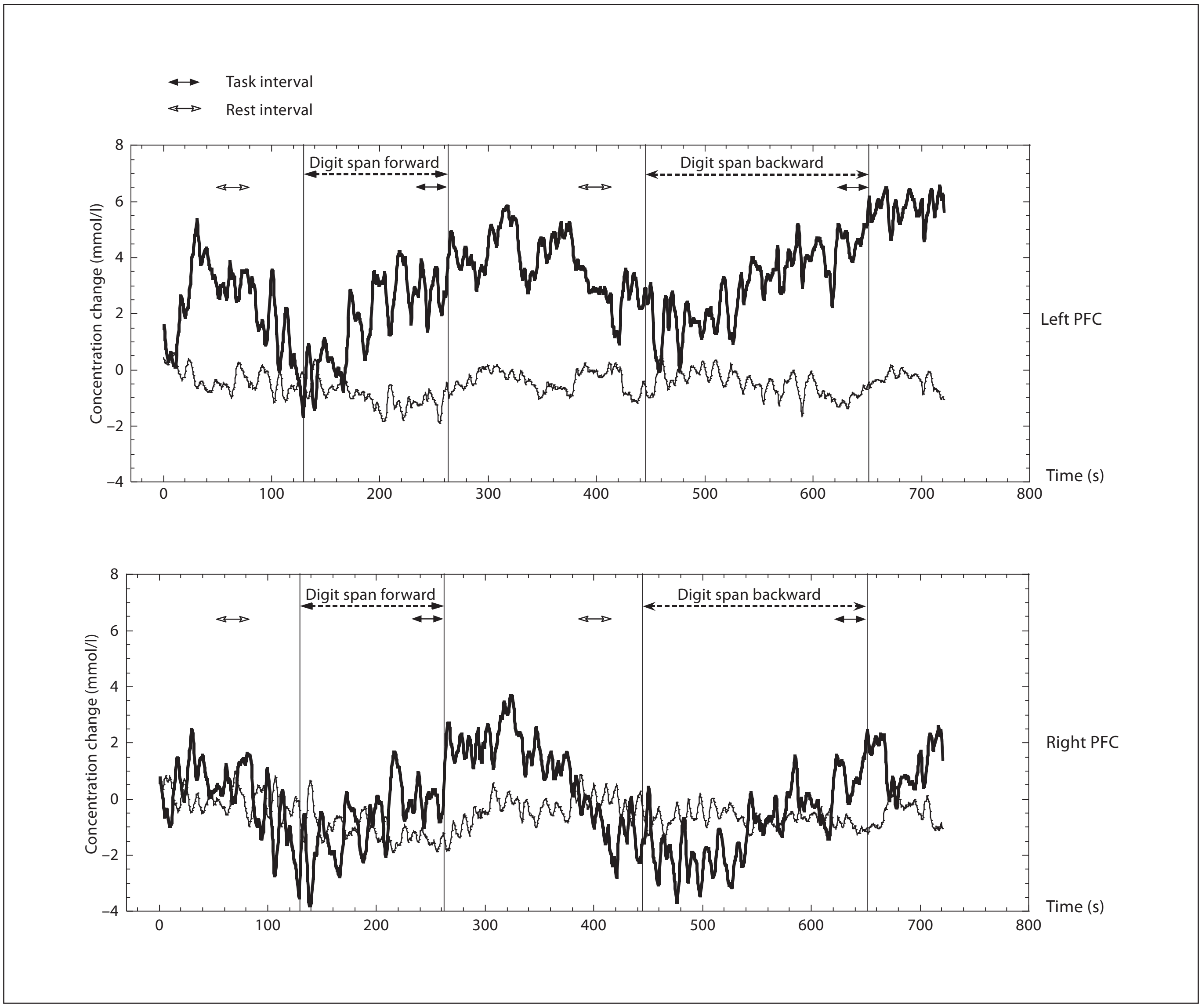

Fig. 1. A typical time course of the concentrations of oxy-Hb and deoxy-Hb during the forward and backward tasks (seen in 1 subject). Bold line = oxy-Hb; fine line = deoxy-Hb. In digit span backward, the concentration of oxy-Hb was higher during the task interval than during the rest interval.

The concept of 2 types of working memories, namely, transient and executive function, has been proposed in a previous study [26]. Transient working memory requires attention and retention of information. Executive function working memory requires the manipulation or transformation of input information in addition to attention and retention. Therefore, digit span backward is associated with executive function working memory rather than transient working memory [26]. Many studies – including lesion studies, neuroimaging studies [27], and NIRS studies [13, 28, 29] – have shown that the PFC plays a role in the executive function working memory. Thus, our results indicate that digit span backward is related to executive functioning, and consequently requires greater PFC activation as compared to the digit span forward task.

Digit span forward is considered to be related to the phonological loop proposed by Baddeley [5] as the multicomponent model of working memory. The phonological loop consists of a phonological store, which retains auditory stimulus, and an articulatory rehearsal. In previous

Table 1. Concentrations of oxy-Hb and deoxy-Hb during the digit span task (n = 22)

	Baseline interval	Task interval	Z-value
Forward			
Oxy-Hb			
Left frontal	1.75 ± 2.8	2.11 ± 2.5	–1.61
Right frontal	1.06 ± 2.5	1.30 ± 2.5	–0.80
Deoxy-Hb			
Left frontal	–0.815 ± 1.2	–1.89 ± 1.8	–3.56***
Right frontal	–1.04 ± 1.3	–2.05 ± 1.5	–3.72***
Backward			
Oxy-Hb			
Left frontal	0.659 ± 2.3	1.66 ± 2.6	–2.19*
Right frontal	–0.443 ± 3.4	0.832 ± 2.8	–1.90†
Deoxy-Hb			
Left frontal	–1.12 ± 1.4	–1.65 ± 1.8	–2.22*
Right frontal	–1.43 ± 1.9	–1.88 ± 1.7	–2.68**

Data presented as means ± SD. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, † $p < 0.10$.

lesion studies, the phonological loop has been suggested to involve the left temporoparietal region [15]. Further, neuroimaging studies have reinforced that the supramarginal gyrus (Brodmann's area, left BA 40) involves the phonological store and Broca's area (left BA 6/44) involves articulatory rehearsal [30]; however, in the present study, we could not assess these regions of the brain. Therefore, further studies should use NIRS measurements to investigate the role of these regions in performing the digit span tasks.

In digit span forward, there was no significant increase in the oxy-Hb concentrations although there was a significant decrease in the concentrations of deoxy-Hb. The significance of the deoxy-Hb concentration change in NIRS measurements has not yet been elucidated [31]. Ikezawa et al. [31] reported that healthy controls exhibited a greater reduction in the deoxy-Hb concentrations as compared to schizophrenia patients while performing the verbal fluency (category fluency), Stroop, and Sternberg tasks, whereas the change in the concentration of oxy-Hb did not significantly differ between the schizophrenia patients and healthy controls. Toichi et al. [32] demonstrated an increase in the oxy-Hb and deoxy-Hb concentrations in the continuous performance test, and a decrease in the deoxy-Hb concentration during Raven's Colored Progressive Matrices in healthy adults. They suggested that deoxy-Hb may be an index of the effort required to pay attention [32]. The inconsistency in the findings concerning changes in the deoxy-Hb concentrations could be attributed partly to the differences in the cognitive tasks that were conducted. More research is required to clarify the interpretation of changes in the deoxy-Hb concentration in NIRS measurements.

While our results suggest that the backward task requires greater activation of the PFC, the oxy-Hb concentration was lower in this task than in the digit span forward task. It is difficult to explain these conflicting results; however, one explanation is that the digit span backward task was too separated from the digit span forward task to allow direct comparison. NIRS data is easily affected by this signal drift, and therefore, the baseline interval is set just before the task interval in many studies. In the present study, the task interval for the digit span backward task was separated by approximately 6 min from that of the digit span forward task. In future studies, the task interval of the digit span backward task should be set shortly after that of the digit span forward task in order to allow direct comparison between these tasks.

In the present study, there was a significant relationship between digit span forward performance and the hemisphere (right or left) for which dominant activation was observed. No such relationship was found for the digit span backward task. Previous studies have shown a critical involvement of the right DLPFC in digit span backward performance [14]. One possible reason for this difference involves the subjects of the present study being predominantly female. Compared to males, females often display more bilateral activity during language tasks [33]. This could help explain why there was no laterality effect observed for digit span backward in the present study. Differences in the methodologies employed in our study and in other studies may also partly explain the discrepancies in the findings. For instance, a previous study [14] employed a 64-channel NIRS device, which can assess larger regions than the 2-channel system used in our study. Moreover, due to the limitations of the apparatus, the hemoglobin concentrations were expressed as a change from the baseline concentrations in arbitrary units. Future research using time-resolved spectroscopy is required to assess the absolute concentrations of hemoglobin [34].

The present study has some limitations. First, the NIRS system we used has only 2 channels, and it is therefore possible that activity within the PFC was missed. Furthermore, regions of the brain other than the PFC are also activated during the digit span task. A previous PET study [16] and an fMRI study [17] have reported that in addition to the PFC, the occipital cortex is significantly activated during the digit span task. However, these brain regions could not be examined in our study. Second, we did not counter-balance administration of the digit span forward and digit span backward tasks, which may have affected the results. Third, we did not use a detailed screening interview when recruiting subjects. Therefore, it is possible that subjects with a history of psychiatric or neurological illness were included in our sample. Fourth, we could not examine deep brain activation using NIRS. NIRS can assess the hemoglobin concentrations up to only 2 or 3 cm below the skull; therefore, activation of the deep brain regions remained unclear. Last, participants may use various strategies such as the visuospatial strategy in some of the tasks [18]. Although participants probably use visuospatial strategy, especially in digit span backward, it is not possible to control the strategy used. Future research should be conducted on the associations between brain activation and visuospatial strategy during the digit span task with NIRS.

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