Spatial working memory encoding type modulates prefrontal cortical activity

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Spatial working memory (SWM) involves both simultaneous and sequential encoding, but the differences in their neural correlates are unclear. We investigated the differences in prefrontal cortex activity related to these SWM encoding types. We also examined the patterns of brain activity influencing individual visuospatial abilities (VSA). We conducted SWM tasks with two different conditions, sequential and simultaneous encoding, and examined hemodynamic activity in 39 healthy adults using near-infrared spectroscopy. The bilateral dorsolateral prefrontal cortex was activated more strongly in the sequential condition compared with the simultaneous condition. This suggests that prefrontal cortex activity underlying SWM is modulated by the type of encoding. We also found that individuals with high VSA showed weaker activation in the right-dorsolateral prefrontal cortex compared with those with lower VSA during the simultaneous condition. This hypoactivation is thought to reflect neural efficiency in the individuals with high ability. These findings are expected to lead to a better understanding of neural substrates for SWM. *NeuroReport* **28:391–396 Copyright © 2017 Wolters Kluwer Health, Inc. All rights reserved.**

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Introduction

Spatial working memory (SWM) involves maintaining spatial information about objects actively in the mind. In humans, several brain regions and networks participate in SWM, such as the lateral prefrontal cortex, the parietal cortex, and frontoparietal connectivity [1–3]. These regions and networks are usually right-lateralized [2,4]. Previous studies have reported that SWM involves two types of encoding: simultaneous and sequential [5,6]. In the former, the spatial locations of multiple objects are encoded at the same time, whereas the latter involves encoding locations one after the other. However, the differences in their neural correlates are unclear because most research has focused on one specific type of encoding. Thus, direct comparisons of the two types of encoding could lead to better understanding of the brain mechanisms underlying SWM.

Simultaneous and sequential encoding in SWM are also known to differ with individual differences in visuospatial abilities (VSA). Performance in working memory tasks has been shown to be related to individual differences in VSA, such as those measured by matrix reasoning and block design [7,8]. Importantly, Beigneux *et al.* [9] suggested that simultaneous encoding in SWM was more strongly associated with age-related declines in VSA compared with sequential encoding. Therefore, simultaneous encoding may be more greatly affected by individual differences in VSA than sequential encoding in healthy adults.

Both VSM and SWM ability have been shown to involve specific patterns of brain activity, especially in the prefrontal cortex. Some researchers have indicated through developmental studies that improvements in SWM ability are supported by increased activity in the prefrontal cortex [10–12]. In another study, enhancements of VSA and SWM through special training produced a dramatic alteration in frontoparietal connectivity for SWM [13]. Given the possibility that VSA may affect the two types of SWM encoding differently, we examined whether the prefrontal activities underlying the two types of encodings alter depending on the level of VSA.

We aimed to investigate differences in brain activity between simultaneous and sequential encoding in SWM, and to reveal differences in the patterns of brain activity in individuals with higher or lower VSA. We primarily focused on the lateral prefrontal cortex, which is the critical region for SWM and is also sensitive to the level of VSA. Functional near-infrared spectroscopy (NIRS) was used to measure brain activities of the regions in a natural setting where the participants could perform their tasks without the mental and physical stresses resulting from a

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restricted environment like that required for functional MRI [14]. We conducted two similar SWM tasks with the same experimental factors, other than the type of encoding – for example, using consistent numbers of objects, shapes, and locations, which enabled us to clarify the influence of the encoding without any other influencing factors. It was expected that the two types of encoding would produce different patterns of NIRS prefrontal activation, whereas the influence of VSA would be highlighted during simultaneous encoding.

Participants and methods

Participants

Thirty-nine healthy adults (13 male; mean age 20.5 years; 30 right-handed) participated in this study. Nine of them were excluded from analysis because of inappropriate channel equipment ($n=3$) and excessive artifacts: specifically, contamination by high-frequency noises ($n=3$) and extraordinarily large changes in oxyhemoglobin (oxy-Hb) (± 1 mmol/mm, $n=3$). We administered the subtests of WAIS-III [15] to the participants either before or after the NIRS experiment, and the remaining 30 participants were divided into two VSA groups based on scaled scores of block design and matrix reasoning, namely higher (>10 in both tests) and lower (≤ 10 in one or both tests) (Table 1). There were no differences in sex, age, and verbal ability (scaled scores of vocabulary and similarities) between the two groups ($P>0.19$). Written informed consent was obtained from all participants before the experiment. The protocol was approved by the ethics committee at the National Center of Neurology and Psychiatry (A2011-003).

Materials and procedure

We used a blocked periodic baseline–activation–baseline design (Fig. 1a). All stimuli were presented against a white background on a 15-inch liquid crystal display screen. The stimulus presentation and data collection were controlled by SuperLab (Cedrus Corp., San Pedro, California, USA). One session consisted of four baseline and three activation blocks, and each block consisted of four trials. A trial consisted of fixation (2 s), an encoding phase (3 s), a delay (2 s), and a response phase (3 s; Fig. 1). In the baseline trials, a 4×4 matrix (12 cm $\times$ 12 cm) was presented during the waiting phase, and one cell of the matrix was filled for participants to touch during the response phase (Fig. 1b, upper panel). In the activation trials, the same matrix was presented with six filled cells during the encoding phase, and participants were asked to memorize their location. In the response phase, five of the six filled cells were presented, and participants were to touch the location of the missing cell.

The experimental sessions were administered in two conditions. In the simultaneous condition the six filled cells were presented together during the encoding phase (Fig. 1b, middle panel). In the sequential condition the six filled cells were presented one by one for 500 ms each (Fig. 1b, lower panel). Participants completed one session in each condition, and the order of the conditions was counterbalanced among participants (Fig. 1).

Table 1 Participants' characteristics by visuospatial ability group

	Lower VSA (mean ± SD)	Higher VSA (mean ± SD)	Statistics	*P*
N	22	8		
Sex (male : female)	18 : 4	6 : 2	$\chi^2(1)=0.22$	0.64
Age (years)	20.82 ± 0.80	21.40 ± 1.68	$t(28)=0.96$	0.37
Block design (SS)	9.27 ± 2.51	13.38 ± 1.92	$t(28)=4.18$	0.00
Matrix reasoning (SS)	8.00 ± 2.96	13.63 ± 1.77	$t(28)=5.03$	0.00
Vocabulary (SS)	10.18 ± 2.56	11.50 ± 2.00	$t(28)=1.31$	0.20
Similarities (SS)	10.36 ± 2.48	11.75 ± 2.71	$t(28)=1.32$	0.20

SS, scaled score; VSA, visuospatial ability.

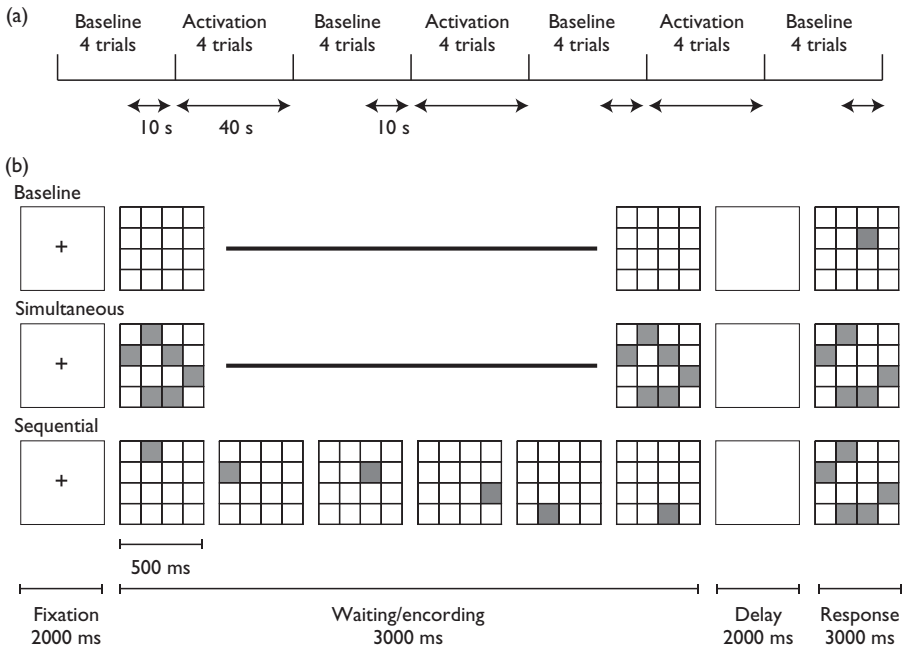
Recordings and analysis

Behavioral measures included accuracy (portion of correct responses) and response times (RTs) for correct trials in the activation blocks. They were submitted to two-way mixed-model analysis of variance (ANOVA) involving the VSA group (higher, lower) and condition (simultaneous, sequential).

NIRS data were recorded using an OEG-16 system (Spectratech Inc., Yokohama, Japan) with 16 channels at a temporal resolution of 655.359 ms. This system uses near-infrared light of two wavelengths (770 and 840 nm) to detect changes in Δoxy-Hb and deoxyhemoglobin (deoxy-Hb) concentrations. Six emitter probes and six detector probes located 3 cm from each emitter probe were arranged in a 6×2 matrix on the forehead (Fig. 2). The center of the probe matrix was placed at Fpz in accordance with the international 10–20 system [16]. The bottom left and right corners of the probe matrix were located around F7 and F8, respectively. Hence, cortical responses were obtained from 16 locations between the emitter and detector probes.

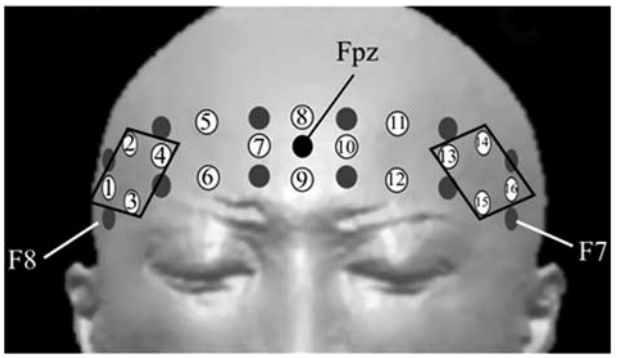
NIRS data were low-pass filtered at 0.2 Hz using fast Fourier transform to reject artifacts caused by minor physical motions of the participants. We used Δoxy-Hb data for the analysis because they are more sensitive to neural activation than Δdeoxy-Hb. We analyzed Δoxy-Hb data during the activation blocks (40 s each), which were corrected by linear fitting using the last 10 s of the baseline blocks immediately before and after them (Fig. 1a). On the basis of visual inspection, activation blocks with artifacts such as a head motion were excluded. All analyzed participants had at least two clean blocks in both conditions, which were averaged separately for the conditions. The average number of blocks accepted for the analysis was 2.93 ± 0.25 (mean ± SD) and 2.87 ± 0.35 for the simultaneous and sequential conditions, respectively. The Δoxy-Hb values were averaged over the regions of interest corresponding to right-dorsolateral prefrontal cortex (DLPFC) and left-DLPFC (right-DLPFC:

Fig. 1



Tasks. (a) A blocked periodic baseline–activation–baseline sequence and epoch for near-infrared spectroscopy analysis (lines with arrows). (b) The task procedure and conditions.

Fig. 2



Locations of near-infrared spectroscopy probes and channels. Gray circles indicate emitter and detector probes, and white circles indicate channels and channel numbers. Black rhombuses show regions of interest (right-DLPFC: 1-, 2-, 3-, and 4-channels; left-DLPFC: 13-, 14-, 15-, and 16-channels). DLPFC, dorsolateral prefrontal cortex.

1-, 2-, 3-, and 4-channels; left-DLPFC: 13-, 14-, 15-, and 16-channels) [16]. Statistical analyses used sums of Δoxy-Hb values in the activation sequence (0–40 s).

Results

Behavioral results

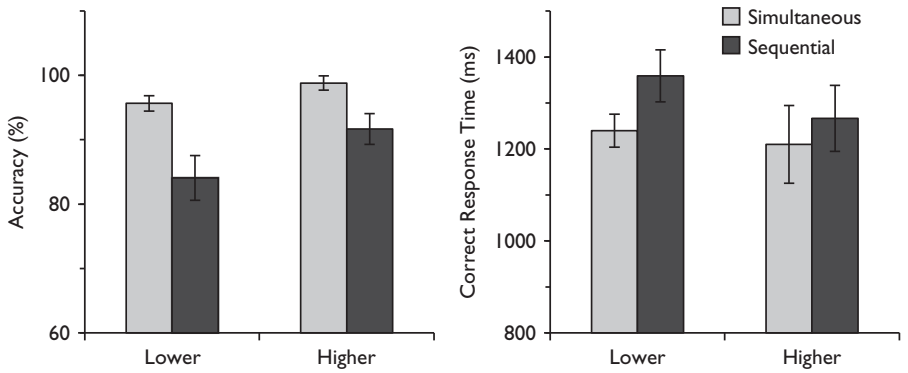
In the baseline trials, participants indicated the filled cell with extremely high accuracy (simultaneous: 0.99 ± 0.01, sequential: 0.99 ± 0.03). Figure 3 shows mean accuracy and correct RTs in activation blocks. Behavioral performance was overall lower in the sequential condition with a significantly lower accuracy (condition: $F_{1,28} = 14.10$, $P = 0.001$, $\eta^2 = 0.14$) and longer correct RT (condition: $F_{1,28} = 9.09$, $P = 0.005$, $\eta^2 = 0.04$). There was no significant effect for either VSA group for accuracy (both $P > 0.15$) or RT (all Ps > 0.60). These results indicate that maintaining sequentially presented objects was more difficult than simultaneous presentation, regardless of VSA (Fig. 3).

Near-infrared spectroscopy results

First, we analyzed data collapsed across groups to examine differences in cortical activity between the two conditions. Figure 4 shows sums of Δoxy-Hb values during the activation phase, which were greater in the sequential condition than in the simultaneous condition, regardless of hemisphere. A two-way ANOVA involving condition and hemisphere revealed a significant main effect of condition ($F_{1,29} = 4.19$, $P = 0.0498$, $\eta^2 = 0.028$). There was no significant effect of hemisphere and no interaction ($P > 0.05$) (Fig. 4).

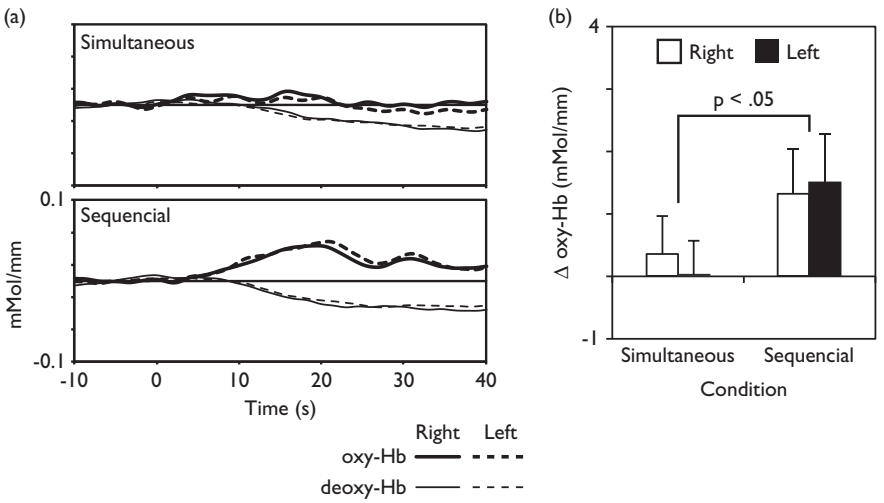
Figure 5 shows grand averaged Δoxy-Hb waveforms for the 50 s period beginning from 10 s before the task started and sums of Δoxy-Hb values during the activation block in the simultaneous condition, separately for each VSA group. ANOVA using group and hemisphere as factors indicated a main effect of group ($F_{1,28} = 4.23$, $P = 0.049$, $\eta^2 = 0.12$) and a group by hemisphere interaction ($F_{1,28} = 5.31$, $P = 0.029$, $\eta^2 = 0.01$). Simple main

Fig. 3



Accuracy and response times for lower and higher visuospatial ability groups in each condition (mean ± SD).

Fig. 4



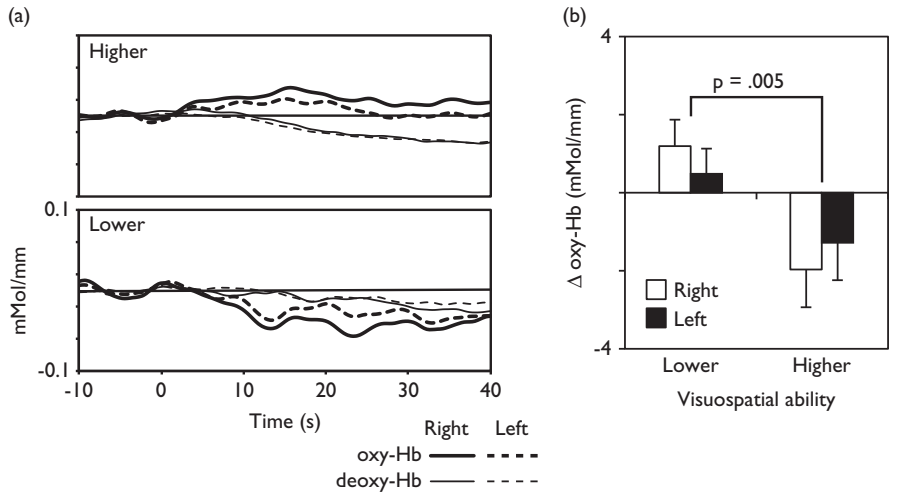
Near-infrared spectroscopy results in each condition. (a) Averaged Δoxy-Hb and Δdeoxy-Hb waveforms of the left and right DLPFCs in each condition. (b) Sums of Δoxy-Hb values of the left and right DLPFCs in each condition. deoxy-Hb, deoxyhemoglobin; DLPFC, dorsolateral prefrontal cortex; oxy-Hb, oxyhemoglobin.

effect tests indicated that Δoxy-Hb values in the right-DLPFC were larger in the lower VSA than in the higher VSA group ($F_{1,28}=6.26$, $P=0.019$, $\eta^2=0.18$), whereas there was no significant difference for the left-DLPFC ($F_{1,28}=2.14$, $P=0.154$, $\eta^2=0.071$). In addition, there was a significant difference between right and left-DLPFCs in the lower VSA group ($F_{1,21}=5.99$, $P=0.023$, $\eta^2=0.01$), which was not found in the higher VSA group ($F_{1,7}=1.22$, $P=0.306$, $\eta^2=0.018$). In the sequential condition, ANOVA revealed no significant effect of group ($F_{1,28}=0.93$, $P=0.344$, $\eta^2=0.03$), hemisphere ($F_{1,28}=1.23$, $P=0.276$, $\eta^2=0.00$), or the two-way interaction ($F_{1,28}=0.88$, $P=0.356$, $\eta^2=0.00$) (Fig. 5).

Discussion

In this study, we examined whether brain activity in prefrontal regions differs depending on the simultaneous or sequential encoding of SWM. Lower accuracy and prolonged RTs were evident in the sequential condition. Moreover, the bilateral DLPFC was activated more strongly in the sequential condition, suggesting that the prefrontal activities underlying SWM were modulated by the type of encoding. The enhanced DLPFC activity in the sequential condition may reflect greater memory load compared with the simultaneous condition, although the two conditions involved the same number of items. In the sequential condition, the participants could not encode the six items as one visual pattern but had to encode each item while holding previously presented items, and they had to repeat this encode-hold process at least six times (i.e. 'forced' path encoding). Conversely, the simultaneous condition enabled them to conduct extrafigural and efficient path encodings, and they could easily maintain the six items as a global visual image. The

Fig. 5



Near-infrared spectroscopy results in the simultaneous condition. (a) Averaged Δoxy-Hb and Δdeoxy-Hb waveforms of the left and right DLPFCs for the lower and higher VSA groups. (b) Sums of Δoxy-Hb values of the left and right DLPFCs for the lower and higher VSA groups in the activation sequence of the simultaneous condition. deoxy-Hb, deoxyhemoglobin; DLPFC, dorsolateral prefrontal cortex; oxy-Hb, oxyhemoglobin; VSA, visuospatial ability.

two experimental conditions in this study required them to adopt a different encoding strategy [6,17], which is revealed in the differences of the behavioral results. Moreover, the patterns of encoding strategy influence prefrontal activity, including the dorsolateral regions [5]. Thus, the strategies in the sequential condition are thought to increase the memory load for participants and induce greater activity in the bilateral DLPFC.

Moreover, the higher VSA group had weaker activation in the right-DLPFC than the lower VSA group during the simultaneous condition, while the two groups did not differ in task performance. This hypoactivation in the higher VSA group can be partly interpreted on the basis of the neural efficiency hypothesis: that more intelligent individuals are characterized by less brain activation than are less intelligent ones [18]. In the case of working memory, individuals with high capacity have been suggested to use minimal brain activity, being able to process information more efficiently [19,20]. Additionally, simultaneous encoding, in which we found differences in DLPFC activity between the two groups, is more influenced by the VSA of individuals compared with sequential encoding [9]. In this study, the individuals in the lower VSA group may have required greater activation of the right-DLPFC, which plays a central role in visuospatial working memory [2,4], to maintain the same level of task performance as those in the higher VSA group.

However, several developmental studies have also suggested that greater activation of the prefrontal cortex may be associated with improvements in SWM ability [10–12]. This is contrary to the present findings and the neural efficiency hypothesis. This disagreement between the previous and present findings is partly due to the maturation of brain functions. During childhood, the development of functionality in the frontal regions plays a key role in cognitive development, and enhanced activity in the relevant regions generally underlies better performance of cognitive tasks like working memory [21]. Further maturation in cognitive functions, however, often involves a reduction in the underlying neural activity [18]. Therefore, it is expected that adults with more mature functioning (i.e. higher ability) show reduced activity. Thus, hypoactivation related to a particular ability may indicate the different state of development between children and adults.

Conclusion

Simultaneous and sequential encoding in SWM appears to involve different prefrontal neural activity. This may be due to differences in memory load and the strategies used to maintain necessary information. We also found that individuals with high VSA had weaker activation in the right-DLPFC compared with those with lower VSA during the simultaneous condition. This hypoactivation may reflect neural efficiency with respect to SWM function. These findings provide a better understanding of SWM and its neural substrates.

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Conflicts of interest

There are no conflicts of interest.

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