fNIRSを用いたLetter N Back課題における文字種混在の比較検討
Comparison of two stimuli in Letter N-back tasks using functional near-infrared spectroscopy

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1. Introduction

WM is constituted by the central executive, and the phonological loop and the visuospatial sketch pad as its lower systems according to Baddeley & Hitch (1974)[1]. The central executive plays a role of proper attention direction, behavioral inhibition, task switching[2]. The visuospatial sketch pad temporarily maintains the visual and spatial information, and the phonological loop temporarily maintains the verbal information. The phonological loop contains the articulatory rehearsal system and the phonological short-term store[3]. The articulatory rehearsal is to reiteratively recall for storing verbal information which were auditorily or visually input. The phonological short-term store is where the recognized verbal information is temporarily maintained. The cognitive system in which verbal information is processed by the interaction between the phonological loop and the central executive is verbal WM (VWM). Until 1980s, WM ability has been measured by behavioral indicators (e.g., accuracy and reaction time).

A task used to measure the verbal WM abilities that include these cognitive processes is the Letter N-back tasks. As a stimulus for this task, either only upper case letters of alphabet (Upper case only version) or the mixture of both upper and lower case letters (Mixed case version) has been commonly used. However, there have been inconsistencies in hemispheric differences in activation patterns between the Upper case only and the Mixed case versions. The former is thought to involve both spatial and verbal processing, while the latter involve verbal processing. The cognitive processing on encoding and rehearsal in the VWM were considered to be different depending on the stimuli. To date, there have been no studies that have examined differences of cognitive processing depending on the stimuli for the same individuals. Thus, in the current study, we aimed to examine the differences of the cognitive processing by measuring brain activation during both two tasks in a within-subject design.

2. Method

(1) Participants & Procedure

Thirty-three healthy adults (17 males and 16 females, M_age 20.94 ± 1.74 years, range 18-24) participated in the experiment. All participants were consistent right handed on the Edinburgh Handedness Questionnaire[4]. A participant who did not properly perform the tasks was excluded from the analysis, and acquired data of thirty-two participants (16 males and 16 females, M_age 20.91 ± 1.76 years, range 18-24) were used for analysis. And a participant was excluded from the behavioral data analysis due to an incomplete measurement. To recruit participants who have no serious medical or psychological problems, all participants were screened for major psychiatric disorders using the M.I.N.I screen[5,6]. This study was approved by the institutional ethics committee of Chuo University, and the protocol was in accordance with the Declaration of Helsinki guidelines.

Participants performed both the upper-case only and mixed versions of Letter N Back task. Twenty consonant letters were used. First, in the 0-back condition, participants were instructed to respond to the target letter "X" by pressing a particular key, and another key for non-targets (Figure 1). Subsequently, the participants were instructed to identity whether the current letter was identical to the letter presented just before (1-back), two letters before (2-back), three letters before (3-back) the current one or not by pressing a key as in 0-back condition. Each condition was repeated three times in random order. There were 10 letters presented for each condition and a target ratio of 33% targets was maintained throughout[7]. The tasks displayed letters with a stimulus duration of 0.5 s, an interstimulus interval of 2.5 s and a blank between condition

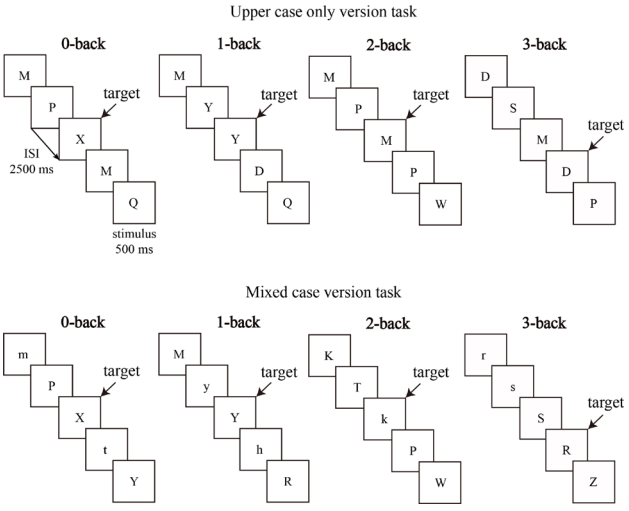

Figure 1. The experimental design of each tasks.

was 15 s. The participants answered by pressing "N" or "M" of keyboard with right index finger and middle finger whether presented letters–were target or non-target stimuli. We used the Psychophysics Toolbox[8,9,10] in a MATLAB R2017b (Mathworks, Natick, MA) environment to create and operate these tasks. After the all tasks, the participants were given 1,500-yen pre-paid card as reward.

(2) fNIRS Measurements

The introduced techniques to measure brain activation enable visualization of brain regions related to verbal working memory. The VWM processing is the activity that is commonly practiced daily. Thus, in this research, it is desirable to measure brain activation under a less-restrictive environment that is as close as possible to daily life. PET and fMRI are highly constrained and require a large amount of effort on the subjects, creating unusual environment. However, fNIRS can measure in an environment that is closer to the subjects daily life because it is less stressful on the subjects and requires to attach a probe only. Considering all these points, we decided that fNIRS is the best way to measure brain activation and used it in this research.

We used the multichannel fNIRS system ETG-4000 (Hitachi Medical Corporation, Kashiwa, Japan), making use of with two wavelengths of near-infrared light (695 nm and 830 nm). We analyzed the optical data based on the modified Beer-Lambert Law[11] as Maki et al. (1995)[12]. This method enabled us to calculate signals reflecting the oxygenated hemoglobin (oxy-Hb), and deoxygenated hemoglobin (deoxy-Hb) concentration changes, obtained in units of millimolar × millimeter (mM × mm). The sampling rate was set to 10 Hz. We placed the fNIRS probes covering the prefrontal regions and the temporal regions, as described in the previous studies (Figure 2). Specifically, we used 3 × 11 multichannel probe-holders that consisted of 17 illuminating and 16 detecting probes arranged alternately at an inter-probe distance of 3 cm. We defined the middle point of a pair of illuminating and detecting probes as a channel position and this resulted in 52 channels (CH). We defined channel position in compliance with international 10-20 system for EEG[13,14]. The lowest probes were positioned along the Fpz, T3 and T4 line (horizontal reference curve) in accordance with the international 10–20 system[13]. Probabilistic spatial registration was employed to register fNIRS data to Montreal Neurological Institute (MNI) standard brain space[15,16]. Specifically, we used a three-dimensional digitizer (POLHEMUS, Patriot) to measure the positions of the fNIRS channels in order to produce the most likely estimate of their locations on the brain for each participant, as well as the spatial variability associated with the estimation[17,18]. Accordingly, we tried to obtain the most likely estimated locations of activated channels and to represent the channels registered to Brodmann areas in reference to a microanatomical brain atlas[19]

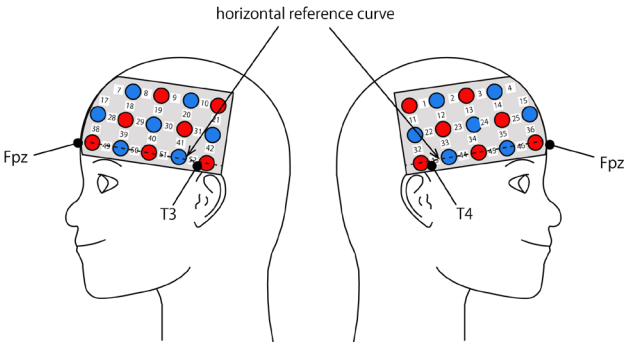

Figure 2. Spatial profiles of fNIRS channels. Left and right sides views of the probe arrangements are exhibited with fNIRS channel orientation. Detectors are indicated with blue circles, illuminators with red circles, and channels with white squares. Corresponding channel numbers are shown in black. Ch 5, 6, 16, 26, 27, 37, 47, and 48 are not visible, but located around or over the midline.

(3) fNIRS data analysis

To elucidate cognitive processing for each version of the Letter N-back task, we used Matlab 2007b (The MathWorks, Inc., Natick, MA, USA) for fNIRS data analysis. We used the oxy-Hb for analysis because the oxy-Hb signals is the most sensitive indicator of regional cerebral hemodynamic response.

We conducted general liner model (GLM) analysis on the fNIRS data. Then, the β values reflecting the cortical activation during the tasks were calculated. The β values for all channels on each task were subjected to one-sample t-tests against zero (two-tails). In addition, to elucidate the cortical activation related to encoding and rehearsal on VWM, the β values for all the channels between 0-back and the others (1-, 2-, 3-back) were subjected to paired t test (two-tails) on the activated areas before.

3. Result

The cortical activation patterns observed in the current study are described as below by integrating the statistical analysis, spatial registration of the channels, and subsequent macroanatomical labeling.

(1) Mixed case version task

For 1-back vs 0-back, the greater cerebral hemodynamic responses were elicited in two channels registered at Brodmann areas 9, the bilateral DLPFC. Furthermore, for 2-back vs 0-back, ten channels registered at Brodmann areas 2, the left S1; 10, the FPA; 21, the left MTG; 22, the left STG; 43, the left subcentral area; 45, the left pars triangularis Broca's area; 46, the left DLPFC were significantly activated (Figure 3). Additionally, for 3-back vs 0-back, nine channels registered at Brodmann areas 2, the left S1; 10, the FPA; 22, the bilateral STG; 43,

the left subcentral area; 46, the right DLPFC were significantly activated (Figure 3).

(2) Upper case only version task

For 2-back vs 0-back, fifteen channels registered at Brodmann areas 2, the bilateral S1; 21, the bilateral MTG; 22, the bilateral STG; 43, the bilateral subcentral area; 45, the bilateral pars triangularis Broca's area were significantly activated (Figure 4). For 3-back vs 0-back, nineteen channels registered at Brodmann areas 2, the bilateral S1; 6, the right Pre-SMA; 21, the bilateral MTG; 22, the bilateral STG; 40, the bilateral supramarginal gyrus part of Wernicke's area; 43, the bilateral subcentral area; 45, the bilateral pars triangularis Broca's area were significantly activated (Figure 4).

4. Discussion

In the current study, we examined the cortical activation tendencies for each version of the Letter N-back task due to the fact that the cognitive processing on encoding and rehearsal in the VWM were considered to be different depending on the stimuli. Our results supported that varying cognitive processing as encoding and rehearsal depending on the stimuli led to the different the cortical activation patterns. In addition, in support of our hypothesis, we confirmed the cortical activation patterns. Especially, the left hemisphere was activated in the Mixed case version task and bilateral hemispheres in the Upper case only version task. These findings suggested that the cognitive process might be different in each task, and that the remembering process might differ depending on the stimulus.

(1) Interpretation of Results

Our results showed the greater activation on the left Broca's area and the left temporal area during 2-back than 0-back on the Mixed case version task. Therefore, we interpreted that the activation of the left Broca's area and the temporal reflected verbal rehearsal and semantic processing[20,21].

On the other hand, on the Upper case only version task, the bilateral Broca's area and the bilateral temporal area was activated. Thus, we interpreted that the activation of the bilateral Broca's area and the bilateral temporal reflected not only verbal processing but also visuospatial rehearsal (inner scribe) and object recognition[3,22-25].

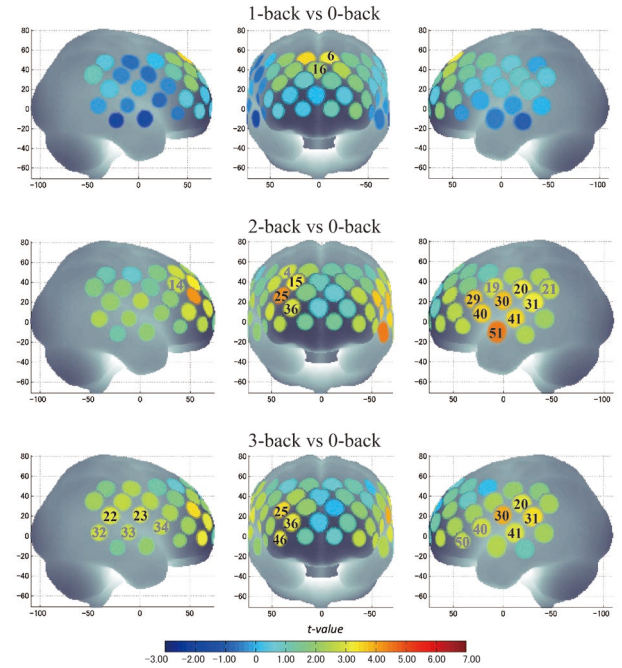

Figure 3. Activation *t*-maps of oxyHb signal increase during Mixed case version N-back task for contrast between 0-back and the other cognitive load. Significance t-values for MNI-registered channels are indicated by the black. Marginally significance t-valaues for MNI-registered channels are indicated by the gray.

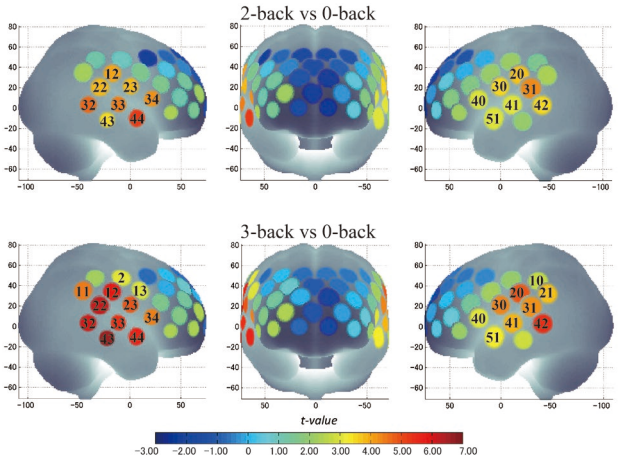

Figure 4. Activation *t*-maps of oxyHb signal increase during Upper case only version N-back task for contrast between 0-back and the other cognitive load. Significance t-values for MNI-registered channels are indicated by the black. Marginally significance t-valaues for MNI-registered channels are indicated by the gray.

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