A Sensitive Indicator of Hemodynamic Changes in The Lateral Prefrontal Cortex Using a Modified Version of “Rock, Paper, Scissors” as a Task Load

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Abstract

Previous studies have used a modified rock, paper, scissors (RPS) task to evaluate cerebral function. Normally, this game requires that participants attempt to win. The LOS task (attempting to lose on purpose) demands inhibition of stereotyped behavior, which is one of the important functions of the prefrontal cortex (PFC). It has also been shown that more activity is induced in the lateral PFC (LPFC) when playing RPS to lose. Many of these studies have therefore focused on the LPFC. Thus, it would be valuable to establish a method of evaluating cerebral function using the modified version of RPS. This study subdivided the LPFC to investigate the reason for the increased hemodynamic changes in the modified RPS task to lose on purpose. And the hemodynamic changes under various task conditions were examined. Near-infrared spectroscopy (NIRS) was used to monitor the hemodynamic changes in the LPFC during the modified RPS task. The subjects were 25 healthy adults. The task was adapted into four versions: “WIN”, “LOSE”, “ALT”, and “RND” tasks. The goal of the “ALT” task was to win and lose alternately, and that of the “RND” task was randomized. The hemodynamic changes during these tasks were compared. The oxyhemoglobin (oxy-Hb) signals were recorded using a block design. The oxy-Hb signals were preprocessed and integrated for analysis. The hemodynamic changes in the right ventrolateral prefrontal cortex (VLPFC) were found to be higher during the LOS task than during the WIN task. This increase was regarded as a logical outcome of VLPFC activation during a task involving the inhibition of stereotyped behavior. This suggested that, when using NIRS to evaluate the LPFC during the modified RPS task, focusing on the coupling of WIN and LOS tasks in the VLPFC may be valuable for evaluating cerebral function.

Keywords: Evaluation, Inhibition of stereotyped behavior, Lateral prefrontal cortex (LPFC), Near-infrared spectroscopy (NIRS), Rock paper scissors (RPS), Ventrolateral prefrontal cortex (VLPFC)

1. Introduction

The prefrontal cortex (PFC) is especially evolved in humans. The lateral prefrontal cortex (LPFC) is an important area for executive function (EF). The dorsal part of the LPFC (DLPFC) (Brodmann areas: BA9, 46) is involved in classic EF, including working memory (WM), set-shifting, sequencing, planning, inhibition, abstract reasoning [1-4], and conflict adjustments [5]. The ventral part of the LPFC (VLPFC) (BA44, 45, 47) is involved in part of the mirror system [6], the important role of cognitive reappraisal [7], social function, and participation in EF. Involvement of the right VLPFC in behavioral inhibition [8] has also been identified. In addition, both the DLPFC and VLPFC are believed to be involved in almost all cognitive processing, together with the anterior cingulate cortex [9].

Previous studies have attempted to evaluate cerebral function using a modified version of the traditional rock, paper, scissors (RPS) task [10-12]. In authentic RPS, players simultaneously present their hands. However, in a modified RPS task, the computer goes first and the player follows, trying
to react to various conditions of tasks. Neuropsychologists have used a modified RPS task to evaluate the inhibition of stereotyped behavior [13]. In a modified RPS procedure, the LOS task (attempting to lose on purpose) is more difficult than the WIN task because it demands inhibition of stereotyped behavior, which is one of the important functions of the PFC [14]. It has also been shown that more activity is induced in the LPFC when playing modified RPS to lose [12]. Many of these studies have therefore focused on the LPFC, and clinical research using this task has shown that treatment for depression increases blood volume in the same area during task loading [15]. In its non-task aspect, a modified RPS procedure is also used in rehabilitation programs in Japan to improve cognitive function [16]. Furthermore, adapting this task to comprise combinations of winning and losing also enables variation of the PFC function required. For example, in addition to simply continuous winning or losing, tasks can be formulated that mix winning and losing, thus varying LPFC activity.

It would thus be valuable to establish a method of evaluating cerebral function using this modified version of RPS. In the present study, the LPFC was subdivided into the VLPFC and DLPFC to investigate the reason for increased hemodynamic changes during the modified RPS task to lose on purpose. The tendency of hemodynamic changes under various task conditions in the LPFC was determined. Near-infrared spectroscopy (NIRS) was used to measure changes in the amount of blood in the brain. This technique is non-invasive and does not require the subject to be restrained [17-21].

2. Materials and methods

2.1 Subjects

25 healthy Japanese volunteers (14 males and 11 females, mean age 28.6 ± 4.8 years) participated in this study after giving their written, informed consent. All were right-handed, as determined using the H.N. Handedness Inventory [22]. This study was approved by the Ethics Committee of Jichi Medical University.

2.2 Device and settings

Changes in oxygenated hemoglobin (Δoxy-Hb, µM [mol/L]), deoxygenated hemoglobin (Δdeoxygen-Hb, µM), and total hemoglobin (Δtotal-Hb, µM) were measured at eight channels using three wavelengths (775, 810, and 850 nm). The NIRS (NIRO-200 oxygenation monitor; Hamamatsu Photonics K.K., Shizuoka, Japan) was used with a multifiber adapter system (C9866; Hamamatsu Photonics K.K.). The path length was presumed to be 180 mm with this device [23].

Photodetectors were placed on the corners of a square with a 3√2-cm side length, and a photo illuminator was placed on the intersection point of the diagonals. The distance between the photo illuminator and each photodetector was 3.0 cm, and the middle point corresponded to a channel. An equilateral triangle was defined to contain the LPFC, the position of which was estimated using virtual spatial registrations [24-27]. Two of three vertices were located on the lateral corner of an eye (Point A in Fig. 1) and external acoustic opening (Point B in Fig. 1). A photodetector was located on the other vertex (Point C in Fig. 1). The position of the square was arranged so that one side of the square and the base of the equilateral triangle were parallel. Four channels (ch1, ch2, ch5, and ch6 in Fig. 1, Table 1) included the LPFC, and another four channels (ch3, ch4, ch7, and ch8 in Fig. 1, Table 1) included the pre-motor and supplementary motor cortex.

![Figure 1. Positions of channels.](image)

Table 1. Identification of the Brodmann areas by virtual spatial registration. Ch2 and ch6 were set on the VLPFC. Ch1 and ch5 were set on the DLPFC.

<table>
<thead>
<tr>
<th>Ch</th>
<th>Brodmann area estimation by MRIcro *</th>
<th>Probability (%)</th>
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<tbody>
<tr>
<td>1</td>
<td>9 - DLPFC</td>
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</tr>
<tr>
<td>2</td>
<td>45 - VLPFC</td>
<td>38.2</td>
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<td>3</td>
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<td>7.4</td>
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<tr>
<td>8</td>
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* MRIcro [27]

VLPFC: ventrolateral prefrontal cortex, DLPFC: dorsolateral prefrontal cortex

2.3 Tasks

For the reasons described above, deceitful RPS (dRPS) [12], in which the computer goes first and the player follows in response to the hands displayed on a computer screen, was adopted. The dRPS is one of the modified RPS tasks. The conditions of dRPS were varied in order to establish a method of evaluating cerebral function using the modified RPS.

RPS is often used as a means of selecting who goes first in an activity. The original game requires at least two players. Each player shapes a hand into a fist for an activity. The original game requires at least two players. For example, in addition to simply continuous winning or losing, tasks can be formulated that mix winning and losing, thus varying LPFC activity.

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RPS is often used as a means of selecting who goes first in an activity. The original game requires at least two players. Each player shapes a hand into a fist for rock, a flat palm for paper, or splays the second and third fingers apart for scissors. The two players simultaneously present one of their hands in one of the shapes described above. The goal of this game is to
The relationship between the hands decides the outcome: a win, loss, or tie. Rock beats scissors; paper beats rock; and scissors beats paper (Fig. 2). If the same hand positions are presented, the result is a tie and the game is replayed until one player wins.

Each task involved a one-condition block design, with a combination of control blocks and stimulus blocks (e.g., ABABABABABA, control block = A, stimulation block = B). Each task took 4 min 24 s (24 s x 11 blocks = 264 s). Subjects had to present one of three RPS hand positions in response to a hand position displayed on the computer screen by following the instructions displayed on the screen (Fig. 3).

During the control block for all tasks, subjects were instructed to present the same hand shape as that of the computer. In the stimulation block, the subjects were asked to perform one of four tasks: a) the “WIN” task ((1) in Fig. 3), in which the subjects were required to win the RPS game on purpose (a natural inclination, stereotyped behavior); b) the “LOS” task ((2) in Fig. 3), which required the subjects to lose the RPS game on purpose (inhibition of stereotyped behavior); c) the “ALT” task ((3) in Fig. 3), which required the subjects to alternate between winning and losing the RPS game on purpose; and d) the “RND” task ((4) in Fig. 3), which required the subjects to randomly win or lose the RPS game on purpose.

The RPS presentation program was compiled using the Hot Soup Processor 3.0 software program, a text-based interpreter system for Windows (ONION software, http://www.onionsoft.net/index_e.html, Japan).

### One-condition block design

![Figure 3. Task design.](image)

Increasing brain activity is accompanied by an increase in oxygen consumption and blood flow [30]. In animal studies, oxyhemoglobin (oxy-Hb) is the most sensitive indicator of changes in cerebral blood flow. Because the direction of change in deoxyhemoglobin (deoxy-Hb) is determined not only by the degree of change in venous blood oxygenation but also by the venous volume, there is a possibility that decreasing deoxy-Hb from decreasing venous blood oxygenation is canceled or masked by increased venous volume [31]. Recent studies have used oxy-Hb as a marker of hemodynamic response in NIRS research [32,33]. Therefore, this study focused on changes in oxy-Hb alone. The oxy-Hb signals were recorded using the block design described above. Figure 4 shows an example of an original oxy-Hb signal before ICA and bandpass-filtering.

![Figure 4. Example of an original oxy-Hb signal.](image)

The hemodynamic waveforms showing changes in oxy-Hb were analyzed in eight channels using MATLAB 2007b (Mathworks Inc., Natick, MA, USA). First, artifacts attributed to body movements were removed using independent component analysis (ICA) by Fast ICA (implemented in MATLAB by Hyvärinen http://www.cis.hut.fi/projects/ica/).
The total duration of a stimulus and a control period, according to the block design paradigm was 48 s (= 0.0208 Hz). It was assumed that fluctuation faster or slower than this period was not related to task-related activation, and the signal was bandpass-filtered at 0.0208 ± 0.01 Hz. Figure 5 shows an example of the signal after ICA and filtering had been carried out. Figure 6 shows an example of the average signal of Fig. 5. This example is the signal of the first subject during the LOS task in the right VLPFC (ch.6). The average of control blocks (CTRL) is indicated from 0 to 24 s. The average of stimulant blocks (STIM) is indicated from 24 to 48 s. Figure 7 shows the average signals of all subjects during the four tasks.

The oxy-Hb signals were recorded using the block design described above. The oxy-Hb signals preprocessed using ICA and bandpass-filtering were calibrated using the z-transform for fair statistical evaluation, because the intensity of the signals differed among channels and subjects. The mean value and standard deviation for the z-transform were calculated with the data from the control blocks of each task. The z-transformed oxy-Hb signals were averaged during each stimulation block, and the averaged waveforms were integrated for each of the 25 subjects (Fig. 8). The mean values of the integrated values from the four task groups were evaluated using the paired t-test with Bonferroni correction (P < 0.05) in order to control type I error (false positive). This is because the focus was on the WIN-LOS activity as indicated in the introduction. Each group included 25 subjects. Moreover, one-way analysis of variance (ANOVA) using SPSS Statistic 20 (IBM, Tokyo, Japan) was simultaneously performed to analyze the effects of conditions on NIRS signals to determine brain activity during the four tasks.

### 3. Results

The rates of correct performance of RPS were: WIN, 99.7% ± 1.3%; LOS, 99.7% ± 0.8%; ALT, 99.2% ± 1.6%; and RND, 98.9% ± 1.8%. There were no significant differences among these variables, as determined using ANOVA. The speeds of performing tasks were 2.4 s (1 subject), 2 s (1 subject), 1.4 s (18 subjects), 1.2 s (2 subjects), and 1 s (3 subjects).

The subjective order of difficulty of the four tasks was recorded. Each participant rated the order of subjective difficulty using a point system varying from 1 (easiest) to 4 (most difficult). The subjective difficulty (order of total points) was WIN < LOS < ALT < RND (Table 2). To test for a bottom-up linear trend of task difficulty, trend analysis was performed using one-way ANOVA. The linear trend was significant (F(1, 24) = 642.2, p < 0.001, partial $\eta^2 = 0.964$).

<table>
<thead>
<tr>
<th>Task</th>
<th>WIN</th>
<th>LOS</th>
<th>ALT</th>
<th>RND</th>
</tr>
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<tbody>
<tr>
<td>Total points</td>
<td>27</td>
<td>53</td>
<td>79</td>
<td>91</td>
</tr>
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</table>

The z-transformed oxy-Hb signals were averaged during each stimulation block, and the averaged waveforms were integrated for each of the 25 subjects. The mean values of the integrations of each of the 25 subjects were lined up in order of task difficulty (Fig. 8).

There was a significant difference between WIN and LOS in one of eight channels (ch6, right VLPFC) using the paired t-test with Bonferroni correction ($t = 2.890, p \leq 0.008$). One-way ANOVA was also performed to analyze the effect of condition on NIRS signals to determine the brain activity for the four tasks. However, no significant difference was found in the amount of hemodynamic responses among the task types.
4. Discussion

Our results show that the only significant difference between the four tasks in eight channels was the increased blood volume in the right VLPCF during the LOS task compared with that during the WIN task. This suggests that when using NIRS to evaluate the LPFC during the performance of the modified RPS task, focusing on WIN-LOS coupling in the right VLPCF provides the most sensitive indicator of activation, a finding that may be valuable for future studies using RPS tasks. In previous studies of RPS tasks using NIRS, the LOS task was found to activate bilateral LPFCs to a greater extent than the WIN task [12], but more precise brain regions were not identified. The present study focused on the LPFC and used virtual registration to subdivide the LPFC into the DLPFC and the VLPCF. Markedly greater activation of the VLPCF was induced by the LOS task compared with the WIN task. The reason for the cerebral hemodynamic changes increasing during the LOS task mainly in the right VLPCF was that this region is involved in behavioral inhibition [34], which was activated during this activity. The present results explain the activation in the right LPFC region found in a previous study [12]. In that study, the activation in the left LPFC was almost the same as that in the right LPFC. With respect to the differences between this study and [12], there are two reasons why a significant difference was not detected in the left LPFC in the present study. One reason is the possibility that the criteria for significance was stricter, since the present study used the Bonferroni correction for the four tasks. The second reason may be that the total amount of data was less than that in [12]. The number of channels used here was small, and a region of interest (ROI) analysis was not used. Therefore, there is a possibility that bilateral LPFCs are activated in the LOS task if the focus is on the whole LPFC region. In the present study, 8-channel NIRS was used because many channels were not required in research that focuses on a specific brain area.

The difference between ALT and RND, both of which comprised mixtures of WIN and LOS tasks, was predictability. There was no significant difference between these two tasks, indicating that there was no predominant activation of the DLPFC, VLPCF, or the pre-motor and supplementary motor cortex during the evaluation of predictability using RPS. These tasks cannot therefore be used as an indicator for prediction. Although it has been reported that the DLPFC (BA46/45) is activated during preparation in predictable tasks such as task switching [35], there was no difference in the DLPFC in the present study. This may have been due to the tasks requiring as fast a response as possible, leaving no time for prediction to be used as a cerebral function during the ALT and RND tasks. The subjects thus dealt with the two types of task using the same type of procedure.

The LPFC has been reported to be involved in task difficulty [36], and therefore the relationship between the subjective degree of difficulty and hemodynamic changes was investigated. As described above, for task difficulty, there was a bottom-up linear trend of task difficulties, as determined using one-way ANOVA. However, using one-way ANOVA for the effect of condition on NIRS signals, no trend was detected in the amount of hemodynamic response among the task types. Therefore, cerebral activity did not appear to increase in proportion to increasing subjective difficulty. There are two possible answers to why it increased for WIN-LOS coupling but not for the other two couplings (WIN-ALT and WIN-RND). One possibility may be the attributes of variations in the degree of difficulty. Previous studies have shown a decline in behavioral performance with increasing WM load [37,38], suggesting that WM has capacity limitations. One functional magnetic resonance imaging study demonstrated maximal hemodynamic responses in the DLPFC caused by a WM task with a middle-level WM load. This characteristic was represented by an inverted U-shaped curve with the hemodynamic response varying with the load of the WM task [39]. It is possible that a similar tendency is also present in VLPCF cerebral activity, which may be most highly active for a subjectively moderate degree of difficulty. However, since the tasks used in the present study were nonparametric tasks requiring multiple cerebral functions, their relationship with the degree of difficulty cannot be definitively asserted. Further investigation focusing on this point is required. The other possibility is that the difference may stem from different activation sites. For example, the ALT task may cause activation in the DLPFC, with the VLPCF not activated, since imaging similarities between alternative tasks and set-shifting tasks have been pointed out [28]. It is therefore possible that activation may
have occurred at different sites, but device limitations meant that this could not be investigated. Multichannel measuring devices should be used in future research.

There remains the possibility that the differences described here may vary by culture. While losing in RPS may cause the inhibition of behavior or conflict among Japanese, people from other countries may show a different pattern. However, it is thought that the characteristics of games like RPS are useful for the elderly and for psychiatric patients as compared to more difficult cognitive tasks. Patterns may also differ by age group. The subjects in this study were relatively young. In addition, the subjects’ own interval was tested as the shortest interval (time) in which they could perform each of the four tasks, and the longest interval from the four tasks during the rehearsal was used in experiments, so subjects’ performance was not influenced by the task performance interval. However, since the results may be influenced by the speed of task performance, further studies should be conducted in which the task is fixed and the task interval is varied.

5. Conclusion

NIRS was used to monitor hemodynamic changes during loading with the modified RPS task under varying conditions. The reason for increased hemodynamic changes in the LPFC during the LOS task was investigated and tendencies in the modified RPS was assessed. Hemodynamic changes were significantly higher in the VLPFC for the LOS task than for the WIN task. This increase was regarded as a logical outcome of VLPFC activation during a task involving the inhibition of stereotyped behavior. This suggests that when using NIRS to evaluate the LPFC during the performance of a modified RPS task, focusing on WIN-LOS coupling in the VLPFC provides the most sensitive indicator for evaluating cerebral function. A brief discussion of the subjective degree of difficulty and cerebral activity in the LPFC region was also provided.

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References


