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博士論文

A screening method for visual attention disabilities

in cerebral palsy with periventricular leukomalacia

(脳室周囲白質軟化症患者における視覚的注意障害のスクリーニング法について)

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Original article

A screening method for visual attention disabilities in cerebral palsy with periventricular leukomalacia

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Abstract

Purpose: Patients with periventricular leukomalacia (PVL) have been reported to have a variety of complications; however, whether these involve impaired visual attention disabilities remains unclear. Therefore, this study aimed to investigate the presence or absence and degree of visual attention disabilities in patients with PVL and propose a screening test that would allow anyone to check for visual attention disabilities easily.

Methods: The study participants were 14 patients with PVL and seven controls with dyskinetic cerebral palsy. All participants performed three types of visual attention tasks: spatial attention tasks, feature-based attention tasks, and object-based attention tasks. The participants also performed counting tasks to determine how many squares of the same size and color could be counted (up to nine). Receiver operating characteristic analysis was used to calculate cutoff values, with disability as the objective variable and the value of the counting task as the explanatory variable.

Results: The results revealed that patients with PVL often had visual attention disabilities, as indicated by a significant reduction in tasks requiring divided attention. Visual attention disabilities could be detected by a score of ≤ 8 in the square counting task.

Conclusions: These findings suggest that family members and teachers of patients with PVL can easily screen for visual attention disabilities at home and school to improve mobility precautions in patients with this disability.

Key words: periventricular leukomalacia, visual attention disability, visual recognition disability

1. Introduction

The number of births in Japan decreased from 1,221,585 in 1990 to 1,037,231 in 2012. By contrast, the birth rate of low birth weight infants increased from 6.3% (76,959) to 9.6% (99,574) [1]. Therefore, despite substantial advances in perinatal medicine, the birth rate of infants with cerebral palsy remains relatively unchanged (only about 0.2%) [2]. Among low birth weight infants born prematurely (< than 33 weeks), 9.1% have periventricular leukomalacia (PVL) [3], which is a type of brain damage involving the periventricular white matter that is a common causal factor in children with cerebral palsy [4]. Depending on the progression of PVL in premature infants, motor paralysis such as spastic diplegia may occur. On the other hand, the patients with PVL have been reported to have complications such as visual recognition disabilities compared to the patients with dyskinetic cerebral palsy (DCP) since 1960s [5]; however, the exact details of this association remain unclear. A recent study using magnetic resonance imaging suggested that PVL around the trigone area of the lateral ventricle, where the optic radiation passes, leads to visual recognition disabilities [6]. It has also been reported that the degree of PVL is related to the degree of visual recognition disabilities [7]. To date, visual recognition disabilities in patients with PVL have been reported to include visual spatial cognition impairment, visual object cognitive impairment [8,9], and disability of the separation of form and ground [10]. Further, in recent years, pulvinar damage has been reported in patients with PVL [11] with possible visual attention disabilities [12]. That is, visual recognition disabilities include not only disabilities involving visual acuity and visual field defects due to damage from optic radiation, but also visual attention disabilities due to pulvinar damage. Visual attention consists of three types: spatial attention, feature-based attention, and object-based attention [13]. However, it remains unclear whether patients with PVL have visual attention disabilities. Some patients with visual recognition disabilities may ignore necessary visual information when getting around in an electric wheelchair or walking with crutches, and thus may be restricted from going out independently to avoid falls and crashing into others, and other safety concerns. Clarifying the details of visual attention

disabilities in patients with PVL could help patients, their families, and their teachers to know the necessary precautions and appropriate behaviors patients should take when going out in an electric wheelchair or walking with crutches. Therefore, the present study aimed to investigate the presence or absence and degree of visual attention disabilities in patients with PVL to expand their activities in accordance with their disability.

2. Materials and Subjects

This cross-sectional study employed an experimental design.

2.1. Subjects

2.1.1. Selection criteria

The participants in the present study were patients with PVL (PVL group) and patients with DCP (DCP group) who were receiving rehabilitation at our hospital. All the patients were diagnosed based on clinical symptoms and findings on brain MRI.

2.1.2. Exclusion criteria [14,15]

The exclusion criteria were: (1) patients with corrected visual acuity < 0.1 , (2) patients with nystagmus and remarkable visual field impairment, (3) patients who were difficult to track, (4) patients who could not answer questions verbally or by pointing a finger, (5) patients who could not fully understand the research method, and (6) patients who were considered to have a high emotional burden regarding the measurements.

2.1.3. Ethical considerations

The experimental procedures were approved by the Medical Ethics Committee of the Hyogo Prefectural Rehabilitation Central Hospital (approval No. 1805). This study adhered to the Declaration of Helsinki in regard to research involving human subjects. All participants and their substitutes received

thorough explanations about the study objectives and measurement procedures and provided written informed consent before the study began.

2.2. Measurement method

2.2.1. Visual acuity

Visual acuity in the participants was measured using Teller Acuity Cards II (TACII; Stereo Optical, Chicago, IL, USA). By using the card-converted visual acuity of 0.1, we confirmed that the participants could select the side with stripes printed on it consecutively five times using a binomial distribution (Bernoulli trial). If the participants could select the side correctly five consecutive times, then a probability of $1/32 \doteq 3\%$. Therefore, it was assumed that their vision acuity was 0.1 or higher [16].

2.2.2. Visual attention

Visual attention was measured using an eye tracker (Tobii Pro TX300; Tobii Technology, Falls Church, VA, USA). The participants sat in a comfortable chair or their own wheelchair depending on their physical ability, and the height of the table and distance from the monitor (approximately 60 cm) were adjusted to situate their eyes at the center of the screen. The participants who had difficulty concentrating took a break if necessary, and then two separate measurements were taken as needed [17].

2.2.3. Visual attention tasks

2.2.3.1. Spatial attention tasks

2.2.3.1.1. Pre-cueing tasks

With reference to Posner's study [18], three squares were displayed side-by-side on the screen. The subjects were requested to choose whether the light spot appeared in either the right, middle, or left square after fixing their eyes on the center square for a certain period. The luminance of the square frame increased just before the light spot appeared in one of the three squares as a pre-cue. Three types of trials were executed in the pre-cueing task: the light spot appeared in the same square pre-cued, in the opposite side from the pre-cued, and without a pre-cue. The subjects answered verbally or by pointing. Each trial

was repeated three times, and the task was composed of nine trials in total. The number of correct answers was counted.

2.2.3.1.2. Visual extinction tasks

Before measuring the visual extinction tasks on the eye tracker screen, the subjects performed a pretest and answered whether each index finger had been bent to evaluate their visual field and judge whether they understood the meaning of the test correctly [19]. After completing the pretest, they participated in a visual extinction task in which two marks were placed on the eye tracker screen before one or both of the marks disappeared briefly. The marks appeared at intervals of 8 cm, 19 cm, or 30 cm on the screen. The subjects were then asked to choose which marks had disappeared. This task was composed of nine trials in total, and the number of correct answers was counted.

2.2.3.2. Feature-based attention tasks (Figure 1)

The feature-based attention tasks used the form-matching tasks from WAVES (Gakken, Tokyo, Japan) [20]. The subjects were asked to choose the identical form to that shown on the left among four similar forms shown on the right. This task was composed of three trials, and the number of correct answers was counted.

2.2.3.3. Object-based attention tasks (Figure 2)

The object-based attention tasks also used the form-matching tasks from WAVES (Gakken) [20]. Similar to the feature-based attention tasks, the subjects were asked to choose the identical form to that shown on the left among four similar forms shown on the right. This task was composed of three trials, and the number of correct answers was counted.

2.2.4. Quantity comparison and counting tasks

2.2.4.1. Quantity comparison tasks

The subjects were then requested to choose the group composed of more squares with the same color and form among two groups shown on the screen. The quantity comparison tasks were composed of six

questions; the numbers of squares were 2 and 4, 3 and 4, 4 and 5, 5 and 6, 6 and 7, and 7 and 8. The number of correct answers was then counted.

2.2.4.2. Counting tasks

Before measuring the counting tasks on the eye tracker screen, the subjects confirmed that they could count up to nine squares of the same color and size by pointing with a finger. They were then asked to answer verbally how many squares they could see with the same color and size on the eye tracker screen. The numbers of squares were increased gradually from two to nine, and the maximum number the subjects miscounted twice in a row was used as the limit value.

2.2.5. Statistical analysis

Statistical analysis was conducted using R version 4.2.2 [21], with the significance level set at 5%. An unpaired t-test or Wilcoxon rank sum test was used to identify the significance differences between the PVL group and the DCP group.

2.2.5.1. Assessment criteria for visual attention disabilities

In the PVL group, receiver operating characteristic (ROC) analysis was carried out to identify the cutoff values for distinguishing PVL with visual attention disabilities. As the objective variable, those who correctly answered all questions in the visual extinction, feature-based attention, and object-based attention tasks were classified as having no disability, and those who incorrectly answered at least one question were classified as having a disability. As the explanatory variable, the limit value of the counting tasks was used.

2.2.5.2. Influence of counting tasks on the feature- and object-based attention tasks

Pearson's product-rate correlation counts were conducted to examine the correlations between counting tasks and GMFCS, and feature- and object-based attention tasks. The PVL group was divided into two groups: those who could count up to five squares (≤ 5 group) in the counting tasks and those who could

count six squares or more (≥ 6 group). An unpaired *t*-test was conducted to identify significance differences between the two groups in the feature- and object-based attention tasks.

3. Results

3.1. Subjects

The study subjects comprised 14 cases of PVL [10 males, 4 females; mean age: 14.3 ± 5.5 years, body mass index (BMI): 17.7 ± 4.0 kg/m², gestational age: 30.1 ± 3.5 weeks, birth weight: 1457.3 ± 549.7 g, Gross Motor Function Measure-66 (GMFM-66): 98.7 ± 50.3 points, Gross Motor Function Classification System (GMFCS): II 4 cases, III 3 cases, IV 3 cases, and V 4 cases, and Communication Function Classification System (CFCS): I 3 cases, II 3 cases, III 6 cases, IV 2 cases] and seven cases of DCP as controls [4 males, 3 females; mean age: 14.9 ± 2.9 years, BMI: 17.8 ± 3.6 kg/m², gestational age: 25.5 ± 9.0 weeks, birth weight: 1218.2 ± 964.4 g, GMFM-66: 59.6 ± 56.2 points, GMFCS: II 1 case, III 1 case, IV 3 cases, and V 2 cases, CFCS: I 3 cases, II 1 case, III 3 cases]. No significant differences in the subjects' background characteristics were seen between the PVL group and the DCP groups (Table 1).

3.2. Measurement results

3.2.1. Visual acuity

All subjects and controls were confirmed to have visual acuity > 0.1 .

3.2.2. Visual attention tasks

3.2.2.1. Spatial attention tasks

3.2.2.1.1 Pre-cueing tasks (Table 2)

On a scale from 0 to 9, the mean score of PVL group was 7.9 ± 2.6 points, and that of the DCP group was 8.9 ± 0.4 points. No significant differences in the pre-cueing tasks were found between the two groups ($p = 0.23$).

3.2.2.1.2. Visual extinction tasks (Table 2)

On a scale from 0 to 9 points, the mean score of the PVL group was 6.4 ± 2.4 points, and that of the DCP group was 8.9 ± 0.4 points. In the visual extinction tasks, the PVL group had significantly lower scores than did the DCP group ($p = 0.0026$).

3.2.2.2. Feature-based attention tasks (Table 2)

On a scale from 0 to 3 points, the mean score of the PVL group was 2.4 ± 0.9 points, and that of the DCP group was 3.0 ± 0.0 . In the feature-based attention tasks, the PVL group had significantly lower scores than did the DCP group ($p = 0.022$).

3.2.2.3. Object-based attention tasks (Table 2)

On a scale from 0 to 3 points, the mean score of the PVL group was 2.4 ± 0.6 points, and that of the DCP group was 3.0 ± 0.0 . In the object-based attention tasks, the PVL group had significantly lower scores than did the DCP group ($p = 0.0057$).

3.2.3. Quantity comparison and counting tasks

3.2.3.1. Quantity comparison tasks (Table 2)

On a scale from 0 to 6 points, the mean score of the PVL group was 5.7 ± 0.6 points, and that of the DCP group was 6.0 ± 0.0 points. In the quantity comparison tasks, no significant differences were found between groups ($p = 0.10$).

3.2.3.2. Counting tasks (Table 2)

In the PVL group, only five of the 14 subjects could count up to nine squares, the limit value, compared with all seven subjects in the DCP group. In the counting tasks, the mean score of the PVL group was 6.6 ± 2.6 , and that of the DCP group was 9.0 ± 0.0 . The PVL group had significantly lower scores than did the DCP group ($p = 0.0058$).

3.2.4. Data and statistical analysis

3.2.4.1. Assessment criteria for visual attention disabilities

The results of the ROC analysis showed that the cutoff value for the counting task was 8 as an assessment criterion of visual attention disabilities, the sensitivity was 0.80 (8 of 10 cases), the specificity was 1.0 (4 of 4 cases), the positive predictive value was 1.0 (8 of 8 cases), the negative predictive value was 0.67 (4 of 6 cases), and the area under the ROC was 0.90 (Figure 3).

3.2.4.2. Influence of the counting tasks on the feature- and object-based attention tasks

In the PVL group, significant correlations were found between the limit value of the counting and GMFCS ($r = -0.60$, $p = 0.024$), between the limit value of the counting and feature-based attention tasks ($r = 0.86$, $p = 0.000082$), and between the limit value of the counting and object-based attention tasks ($r = 0.81$, $p = 0.00049$) (Figure 4). The ≤ 5 group had five subjects and the ≥ 6 group had nine subjects in the PVL group. In the feature-based attention tasks, the mean score of the ≤ 5 group was 1.40 ± 0.33 points, and that of the ≥ 6 group was 2.89 ± 0.33 points. The ≤ 5 group had significantly lower scores than did the ≥ 6 group ($p = 0.018$). In the object-based attention tasks, the mean score of the ≤ 5 group was 1.80 ± 0.45 points, and that of the ≥ 6 group was 2.78 ± 0.44 points. The ≤ 5 group had significantly lower scores than did the ≥ 6 group ($p = 0.0040$) (Table 3).

4. Discussion

Our study newly revealed three major findings. First, patients with PVL often have visual attention disabilities, among which, divided attention is most likely to be damaged. Second, visual attention disabilities can be detected by a score of ≤ 8 in a nine-square counting task. Third, patients who score ≤ 5 on a counting task are neither likely to distinguish five different forms on the screen nor choose proper answers in feature- or object-based attention tasks.

Regarding the first finding, the attention types have been reported to have four components, sustained, selective, alternating, and divided, with divided attention the most likely to be diminished [22]. Unlike the pre-cueing tasks, the visual extinction tasks in this study require divided attention while gazing at both

left and right markers simultaneously. In addition, children aged 3 years who are unable to count marbles have been reported to be able to tell which is more between 4 or 7 and 6 or 9 [23]; however, how they make these judgments remains unclear [24]. In addition, counting tasks also require divided attention while capturing three squares scattered both centrally and peripherally in the visual field at the same time. The differences between the pre-cueing, visual extinction, quantity comparison, and counting tasks suggest that patients with PVL are more likely to be particularly impaired in terms of divided attention.

Regarding the second finding, the cutoff value of 8 for counting nine squares of the same color and size is useful to screen possible visual attention disabilities quickly and easily for early detection.

Regarding the third finding, five forms were displayed on the screen at the same time in the feature- and object-based attention tasks. Therefore, it was difficult to answer the task correctly without recognizing the five forms presented on the screen separately. In fact, the cases able to count fewer than five squares in the counting tasks had significantly fewer correct answers in the feature- and object-based attention tasks than did those who were able to count six or more. In other words, they seemed to have difficulty recognizing five forms at the same time, and some could not adequately compare the forms on both sides. This finding is similar to a previous report suggesting that the visual recognition disabilities in patients with PVL feature the difficulties on focusing on the appropriate part after grasping the whole [25]. Therefore, when performing feature- and object-based attention tasks, it is first preferable to assess how many forms can be counted. Subsequently, less than or equal to the number of forms that could be counted should be presented to enable the subjects to focus their attention on the differences of forms.

By the way, the intelligence of the subjects might affect the performance of the tasks in this study. As an intelligence quotient assessment, the study participants were assessed by CFCS. The results of CFCS showed no significant differences between the two groups. As the reason, the subjects in this study were required a certain intellectual level, because the criteria excluded those who had difficulty understanding the task or could not point or respond verbally. While a low intelligence quotient reduced working

memory, providing appropriate visual attention cues during working memory tasks improved scores among the older subjects [26], and lower scores on working memory tasks timing related to lower attention task scores among the young subjects [27], therefore, working memory and visual attention are likely to be positively correlated. Although visual attention may be reduced due to a decrease in intelligence quotient and working memory, the level of the effects was likely to be varied depending on how the tasks were presented in this study.

This study did have some limitations. First, the number of cases was small. Second, the negative predictive value of 0.67 suggests that 33% of the subjects in the PVL group who could count up to nine squares might still have incorrectly answered the visual attention tasks. In a future study, whether reduced divided attention could be improved by performing the tasks should be investigated. In addition, further research is needed to investigate the degree to which visual attention disabilities affect activities of daily living, such as mobility, at home, school, and in the community.

Motor paralysis in patients with cerebral palsy is easy to understand by family members and teachers, in contrast to visual recognition disabilities. Therefore, gaining a better understanding of visual recognition disabilities could be helpful for families and teachers to expand patients' activities. To achieve this, visual recognition disabilities should be properly evaluated one-by-one to elucidate their conditions, which until now, have been ambiguously referred to as visual perception disorders.

Author Contributions

ST was responsible for designing the study, conducting the study, and analyzing the data. YM was responsible for guiding the study design. Both authors contributed to the writing of the final manuscript.

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Disclosure of Conflicts Interest (COI)

The authors declare no competing interests.

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Table 1. Characteristics of the participants in the periventricular leukomalacia (PVL) and dyskinetic cerebral palsy (DCP) groups.

	PVL group (n = 14)	DCP group (n = 7)	P-value
Gender (male/female)	10/4	4/3	0.55
Age (years)	14.3 ± 5.5	14.9 ± 2.9	0.76
BMI (kg/m ²)	17.7 ± 4.0	17.8 ± 3.6	0.99
Gestational age (weeks)	30.1 ± 3.5	25.5 ± 9.0	0.43
Birth weight (g)	1457.3 ± 540.7	1218.2 ± 964.4	0.74
GMFM-66 (points)	98.7 ± 50.3	59.6 ± 56.2	0.24
GMFCS			
II	4	1	0.50
III	3	1	
IV	3	3	
V	4	2	
CFCS			
I	3	3	0.32
II	3	1	
III	6	3	
IV	2	0	

Mean ± standard deviation, unpaired t-test or Wilcoxon rank sum test.

BMI; *Body Mass Index*, GMFM-66; Gross Motor Functional Measure, GMFCS; Gross Motor Function Classification System, CFCS; Communication Function Classification System.

Table 2. Results of the visual attention tasks and quantity comparison and counting tasks.

	PVL group (n = 14)	DCP group (n = 7)	P-value
Visual attention tasks			
Spatial attention tasks			
Pre-cueing tasks (maximum points: 9)	7.9 ± 2.6	8.9 ± 0.4	0.23
Visual extinction tasks (maximum points: 9)	6.4 ± 2.4	8.9 ± 0.4	0.0026
Feature-based attention tasks (maximum points: 3)	2.4 ± 0.9	3.0 ± 0.0	0.022
Object-based attention tasks (maximum points: 3)	2.4 ± 0.6	3.0 ± 0.0	0.0057
Quantity comparison tasks (maximum points: 6)	5.7 ± 0.6	6.0 ± 0.0	0.10
Counting tasks (maximum value: 9)	6.6 ± 2.6	9.0 ± 0.0	0.0058

Mean ± standard deviation, unpaired t-test or Wilcoxon rank sum test.

PVL; periventricular leukomalacia, DCP; dyskinetic cerebral palsy.

Table 3. Results of influence of counting tasks between feature-based attention tasks and object-based attention tasks.

	the ≤ 5 group (n = 5)	the ≥ 6 group (n = 9)	P-value
Feature-based attention tasks (maximum points: 3)	1.40 ± 0.33	2.89 ± 0.33	0.018
Object-based attention tasks (maximum points: 3)	1.80 ± 0.45	2.78 ± 0.44	0.0040

Mean ± standard deviation, unpaired t-test.

The ≤ 5 group; those who could count up to five squares in the counting tasks.

The ≥ 6 group; those who could count six squares or more in the counting tasks.

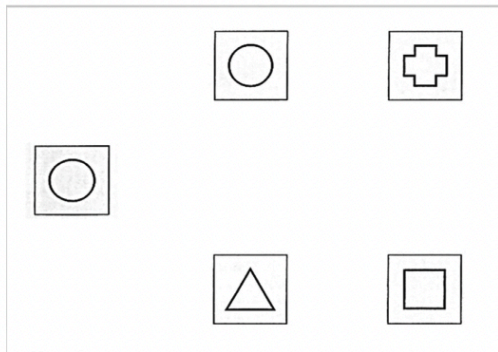


Fig. 1. Feature-based attention tasks.

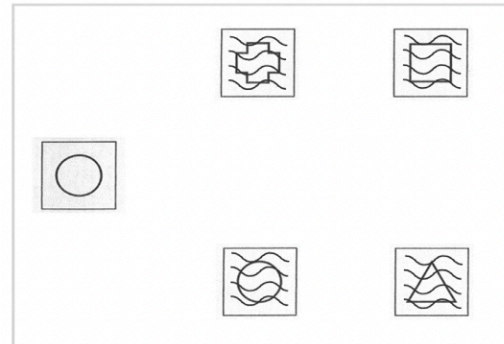


Fig. 2. Object-based attention tasks.

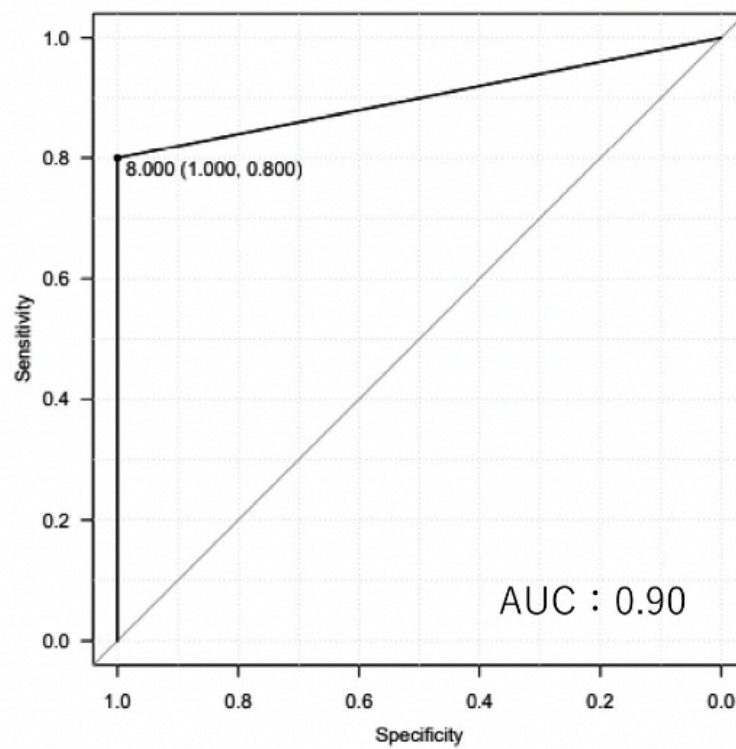


Fig. 3. Assessment criteria for visual attention disabilities. AUC; area under the curve.

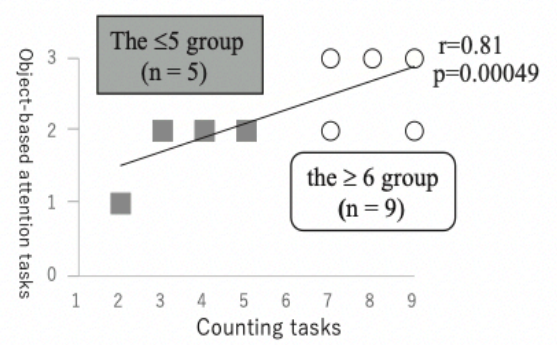
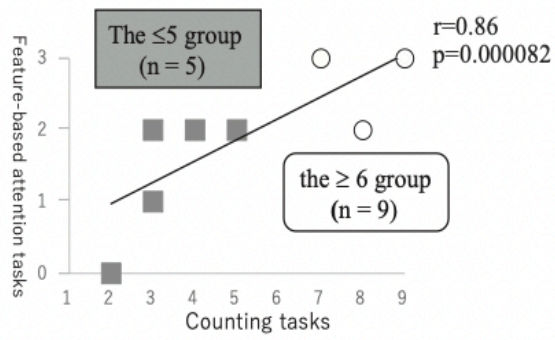


Fig. 4. Results of correlation between counting tasks and feature-based attention tasks or object-based attention tasks in PVL group.