

A Study on Neuropsychological Characteristics and the Lesion Site of Right Hemisphere Damaged Patients with Indifference Reaction

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Abstract

The relationship between indifference reaction and neuropsychological symptoms in right hemisphere damaged patients (RHD) was investigated. 78 patients with RHD were included in this study. According to the lesion site, the subjects were classified into six groups as follows: extensive cortical lesion, anterior cortical lesion, posterior cortical lesion, extensive basal ganglia lesion, limited basal ganglia lesion, and thalamic lesion groups. The Neuropsychiatric Inventory (NPI) was used to evaluate indifference reactions. The subjects showed neuropsychological symptoms that included anosognosia, attention disorder, unilateral spatial neglect, amnesia, dysexecutive syndrome, apraxia, and agnosia. Subjects with extensive cortical lesions and extensive basal ganglia lesions showed high NPI scores, whereas subjects with anterior cortical lesions and limited basal ganglia lesions showed low NPI scores. Multiple logistic regression analysis was applied to assess the factors that influenced indifference reaction, and the attention disorder was significantly correlated with indifference reaction. Hence, lesions in the right hemisphere might cause indifference reaction due to inability to perceive external stimuli caused by attention disorder.

1. Introduction

Gainotti^{1,2)} first evaluated the emotional behavior of patients with unilateral brain damage. He showed that patients with right hemisphere damage (RHD) were more likely to present indifference and euphoric reactions than those with left hemisphere damage (LHD). Babinski³⁾ first reported indifference reaction in RHD. Then, Goldstein⁴⁾ revealed that indifference reaction is an abnormal reaction associated with denial of disability in RHD. Moreover, Ohigashi⁵⁾ recently revealed that indifference reaction was not commonly included to apathy-like symptoms in RHD. Although indifference reaction has been observed in patients with RHD for a long time, its symptoms and mechanism are still unknown. After the study of Gainotti^{1,2)}, no research has assessed indifference reactions in RHD in detail. As shown by Gainotti^{1,2)}, patients with RHD predominantly presented the indifference reaction. Less serious symptoms could be classified into four groups as follows: indifference to surroundings, tendency to joke, lack of awareness to their disability, and evaluating their disability as mild state. The indifference reaction was significantly correlated with

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unilateral spatial neglect. Therefore, this study aimed to examine the lesion sites in the right hemisphere and incidence of neuropsychological symptoms in patients with and without indifference reaction. Then factors influencing indifference reaction were assessed.

2. Methods

2.1 Participants

Patients with RHD who were admitted for 5 years in the convalescent rehabilitation ward at Kurashiki Kinen Hospital were enrolled in this study. The participants were right-handed and did not have a history of previous strokes. And they had stable symptoms and did not show confusion at 3 months from the onset of their stroke. The exclusion criteria were consciousness disorder, lesion under tent, head trauma, subarachnoid hemorrhage, subdural hemorrhage and psychiatric disorders including depression. 78 patients with RHD were finally included.

2.2 Procedures

We assessed the site of the lesion, severity of indifference reaction, and neuropsychological symptoms. Four speech therapists who were in charge of the subjects evaluated the above mentioned items. The assessment sheet was distributed to all evaluators in advance, and the researcher explained the evaluation method.

2.2.1 Evaluation of lesion site

Computed tomography scan images (CT) and magnetic resonance imaging (MRI) of the head were investigated based on the diagnosis of the attending physician. According to lesion location, the patients were classified into six groups, which were as follows: extensive cortical lesion (frontal and parietal, temporal, or occipital lobe lesion), anterior cortical lesion, posterior cortical lesion, extensive basal ganglia lesion, limited basal ganglia lesion, and thalamic lesion.

2.2.2 Evaluation of indifference reaction

The items in the Neuropsychiatric Inventory (NPI) Japan version⁶⁾ for indifference reaction were used. The NPI score ranged from 0 to 12 points, and a higher score indicated more severe symptoms.

2.2.3 Evaluation of neuropsychological symptoms

Neuropsychological symptoms were evaluated based on the Bisiach scale for anosognosia, the Clinical Assessment of Attention Deficit was used for evaluating attention disorders, the Behavioral Inattention Test for unilateral spatial neglect, the Wechsler Memory Scale-Revised for amnesia, the Behavioral Assessment of the Dysexecutive Syndrome for disexecutive syndrome, the Standard Performance Test of Apraxia for apraxia, and the Visual Perception Test of Agnosia for agnosia was also used for the evaluation. Based on the cutoff scores for each evaluation method, each symptom was evaluated as present (1) and not present (0). If the test did not reach the cutoff score, a lower score than the other evaluation items was evaluated as present (1), otherwise as not present (0).

2.3 Statistical analysis

We used Excel (Bell Curve for Excel) version 2.02 for the statistical analysis. The Mann-Whitney U test was used to assess the differences in score between two samples, and a multivariate analysis of variance was used for three or more samples. The Steel-Dwass test was applied in multiple comparison correction analysis. A multiple logistic regression analysis was applied to assess factors influencing indifference reaction. The significance level in all analyses was set at <5%.

2.4 Research ethics

This study was approved by the Medical Welfare Ethics Committee of Kawasaki University of Medical Welfare (approval number: 18-050) and the Ethics Committee of Kurashiki Kinen Hospital (approval number: 30-1).

3. Results

3.1 Severity of indifference reaction according to the site of damage

There were no statistically significant differences in terms of number of subjects, age, and Mini-Mental State Examination (MMSE) scores among the groups of lesion sites (Table 1). To validate the severity of indifference reaction in patients with right hemisphere lesions, the differences in NPI scores were evaluated using the Kruskal-Wallis test. Results showed that there was a significant difference in the scores ($p < 0.01$) among the groups. Based on the multiple comparison correction analysis, the NPI score was significantly higher in the extensive cortical lesion group than in the anterior cortex lesion group ($p < 0.01$) and the restricted basal ganglia lesion group ($p = 0.01$). And the score was significantly higher in the extensive basal ganglia lesion group than in the anterior cortical lesion group ($p < 0.01$).

Table 1 Median score of age, MMSE and NPI of respective lesion sites in right hemisphere damaged patients

	ext cortex	ant cortex	pos cortex	ext ganglia	lim ganglia	thalamus	<i>p</i> value	analysis
male	13	9	5	6	8	8	0.82	*
female	4	7	4	4	6	4		
age	64 (60-67)	67.5 (60.2-75)	67 (63-73)	62 (68.7-64.5)	66.5 (63.2-70.7)	68 (60.7-72)	0.66	**
total points of MMSE	23 (18-26)	21.5 (14.5-28)	25 (15-28)	20.5 (13.2-26.7)	23.5 (18.7-26.7)	21 (18-24.2)	0.93	**
total points of NPI							<0.01	**
ext cortex VS ant cortex							<0.01	***
ext cortex VS pos cortex							0.43	***
ext cortex VS ext ganglia							0.99	***
ext cortex VS lim ganglia							0.01	***
ext cortex VS thalamus							0.79	***
ant cortex VS pos cortex							0.27	***
ant cortex VS ext ganglia	8 (4-12)	0	0 (0-8)	12 (4.2-12)	0 (0-3.7)	5 (0-8)	<0.01	***
ant cortex VS lim cortex							0.44	***
ant cortex VS thalamus							0.05	***
pos cortex VS ext ganglia							0.36	***
pos cortex VS lim ganglia							0.96	***
pos cortex VS thalamus							0.99	***
ext ganglia VS lim ganglia							0.05	***
ext ganglia VS thalamus							0.62	***
lim ganglia VS thalamus							0.49	***

Statistical analysis: *chi-squared test, **Kruskal-Wallis test, ***Steel-Dwass test

3.2 Comparison of neuropsychological symptoms in patients with and without indifference reaction

Based on the NPI score, the participants were divided into two groups according to whether they have indifference reaction or not. There was no statistically significant difference in terms of number of subjects and age between the two groups. However, the MMSE score was significantly lower in the group with indifference reaction than in the group without indifference reaction (Table 2). To validate the neuropsychological symptoms based on the presence of indifference reaction, the difference in the incidence of neuropsychological symptoms between the two groups was assessed using the Mann-Whitney U test. Results showed that the proportion of patients with anosognosia, attention disorder, unilateral spatial neglect, and amnesia was significantly higher in the group with indifference reaction than in the group without indifference reaction ($p < 0.01$; Table 3).

Table 2 Median score of age and MMSE in patients with and without indifference reactions

	with indifference reaction	without indifference reaction	<i>p</i> value	analysis
male	27	22	0.95	*
female	15	14		
age	66 (61.25-70)	65.5 (60-65.5)	0.75	**
total points of MMSE	20.5 (15.25-24.75)	24 (17.75-28)	0.02	**

Statistical analysis: *chi-squared test, **Mann-Whitney U test

Table 3 Incidence of neuropsychological symptoms in patients with and without indifference reactions

	with indifference reaction	without indifference reaction	<i>p</i> value
Anosognosia	0.64	0	<0.01
Attention	0.75	0.19	<0.01
Unilateral neglect	0.41	0.05	<0.01
Amnesia	0.52	0.14	<0.01
Disexecutive	0.26	0.15	0.08
Apraxia	0.15	0.09	0.25
Agnosia	0.1	0.02	0.05

Statistical analysis: Mann-Whitney U test

3.3 Factors affecting indifference reaction

A multiple logistic regression analysis was applied to identify the factors influencing indifference reaction. The dependent variable was the presence of indifferent reaction based on NPI scores. To assess differences in the incidence of neuropsychological symptoms in patients with or without indifference reaction, explanatory variables such as anosognosia, attention disorder, unilateral spatial neglect, and amnesia were used. Results showed the following values for each independent variable: anosognosia, 3.59; attention deficit disorder, 15.98; unilateral spatial neglect, 5.55; and amnesia, 0.63 (Figure 1).

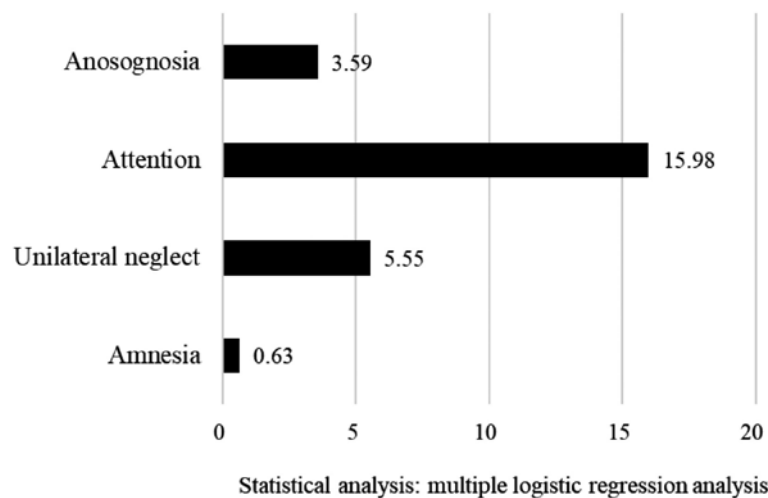


Figure 1 Factors affecting indifference reaction

4. Discussion

4.1 Relationship between indifference reaction and site of brain lesion

Based on the severity of indifference reaction according to the site of RHD, the extensive cortex and extensive basal ganglia lesion groups had severe indifference reaction, and the anterior cortex and restricted basal ganglia lesion groups had mild indifference reaction. Gainotti^{1,2)} showed a significant correlation between RHD and indifference reaction. However, no studies have assessed the relationship between severity of indifference reaction and right hemisphere lesions. As Gainotti²⁾ pointed out, the exclusion criteria for brain damage were not established, and patients with head trauma were included in the previous study. Hence, the risk of diffuse axonal or bilateral hemisphere damage could not be ruled out. The present study is significantly different from those of previous studies. That is, the etiology of subjects was limited to cerebrovascular disease in the right hemisphere, and those with head trauma, under tent lesions, subarachnoid hemorrhage, and subdural hemorrhage were excluded.

4.2 Relationship between indifference reaction and neuropsychological symptoms

Gainotti²⁾ evaluated the emotional behavior of patients with unilateral hemisphere damage. Results showed a relationship between LHD and catastrophic reaction and RHD and indifference reaction. Moreover, there was a significant correlation between catastrophic reactions and aphasia in LHD and between indifference reaction and unilateral spatial neglect in RHD. However, Gainotti²⁾ examined the relationship between catastrophic reaction and aphasia as well as indifference reaction and unilateral spatial neglect. However, the relationship between emotional behavior and other neuropsychological symptoms was not evaluated. In the current study, the proportion of patients with cognitive disorder, anosognosia, attention disorder, unilateral spatial neglect, and amnesia was significantly higher in the subjects with indifference reaction than in the subjects without indifference reaction. Hence, in RHD, indifference reaction is characterized by not only unilateral spatial neglect but also various right hemisphere symptoms. This result matches with those of studies showing that cortex and basal ganglia lesions are associated with severe indifference reaction. And the indifference reaction to the surroundings is thought to be one of right hemisphere symptoms caused by extensive damage in the cortex and basal ganglia.

4.3 Factors affecting indifference reaction

A multiple logistic regression analysis was applied to identify factors influencing indifference reaction. Results showed that visual attention disorder by unilateral spatial neglect had the strongest effect. Recent studies have shown that spatial attention network was considered the mechanism underlying unilateral spatial neglect⁷⁾, and a significant correlation was noted between spatial attention network and unilateral spatial neglect. Therefore, we tried to explain the association among indifference reaction, unilateral spatial neglect and visual attention disorder which was based on the spatial attention network. Corbetta et al.^{7,8)} showed unilateral spatial neglect caused by two spatial attention networks. The dorsal spatial attention network consciously directs attention to the target (active attention function), and the frontal lobe of the bilateral hemisphere is important for this network. By contrast, the ventral attention network inputs an unexpected stimulus from the external environment and we appropriately pay attention to the stimulus (passive attention function), and the role of the posterior region of the right hemisphere is important. Based on this information, the patients who have the bilateral frontal lobe do not intentionally pay active attention to the target. However, damage to the posterior part of the right hemisphere results in difficulties in responding passively to external stimuli, and this mechanism causes unilateral spatial neglect⁸⁾. Based on this hypothesis, RHD is associated with an inability to accurately recognize environmental stimuli which is caused by decreased passive attention function. And this disorder causes unilateral spatial neglect and various inferior hemisphere symptoms. As a result, the indifference reaction is thought to be one of these behavioral disorders. This finding was supported by the current study. That is, the anterior lesioned subjects had a mild indifference reaction. Therefore, indifference reaction was caused by broad lesions including those in the posterior cortex of the right hemisphere.

4.4 Limitations of the study

This study showed the relationship among indifference reaction, right hemisphere lesions, attention disorder and unilateral spatial neglect. Although indifference reaction was found to be associated with passive attention disorder, this study did not examine spatial attention disorder in detail. Moreover, indifference and euphoria to disability, which are the characteristics of indifference reaction, cannot be explained by perceptual impairment caused by environmental stimuli. And furthermore, this study examined only morphological lesions by CT and MRI, without consideration of brain dysfunction. Thus, further research on examination of brain dysfunction to clarify related lesions in more detail, and the feelings of individuals with indifference reaction should be conducted.

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