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An Impairment of Recognizing Emotional Facial Expressions in Parkinson's Disease

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Parkinson's disease (PD), one of the most common neurodegenerative disorders, is characterized by motor and non-motor symptoms. We evaluated the impairment in recognizing emotional facial expressions in PD patients using morphing techniques and investigated the related structures with brain perfusion on single photon emission CT (SPECT) using the three-dimensional stereotactic surface projection (3D-SSP) technique. Finally, we demonstrated that PD patients displayed a prominent degree of hypoperfusion in the occipital lobe, while also demonstrating an impairment in recognizing the facial emotions for both anger and happiness.

The ability to recognize the facial emotions for happiness has been shown to be closely associated with a decreased cerebral blood flow (CBF) in the right occipital lobe.

In PD patients, an impairment in recognizing emotional facial expressions might be partially due to an occipital cortical dysfunction. As the present study is a preliminary one, further studies are thus needed to elucidate the mechanism of such impairments in recognizing emotional facial expressions in PD patients.

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Keywords:

Introduction

Parkinson's disease (PD) is a neurodegenerative disorder that is clinically characterized by motor symptoms, such as bradykinesia, rigidity, and resting tremors, mostly due to the loss of dopaminergic neurons in the substantia nigra pars compacta. In addition, non-motor symptoms, which include sleep disorders, neuropsychiatric symptoms, autonomic disturbances, gastrointestinal symptoms and sensory symptoms, develop in either the early or late stages of PD, and are closely associated with disabilities in moderate to advanced PD patients. These symptoms are mainly related with a dysfunction of both the dopaminergic neurons outside the substantia nigra and non-dopaminergic neuron, such as noradrenergic, serotoninergic and cholinergic neurons in the central nervous or peripheral nervous system. In the pathological process underlying PD; the evolution of Lewy Body (LB) deposits, the non-dopaminergic brain stem nuclei, such as the noradrenergic locus caeruleus and the serotonergic raphe nuclei, are thought to be involved prior to nigral degeneration. Subsequently, the LB pathology progresses to the cholinergic structures in the basal forebrain, limbic structures, such as the amygdala and hippocampi, and finally to the neocortical regions including

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the frontal and temporoparietal association cortices[1,2]. All of these structures may be related to cognitive functions and emotional processing.

The prevalence of dementia is as high as 40% of all PD patients[3] and the cumulative prevalence at long-term follow-up is as high as 80% of all PD patients[4,5]. However, the time from the onset of PD to dementia varies considerably with some patients developing dementia within the first 3 to 5 years after the onset of PD, whereas others remain cognitively more or less intact for 20 to 30 years[6]. On the other hand, a substantial number of non-demented PD patients exhibit subtle cognitive impairment (CI), such as attentional-executive dysfunction, visuospatial defects and free-recall memory problems. In particularly, recent studies have reported emotional processing, such as facial expression recognition, to be impaired in PD patients[7-9]. However, it remains controversial as to whether or not PD patients indeed have an impaired recognition of emotional facial expressions, and the factors related to the pathogenesis still remain to be elucidated[10,11].

The aim of this study is to evaluate the recognition of emotional facial expressions in PD patients using morphing techniques and to also investigate the factors associated with brain perfusion on single photon emission CT (SPECT) using the three-dimensional stereotactic surface projection (3D-SSP) technique.

Materials and Methods

Subjects (Table 1); 11 PD patients (7 men and 4 women) under a definitive diagnosis based on the PD diagnostic criteria of the British Brain Bank[12] were registered. All patients evaluated in this study had been already diagnosed and regularly treated at Nagasaki University Hospital, and were taking anti-Parkinsonian medication. The clinical evaluation of motor symptoms was made using the Unified Parkinson's Disease Rating Scale (UPDRS) Part Ⅲ. Other tests and clinical evaluations were carried out two hours after the patients had received their morning medication.

All participants could understand the nature of this study and gave their informed consent. All PD patients were right-handed. Their ages ranged from 44 to 71 years old, with an average age of 59.9 years old. The duration of the disease ranged from 2 to 19 years, and the modified Hoehn & Yahr classification was stage Ⅰ: 2 patients, stage Ⅱ: 4 patients, stage Ⅲ: 3 patients, and stage Ⅳ: 2 patients. The Mini-Mental State examination (MMSE) score ranged from 26 to 30 with no cases showing any clear decline in their cognitive functions. The Beck Depression Inventory Second Edition (BDI-II) score ranged from 1 to 25, with an average score of 9.5. We used the UPDRS Ⅲ as a parameter of motor symptoms, and the scale ranged from 10 to 71, but two of PD patients were not evaluated for this measurement. All patients were examined by N-isopropyl-p[^{123}I] iodoamphetamine SPECT. No patients with severe complications (for example, cerebral infarction and so on) were included in this study.

The participants had no underlying diseases or impairments in their higher brain function, and they demonstrated no abnormal findings except for some abnormalities due to aging on MRI. In addition, any patients that were diagnosed to have diffuse Lewy body disease (DLB) were excluded from this research because of the difficulty in clinically distinguishing DLB and PD from dementia.

^{123}I-IMP SPECT was carried out in 8 PD patients. The 3D-SSP technique, which was able to accurately identify abnormalities associated with such functional diseases as Alzheimer's disease, was used to obtain data using the image-analysis software package, iSSP ver.3.5, and statistical images of the cerebral blood flow (CBF) were created as Z-score images. The stereotactic extraction estimation (SEE) method was applied to these Z-score images and the regional CBF of each region was analyzed and evaluated using the parameters indicated in Table 1. The variations in the CBF were evaluated with the mean Z-score (severity) and extent ratio. Cognitive tests regarding emotional information: Facial expression images created using an information processing technology called morphing were used to measure the patients' ability to recognize three basic facial expressions for anger, happiness and sadness. The morphing technique is a useful technique for generating facial expression images of a moderate intensity by means of engineering treatment (Figure 1). One facial expression was shown to the participant in the upper half of the PC screen and 4 images were then shown in the lower half of the screen. Each facial expression trial was presented to the participant as a multiple choice question (Figure 2). The patients were asked to select the same facial image by pointing with his/-her finger. Each trial had 96 black-and-white images, consisting of 6 male and female facial stimuli (3 males and 3 females); 3 facial expressions (anger, happiness and sadness); morphed 5-level intensity (20, 40, 60, 80 and 100%) and 6 neutral faces. There was no time limit for viewing the images.

The threshold values of the emotional intensity of the cases were analyzed. Logistic curve fitting was carried out for the relationship between the percentage of correct

Table 1. Clinical features of PD patients

	age	sex	Onset (y/o)	Duration (Year)	H-Y stage	UPDRS III	MMSE	BDI-II
1	68	M	66	2	2	17	30	6
2	55	F	48	7	3	28	29	9
3	44	M	38	6	2	10	30	1
4	46	M	36	10	3	45	30	25
5	60	M	41	19	4	71	26	14
6	70	F	68	2	1	19	29	ND
7	57	M	54	3	1	15	28	2
8	65	M	60	5	4	ND	30	21
9	57	F	49	8	2	ND	27	10
10	71	F	66	5	2	29	30	22
11	66	M	56	10	3	35	30	1
mean	60	—	54	6	2	28	30	9.5

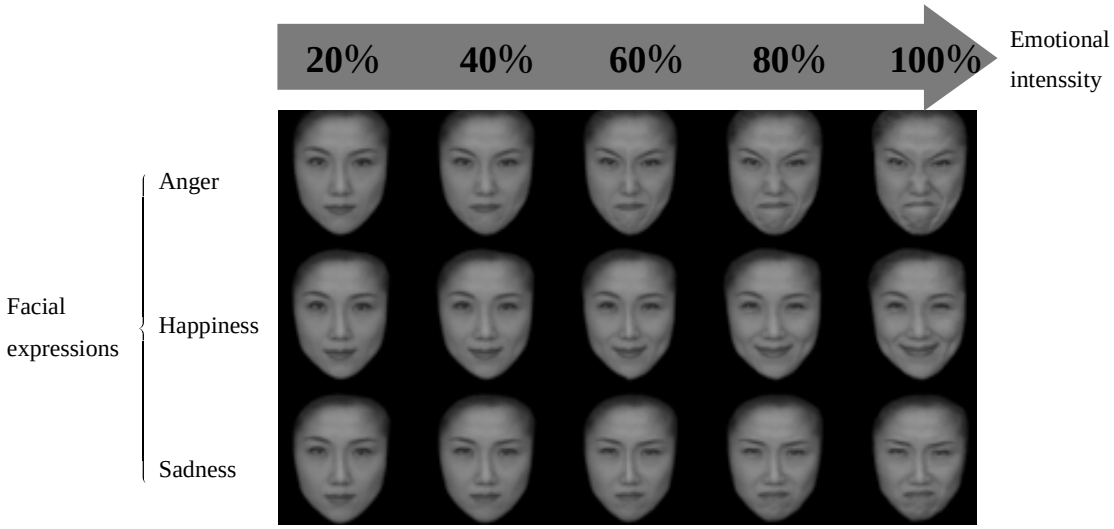

Figure 1. Emotion categorization task using morphing images

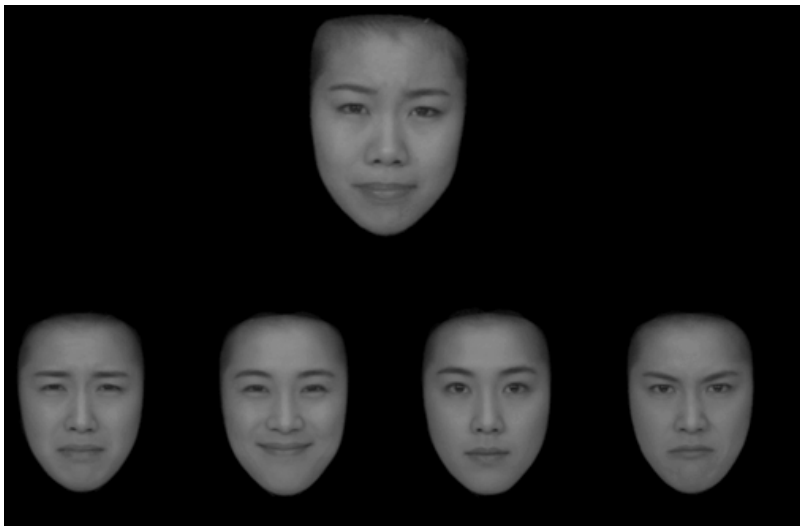

Figure 2. One emotion categorization task

answers and the emotional intensity regarding each facial expression, after which the emotional intensities with 50% correct answers were estimated (Figure 3). The correlation coefficient between the obtained threshold value and the Z-score for the cerebral blood flow of each region was calculated. Regarding comparisons with the healthy control group, Hu (Unbiased Hit Rate), which is used as an index for the percentage of correct answers, eliminating any response bias, was calculated regarding the emotional intensities of each facial expression and then the findings were compared between each group.

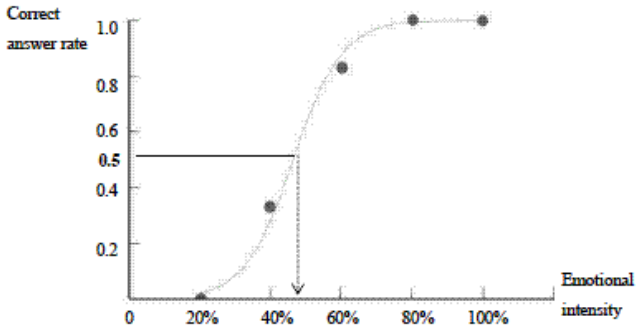

Figure 3. Estimation of the emotional intensity

Logistic curve fitting was carried out for the relationship between the percentage of correct answers and the emotional intensity regarding each facial expression, after which the emotional intensities with 50% correct answers were estimated.

Results:

A SPECT analysis on the regional CBF was performed on 8 PD patients. In the analysis of a decreased CBF for the lobar levels obtained by estimating the voxels above 1.5 for the Z-score (Table 2). A decrease in the CBF in both the mean Z-score and the extent ratio was detected in the frontal lobe for 2 patients, the parietal lobe for 5 patients, the temporal lobe for 5 patients and occipital lobe for 7 patients. The hypoperfusion of the occipital lobe was very prominent and the CBF on the right side tended to decrease more than that on the left side in all lobes.

A cognitive test to identify emotional facial expressions was performed on 11 PD patients. The emotional intensities for the 50% correct answer threshold for anger, happiness and sadness were calculated as shown in Table 3. The higher the threshold value, the greater the decline in cognitive function for facial expressions has been suggested. The mean values of the emotional intensity ranges regarding anger, happiness and sadness in the PD group were 55.58, 51.53, and 52.39, respectively. Compared to the healthy control group, according to an analysis of variance, the emotional intensity ranges of anger and happiness significantly increased in the PD group ($p<0.001$), as shown in Figure 4. Furthermore, the duration and severity of parkinsonism and depression were not correlated with the recognition of emotional facial expressions.

Table 2. A decreased CBF at the lobar level

Lobe	Frontal lobe				Parietal lobe				Temporal lobe				Occipital lobe			
Side	Left		Right		Left		Right		Left		Right		Left		Right	
Pt	Extent ratio(%)	Mean Z-score	Extent ratio(%)	Mean Z-score	Extent ratio(%)	Mean Z-score	Extent ratio(%)	Mean Z-score	Extent ratio(%)	Mean Z-score	Extent ratio(%)	Mean Z-score	Extent ratio(%)	Mean Z-score	Extent ratio(%)	Mean Z-score
1	1.4	1.7	4.5	2.0	10.7	2.0	5.7	2.1	14.2	2.0	24.7	2.1	15.1	2.2	32.7	2.6
2	9.5	1.9	20.0	1.9	6.5	2.0	12.0	1.7	1.3	1.6	6.0	1.7	0.6	1.6	6.9	1.7
3	2.5	1.8	4.4	1.8	6.0	1.9	0.3	1.7	0.0	Null	2.7	1.8	30.7	2.0	40.9	2.5
4	1.9	1.8	11.3	1.9	2.3	1.8	11.7	1.8	3.9	2.2	13.4	2.0	13.0	2.0	26.6	2.0
5	0.6	1.8	7.5	2.0	16.8	2.1	45.7	2.4	6.2	1.8	33.5	2.5	44.8	2.4	47.8	2.7
6	4.1	2.0	1.9	2.1	0.2	1.5	2.1	1.7	0.9	1.7	4.4	1.8	20.9	2.0	30.4	2.6
7	2.2	1.9	3.4	1.9	4.6	1.7	24.7	2.2	0.0	Null	17.4	2.2	52.9	2.0	28.4	2.1
8	4.6	2.0	5.0	2.0	5.7	2.1	4.9	2.1	4.4	1.7	9.5	2.1	10.1	1.9	23.1	1.9

Shaded boxes mean a significantly decreased CBF: Extent ratio > 10%, and Z-score > 1.5.

Table 3. Thresholds of the emotional intensities

Pt	Anger	Happiness	Sadness
1	66.8	60.08	59.68
2	49.52	40.08	39.44
3	63.52	60.08	40.32
4	53.36	63.36	46.24
5	48.64	71.52	53.52
6	66.64	40.56	60.08
7	28.8	42.56	39.92
8	79.44	56.64	51.2
9	55.68	60.08	84.88
10	42.56	43.28	49.84
11	56.4	28.64	51.2
Average	55.58	51.53	52.39

Table 4. Correlation between a decreased CBF at the lobar level and the thresholds for each type of emotional intensity

			Extent ratio			Mean Z-score		
			Correlation coefficient	p	n	Correlation coefficient	p	n
Frontal lobe	Lt	Anger	0.11	0.79	8	-0.28	0.51	8
		Happiness	-0.54	0.17	8	**-0.73**	**0.04**	8
		Sadness	-0.26	0.54	8	0.01	0.98	8
	Rt	Anger	-0.08	0.85	8	-0.16	0.70	8
		Happiness	0.01	0.98	8	-0.13	0.76	8
		Sadness	-0.32	0.44	8	0.62	0.10	8
Parietal lobe	Lt	Anger	-0.07	0.86	8	-0.52	0.19	8
		Happiness	0.63	0.09	8	0.36	0.38	8
		Sadness	0.20	0.63	8	-0.29	0.49	8
	Rt	Anger	-0.20	0.63	8	-0.47	0.29	7
		Happiness	0.42	0.30	8	0.40	0.38	7
		Sadness	0.09	0.83	8	0.19	0.68	7
Temporal lobe	Lt	Anger	0.20	0.64	8	0.09	0.86	6
		Happiness	0.49	0.22	8	0.60	0.21	6
		Sadness	0.59	0.12	8	0.06	0.91	6
	Rt	Anger	0.01	0.97	8	-0.11	0.79	8
		Happiness	0.62	0.10	8	0.57	0.14	8
		Sadness	0.45	0.27	8	0.32	0.44	8
Occipital lobe	Lt	Anger	-0.33	0.43	8	-0.07	0.87	8
		Happiness	0.10	0.82	8	0.62	0.10	8
		Sadness	-0.12	0.77	8	0.49	0.21	8
	Rt	Anger	0.29	0.48	8	0.51	0.20	8
		Happiness	**0.71**	**0.04**	8	0.54	0.17	8
		Sadness	0.41	0.31	8	**0.75**	**0.03**	8

Shaded boxes mean a significant correlation ($p<0.05$).

Table 5. Correlation between a decreased CBF at the gyrus level and the thresholds for each type of emotional intensity

Gyrus	Side	Anger			Happiness			Sadness		
		Correlation coefficient	P	n	Correlation coefficient	P	n	Correlation coefficient	p	n
Superior Frontal Gyrus	Lt	-0.24	0.56	8	-0.28	0.50	8	-0.68	0.06	8
	Rt	-0.16	0.71	8	-0.09	0.83	8	-0.52	0.18	8
Middle Frontal Gyrus	Lt	0.05	0.92	8	0.02	0.96	8	-0.17	0.69	8
	Rt	-0.34	0.41	8	-0.04	0.92	8	-0.52	0.19	8
Inferior Frontal Gyrus	Lt	0.16	0.70	8	**-0.73**	**0.04**	8	0.05	0.91	8
	Rt	0.29	0.48	8	0.53	0.18	8	-0.27	0.52	8
Medial Frontal Gyrus	Lt	-0.29	0.49	8	-0.63	0.10	8	-0.39	0.35	8
	Rt	-0.36	0.39	8	-0.47	0.24	8	-0.20	0.64	8
Orbital Gyrus	Lt	0.27	0.60	6	-0.39	0.45	6	0.43	0.40	6
	Rt	0.04	0.95	5	-0.24	0.70	5	0.53	0.36	5
Rectal Gyrus	Lt	-0.41	0.37	7	-0.46	0.30	7	0.14	0.76	7
	Rt	0.38	0.41	7	-0.17	0.71	7	0.16	0.74	7
Paracentral Lobule	Lt	-0.11	0.79	8	0.10	0.81	8	-0.24	0.56	8
	Rt	**0.79**	**0.02**	8	0.12	0.77	8	0.13	0.75	8
Precentral Gyrus	Lt	-0.41	0.32	8	0.05	0.91	8	-0.75	0.03	8
	Rt	-0.15	0.72	8	0.25	0.55	8	-0.23	0.59	8
Subcallosal Gyrus	Lt	-0.12	0.80	7	-0.24	0.61	7	0.30	0.51	7
	Rt	0.64	0.36	4	-0.01	0.99	4	**1.00**	**0.01**	4
Superior Parietal Lobule	Lt	-0.24	0.58	8	-0.02	0.96	8	0.16	0.70	8
	Rt	-0.35	0.39	8	0.28	0.49	8	0.07	0.87	8
Inferior Parietal Lobule	Lt	0.33	0.43	8	**0.96**	**0.01**	8	0.39	0.34	8
	Rt	-0.57	0.14	8	0.20	0.63	8	-0.03	0.94	8
Angular Gyrus	Lt	0.47	0.24	8	**0.76**	**0.03**	8	0.57	0.14	8
	Rt	-0.04	0.94	6	0.58	0.23	6	0.26	0.62	6
Postcentral Gyrus	Lt	-0.29	0.49	8	0.38	0.35	8	-0.18	0.67	8
	Rt	-0.38	0.35	8	0.31	0.45	8	0.14	0.74	8
Precuneus	Lt	-0.02	0.96	8	0.14	0.74	8	0.09	0.83	8
	Rt	-0.50	0.20	8	0.38	0.35	8	0.05	0.91	8
Supramarginal Gyrus	Lt	0.33	0.42	8	**0.98**	**0.01**	8	0.19	0.65	8
	Rt	-0.50	0.20	8	0.31	0.46	8	-0.03	0.94	8
Superior Temporal Gyrus	Lt	-0.31	0.45	8	0.39	0.34	8	0.36	0.38	8
	Rt	-0.16	0.70	8	0.46	0.2	8	0.40	0.33	8
Middle Temporal Gyrus	Lt	0.20	0.64	8	0.26	0.54	8	**0.75**	**0.03**	8
	Rt	-0.48	0.23	8	0.52	0.19	8	0.08	0.85	8
Inferior Temporal Gyrus	Lt	0.29	0.49	8	0.60	0.11	8	0.48	0.23	8
	Rt	0.04	0.92	8	**0.71**	**0.05**	8	-0.06	0.90	8
Transverse Temporal Gyrus	Lt	-0.75	0.15	5	-0.44	0.46	5	0.27	0.66	5
	Rt	0.36	0.49	6	0.79	0.06	6	0.63	0.18	6

Superior Occipital Gyrus	Lt	-0.07	0.87	7	-0.56	0.19	7	0.03	0.95	7
	Rt	-0.31	0.50	7	0.45	0.31	7	-0.27	0.56	7
Middle Occipital Gyrus	Lt	**-0.83**	**0.01**	8	-0.43	0.29	8	-0.25	0.55	8
	Rt	-0.50	0.21	8	0.37	0.36	8	-0.60	0.11	8
Inferior Occipital Gyrus	Lt	**-0.83**	**0.02**	7	-0.26	0.58	7	-0.35	0.44	7
	Rt	0.14	0.73	8	0.22	0.60	8	-0.37	0.36	8
Cuneus	Lt	-0.24	0.56	8	0.61	0.11	8	0.26	0.54	8
	Rt	0.07	0.88	8	0.49	0.22	8	0.59	0.12	8
Fusiform Gyrus	Lt	-0.28	0.51	8	0.26	0.54	8	0.27	0.52	8
	Rt	0.22	0.60	8	0.42	0.30	8	-0.37	0.37	8
Lingual Gyrus	Lt	-0.17	0.69	8	0.28	0.51	8	-0.08	0.85	8
	Rt	0.08	0.86	8	0.29	0.48	8	0.25	0.55	8
Thalamus	Lt	-0.04	0.93	8	-0.50	0.21	8	0.18	0.67	8
	Rt	0.30	0.48	8	0.35	0.40	8	0.32	0.44	8
Cingulate Gyrus	Lt	-0.49	0.22	8	-0.34	0.40	8	-0.14	0.74	8
	Rt	-0.41	0.31	8	-0.42	0.30	8	-0.55	0.15	8
Parahippocampal Gyrus	Lt	0.38	0.40	7	0.24	0.60	7	**0.81**	**0.03**	7
	Rt	0.61	0.11	8	-0.33	0.43	8	**0.72**	**0.04**	8
Anterior Cingulate	Lt	0.07	0.87	8	-0.48	0.23	8	0.08	0.85	8
	Rt	0.27	0.60	6	0.01	0.98	6	0.68	0.14	6
Posterior Cingulate	Lt	-0.34	0.41	8	0.33	0.42	8	0.12	0.78	8
	Rt	-0.11	0.80	8	0.463	0.25	8	0.46	0.26	8
Uncus	Lt	0.73	0.16	5	0.40	0.50	5	0.79	0.11	5
	Rt	-0.11	0.79	8	-0.30	0.48	8	0.33	0.43	8

Shaded boxes mean a significant correlation ($P < 0.05$).

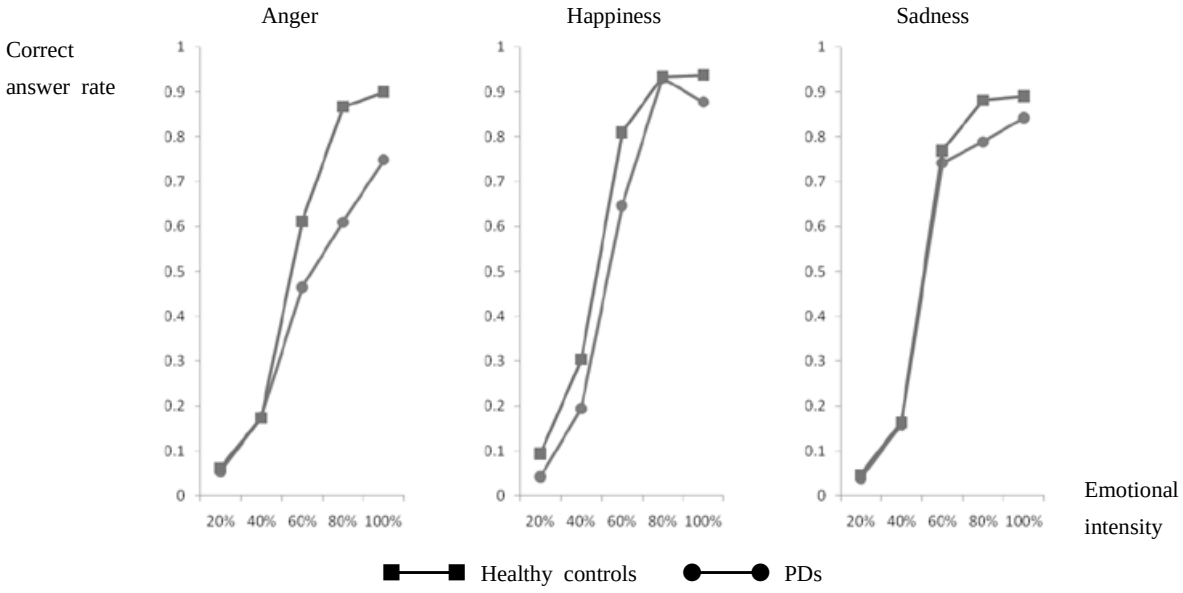

Figure 4. Comparison between the healthy controls and PDs

Compared with the healthy control group, according to an analysis of variance, the emotional intensity range of anger and happiness significantly increased in the PD group ($p<0.001$).

When analyzing the correlation between a decreased CBF on the lobar level and the thresholds for the emotional facial expressions, the extent ratio of a decreased CBF in the right occipital lobe correlated with the threshold for happiness (p=0.049). The mean Z-score for a decreased CBF in the left frontal lobe correlated with the threshold for sadness, a decline in the blood flow of the left frontal lobe correlated with the threshold for sadness (P=0.031). When analyzing the correlation with a decreased CBF (mean Z-score) in the gyrus level obtained by estimating the voxels above 1.0 for the Z-score (Table 5), the threshold for anger correlated with a decreased CBF in the right paracentral lobule (p=0.019), left middle occipital gyrus (p=0.014), and left inferior occipital gyrus (p=0.022). Moreover, the threshold for happiness correlated with a decreased CBF in the left inferior frontal gyrus (p=0.038), left inferior parietal lobule (p=0.0001), left angular gyrus (p=0.029), and right inferior temporal gyrus (p=0.047). The threshold for sadness correlated with a decreased CBF in the right subcallosal gyrus (p=0.003), left middle temporal gyrus (p=0.031), and the right parahippocampal gyrus (each p = 0.029, 0.043).

Discussion:

Previous perfusion SPECT studies have reported hypoperfusion in the occipital lobes and hyperperfusion in the basal ganglia and thalamus in PD patients [13-16]. In several studies, brain ^{123}I-IMP SPECT imaging using the 3D-SSP method was applied for PD. Mito et al. demonstrated cerebral perfusion of non-demented PD patients to decrease at the anterior cingulate cortex and the primary visual cortex, and this was significantly observed in PD patients with postural instability and gait difficulty. This finding is similar to the pattern of glucose hypometabolism demonstrated by FDG-brain PET[17, 18, 22]. However, no pathological changes or atrophy were significantly detected in the occipital lobe of PD patients[19-21]. Therefore, a blood flow reduction in the occipital lobe is thought to reflect either retinal dysfunction or corticostriatal differentiation in the dopaminergic neurons or the other neurotransmitter neurons, which may be attributed to the various impairments of visual recognition such as visuospatial perception[22].

A large number of different structures participate in the recognition of facial expressions showing emotions: among them, the occipito-temporal cortex, the amygdala, the orbito-frontal cortex, the basal ganglia, and the right parietal cortex[23]. PD patients are generally known to display an impairment in the ability to recognize emotional facial expressions[24]. This phenomenon has been reported to be primarily associated with a dysfunction of the fronto-subcortical systems caused by dopamine depletion[25]. However, some studies have suggested that the emotional cognitive impairments in PD are associated with amygdala dysfunction. Functional magnetic resonance imaging (fMRI) and volumetric MRI studies have demonstrated that the levels of dopamine may modulate the amygdala's response in PD patients, especially regarding the identification of scary faces[26] and that PD patients also show volumetric reductions in the amygdala[27].

In the present study, we demonstrated that PD patients tend to display a prominent degree of hypoperfusion in the occipital lobe by using 3D-SSP and an impairment in recognizing the facial emotion for anger and happiness using the morphing technique. The recognition of the facial emotion for happiness has been shown to be closely associated with a decreased CBF in the right occipital lobe, while the association between other regional CBFs and the recognition of emotional facial expressions remain unclear.

In PD patients, an impairment in recognizing emotional facial expressions might be partially due to an occipital cortical dysfunction. Further studies are therefore needed to elucidate the mechanism of such impairments in recognizing emotional facial expressions in PD patients because we did evaluate the correlation between anti-parkinsonian drugs and the cognitive functions in this study.

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Author Nakajima Hideki, Tsujino Akira, and all other authors declare that they have no conflicts of interest.

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