In Parkinson’s disease, the striatum dopamine amount decreases because of degeneration of the substantia nigra, and peculiar and various movement disorders occur. Recently, many reports have demonstrated that disorders of cognitive functions, such as decision making, visuospatial skills, procedural memory, and working memory, are seen from the early stages of the disease.1 These disorders were seen also in nondemented patients.2 Such cognitive disorders are similar to the condition seen in the patients with frontal lobe disorders. In fact, frontal lobe dysfunction has been reported in Parkinson’s disease.3

The frontal assessment battery (FAB) was developed by Dubois et al4 to evaluate frontal lobe function easily within a short time. FAB was reported to be closely correlated with the Wisconsin Card Sorting Test4 and to be able to distinguish patients with frontal lobe dysfunction from control patients with 90% sensitivity. In Parkinson’s disease, FAB score was reported to decrease because of frontal lobe dysfunction.5

Recently, new analysis techniques for single photon emission computed tomography (SPECT) such as 3-dimensional stereotactic surface projections (3D-SSP)6 or statistical parametric mapping (SPM)7 have been developed, and we are able to study brain functional image more easily and accurately than before.

We might take it for granted that patients with Parkinson’s disease and low FAB score show frontal hypoperfusion, but there have been few imaging studies about FAB score in Parkinson’s disease. The aim of this study was to compare brain perfusion images using 3D-SSP analysis of N-isopropyl-p-123I iodoamphetamine (123I-IMP) SPECT between Parkinson’s disease patients with high FAB score and those with low FAB score and to investigate the correlation between FAB and brain perfusion image.

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METHODS

Subjects
Forty-one patients with Parkinson's disease admitted to the Department of Neurology, Sumitomo Hospital, were studied. All of the patients fulfilled the UK Parkinson's Disease Society Brain Bank criteria for idiopathic Parkinson's disease, and dopaminergic treatment was effective for parkinsonian symptoms in all patients. Fully informed consent was obtained, and all patients agreed to participate in this study. No patients had other central nervous diseases. Patients with questionable other parkinsonism such as multiple system atrophy were not enrolled. We performed Mini-Mental State Examination (MMSE) and FAB at the same time and on-stage. Eleven patients who had dementia (diagnosed according to the Diagnostic and Statistical Manual of Mental Disorders, 4th edition) or whose MMSE score was 23 or less were excluded because dementia might influence both FAB score and brain perfusion images. We divided the remaining patients into 2 groups: a high-FAB group whose FAB score was 12 or more \((n = 21)\) and a low-FAB group whose FAB score was 11 or less \((n = 9)\). Details of patient profiles are given in Table 1. In comparison between the 2 groups, the Mann–Whitney \(U\) test was used for nonparametric data, and the unpaired \(t\) test was used for parametric data. Significance was accepted at \(P < .05\). Sex, age, Hoehn–Yahr stage, Unified Parkinson's Disease Rating Scale (UPDRS) motor score, disease duration, levodopa dosage, and MMSE score did not show significant difference. Hoehn–Yahr stage and UPDRS motor score were recorded at on-stage. The only significant difference was seen in dopamine agonist medication.

FAB
The FAB consists of 6 subtests exploring different functions related to the frontal lobes. The 6 subtests of the FAB explore the following: (1) conceptualization and abstract reasoning (similarities test); (2) mental flexibility (verbal and fluency test); (3) motor programming and executive control of action (Luria motor sequences); (4) resistance to interference (conflicting instructions); (5) inhibitory control (go/no-go test); and (6) environmental autonomy (prehension behavior). Each subtest is scored from 3 (better score) to 0, for a maximum score of 18. The FAB has shown good validity and interrater reliability.

SPECT
Measurements were carried out on-stage in a quiet dimly lit room with the subjects at rest in the supine position and with their eyes closed. SPECT imaging was performed using Starcam3000XR/T (General Electric Company, Fairfield, Conn). The resolution was 10.5 mm full-width half maximum, and the computer slice width was 6 mm. The SPECT data were obtained in a 128 \(\times 128\) format for 64 angles with 30 seconds per angle. The study was initiated 15 minutes after the intravenous injection of 167 MBq of \(^{123}\)I-IMP, and each total period of data acquisition was 32 minutes. The filtered back-projection method was used for image reconstruction after we preprocessed projection data with a Butterworth filter. A series of slices were reconstructed to be parallel to the orbitomeatal line.

3D-SSP analysis
We used the computer software iSSP3 (Nihon Medi-Physics Co Ltd, Nishinomiya City, Japan) for data analysis of \(^{123}\)I-IMP scintigraphy. In the standard stereotactic system, pixels located on the outer and medial surfaces of both hemispheres are predetermined along with 3-dimensional vectors perpendicular to the surface at each pixel. For each predetermined surface pixel, the algorithm searches for the highest pixel value in a direction inward along the vector to a 6-pixel depth (13.5 mm) into the cortex on an individual's anatomically standardized SPECT image set and assigns the maximum value to the surface pixel. Surface pixel sets extracted from each individual's SPECT data were used in the subsequent data analysis.

It is common practice in SPECT analysis to normalize a data set to a reference region. In the present work, the algorithm normalized each pixel value with stereotactic surface coordinates \((x, y, z)\) to the global perfusion as follows:

\[
\text{Normalized perfusion rate } (x, y, z) = \text{perfusion rate } (x, y, z)/\text{global perfusion rate}
\]

Because of this normalization, the method was applicable to nonquantitative reconstructed image sets.

We used the computer software iSSP3 2tZ in iSSP3 set for comparison between 2 groups. The extracted cortical activity of low-FAB patients was compared with that

<table>
<thead>
<tr>
<th>Value</th>
<th>Low-FAB Group</th>
<th>High-FAB Group</th>
<th>(P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient (n)</td>
<td>9</td>
<td>21</td>
<td>(&lt;.0001)</td>
</tr>
<tr>
<td>FAB</td>
<td>9.8 ± 2.1</td>
<td>15.3 ± 1.8</td>
<td>(&lt;.0001)</td>
</tr>
<tr>
<td>Sex (male/female)</td>
<td>5/4</td>
<td>9/12</td>
<td>NS</td>
</tr>
<tr>
<td>Age (y)</td>
<td>68.9 ± 4.2</td>
<td>66.1 ± 8.4</td>
<td>NS</td>
</tr>
<tr>
<td>Hoehn–Yahr (stage)</td>
<td>3.0 ± 0.5</td>
<td>3.2 ± 0.7</td>
<td>NS</td>
</tr>
<tr>
<td>UPDRS motor score</td>
<td>33.8 ± 5.7</td>
<td>33.9 ± 10.5</td>
<td>NS</td>
</tr>
<tr>
<td>Disease duration (y)</td>
<td>8.3 ± 4.2</td>
<td>6.8 ± 4.9</td>
<td>NS</td>
</tr>
<tr>
<td>L-dopa (mg)</td>
<td>283 ± 46</td>
<td>179 ± 123</td>
<td>NS</td>
</tr>
<tr>
<td>Dopamine agonist user (patient)</td>
<td>8</td>
<td>10</td>
<td>.0376</td>
</tr>
<tr>
<td>MMSE</td>
<td>26.4 ± 1.9</td>
<td>277 ± 1.9</td>
<td>NS</td>
</tr>
</tbody>
</table>

Note: FAB = frontal assessment battery; NS = not significant; UPDRS = Unified Parkinson's Disease Rating Scale; MMSE = Mini-Mental State Examination. Data shown depict the mean ±1 SD. Mann–Whitney \(U\) test was used for nonparametric data, and unpaired \(t\) test was used for parametric data.
of high-FAB patients using a two-sample Student t test on a pixel-by-pixel basis. Calculated $t$ values were converted to $Z$ values using a probability integral transformation. The pixels showing that brain perfusion of the low-FAB group decreased significantly compared with the high-FAB group were expressed on standardized brain magnetic resonance images. Using Bonferroni correction, we found $Z$ values greater than 4.53 to be statistically significant ($P < .05$). Figure 1 shows the regions with $Z$ values greater than 4.6, and Figure 2 shows the regions with $Z$ values greater than 2.0.

RESULTS

Figure 2 shows that the parietal and temporal area perfusions of the low-FAB group decreased compared with the high-FAB group. After Bonferroni correction, Figure 1 and Table 2 show that the left inferior parietal lobule and left supramarginal gyrus perfusion of the low-FAB group were decreased significantly compared with those of the high-FAB group. There was a significant correlation between the FAB score and the perfusion rate in the coordinates (90, 76, 17) ($r = .563, P = .0009$) (Figure 3).
Adding to the decreased perfusion analysis, we analyzed the increased perfusion regions in the low-FAB group, but there were no significantly increased regions.

**DISCUSSION**

FAB was devised to evaluate frontal lobe functions. The basis of cognitive disorders in Parkinson’s disease has been considered to be frontostriatal circuit impairment. Dennis\textsuperscript{11} reviewed the frontostriatal circuit impairment in Parkinson’s disease and suggested that the anterior cingulate cortex is related to conflict monitoring, motivation, response initiation, and apathy; the dorsolateral prefrontal cortex is related to working memory, set shifting, conditioned associate learning, response generation, set maintenance, and memory retrieval; and the orbitofrontal cortex is related to stimulus-driven behavior, disinhibition, impulse control, perseveration, decision making, and depression. The decrease of FAB score in Parkinson’s disease has been considered attributable to frontostriatal circuit impairment. However, this study found that the decrease of FAB score in Parkinson’s disease was closely related not to decreased perfusion in the frontal lobe but to that in the parietal and temporal lobes. This result produced by functional imaging seemed to be inconsistent with previous reports about cognitive functional tests in Parkinson’s disease. Significant correlations have been shown between the subtests of the FAB and frontal metabolism using 2-deoxy-2-[\textsuperscript{18}F]fluoro-D-glucose positron emission tomography in patients with various frontal lobe damage.\textsuperscript{12}

However, Maruyama et al\textsuperscript{13} reported similar results by SPM analysis of \textsuperscript{99m}Tc-ethyl cysteinate dimer (\textsuperscript{99m}Tc-ECD) SPECT. They demonstrated that brain perfusion not in the frontal lobe but in the supplementary motor area, parietal lobe, and left thalamus was correlated with FAB score in Parkinson’s disease patients without dementia. Rothlind et al\textsuperscript{14} reported a decreased score on the frontal–subcortical assessment battery (FSAB), which is very similar to FAB, even after correcting by MMSE score, in Alzheimer’s disease. They suggested the possibility that language and memory impairment in Alzheimer’s disease had some influence on FSAB.\textsuperscript{14} Recently, some reports described that the performances considered to reflect the frontal functions, such as working memory, script generation, or Wisconsin Card Sorting Test, may also have close relations with parietal lobe functions.\textsuperscript{15-17}

We think that previous studies including that of Sarazin et al\textsuperscript{12} do not conflict with our study. Frontal hypofunction exists in Parkinson’s disease, and the performances that have been considered to represent frontal lobe functions will have close relations with frontal hypoperfusion and hypometabolism. However, we propose that performance will deteriorate if hypofunction in some part of the parietal lobe is added. In Parkinson’s disease without dementia, not only frontostriatal circuit impairment but also parietal lobe impairment, especially left inferior parietal lobule and left supramarginal gyrus impairment, may cause decreased FAB score.

In conclusion, patients with Parkinson’s disease may have frontal lobe dysfunction, but their decreased FAB score may be caused not by progressed frontal lobe dysfunction but by parietal lobe dysfunction added to the preexisting frontal lobe impairment.

**References**


