The effect of age and disease duration on cerebral glucose metabolism in patients with Parkinson's disease

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The effect of age and disease duration on cerebral glucose metabolism in patients with Parkinson's disease

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Hyun Sook Kim

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ABSTRACT

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Background: Although the core pathology of Parkinson's disease (PD) is the uniform dopaminergic cell loss in the substantia nigra, the clinical features are markedly diverse. Neuronal degenerations associated with PD itself and in aging may affect the evolution of PD in additive or augmentative manner. Those degenerations also have been focused to explain the clinical diversity. However, no systematic study has been reported on the clinical deficits and topography of dysfunctional brain areas correlating with the age of patients and duration of disease, respectively. **Methods**: The present study included 128 non-demented PD patients. The severity of parkinsonian motor deficit was measured using unified Parkinson's disease rating scale (UPDRS) motor scores. All underwent brain magnetic resonance imaging and [^{18}F]-fluorodeoxy glucose positron emission tomography studies. Multiple linear regression analysis was used to find parkinsonian motor deficits of which severity correlate with the age of patients and severity correlate with the disease duration. A multiple regression model was used to find brain areas in which cerebral glucose metabolism (CMRglu) correlates with age of patients and disease duration. **Results:** The mean (SD) age of patients was 64.6 (8.1) years and the mean

of disease duration was 49.3 (49.7) months. The mean of total UPDRS motor score was 28 (13.6). Mean UPDRS motor score of the severity of tremor was 3.6 (3.3), rigidity was 5.3 (3.7), bradykinesia was 9.5 (4.5) and axial symptoms was 4.3 (3.2). The age of patients correlated positively with total UPDRS motor scores. It also correlated with the severity of bradykinesia and axial motor deficits, but not with that of tremor and rigidity. The disease duration correlated with the total UPDRS and all four UPDRS subscores representing tremor, rigidity, bradykinesia, and axial mtor deficit. The age of patients correlated inversely with the regional glucose metabolism of the prefrontal, orbitofrontal, superior temporal, anterior and posterior cingulate cortices, parahippocampal gyrus, caudate and thalamus. In contrast, disease duration correlated inversely with the metabolism of occipital cortex. **Conclusions**: In PD, age and disease duration have independent, additive effects on the deterioration of cortical metabolism, which leads to various clinical disabilities in PD patients. Moreover, age-related widespread, particularly frontal, dysfunction may accelerate deterioration of bradykinesia and axial motor deficits.

Key Words: Parkinson's disease, aging, duration of disease, positron emission tomography

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I. INTRODUCTION

The core pathology of Parkinson's disease (PD) is dopaminergic cell loss in the substantia nigra; however, PD patients show marked diversity in predominant symptoms, amount of response to treatment, rate of progression and degree of functional disability. In particular, old PD patients with longer disease duration are frequently disabled due to severe levodopa-resistant neurological deficits, including gait disturbances, postural instability, dysphagia, dysarthria and cognitive decline.[1-3] Age and disease duration, as time-related factors, have been focused to explain the clinical diversity and those factors are closely related with the disability of PD. [4,5]

Neuronal degenerations associated with PD itself and in aging may differentially affect many extranigral structures, as well as nigrostriatal dopaminergic neurons.[6,7] A study examining PD patients at off-medication

demonstrated independent additive effect of age and disease duration on the deterioration of bradykinesia.[8] More recent study reported an interaction between disease duration and age of patients on bradykinesia, reduced facial expression, speech disturbance and axial impairment. Among them, most significant interaction was found for axial motor impairment including speech and gait disturbances, and postural instability.[9] However, there is no functional imaging study on the differential effect of aging and disease duration on the brain function and clinical deficit.

[^{18}F]fluoro-2-deoxy-D-glucose (FDG)/ position emission tomography (PET) studies have been used to identify the dysfunctional brain areas. Decreased cerebral glucose metabolism rates (CMRglu) reflect reduced synaptic activities caused by reduced dendritic branching, dendritic spines or afferent axons, in addition to neuronal loss in a certain brain area.[10] In 40 normal individuals with age ranged from 18 to 78, FDG PET study demonstrates that CMRglu decline in all brain areas in age-dependent manner. The ratio of superior frontal to superior parietal CMRglu declines with age and this indicates selective vulnerability of the frontal cortex to aging.[11] In patients with PD, previous PET and SPECT studies have demonstrated global cortical hypometabolism or decreased glucose metabolism in the frontal, inferior parietal, and occipital areas.[12-14]

To find the differential effect of ageing and disease duration on PD, we

studied brain areas in which CMRglu correlates with the age and disease duration, respectively.

II. MATERIALS AND METHODS

1. Included subjects

From July 2004 to November 2007, we enrolled 186 patients fulfilling UK PD brain bank (PDBB) criteria.[15] All patients underwent axial T1-weighted magnetic resonance imaging (MRI) studies and Korean version of Mini Mental Status Examination score (K-MMSE). Among them, we excluded 58 patients with K-MMSE score lower than 24, onset age younger than 45, or old stroke lesions on T2-weighted brain MRI studies. All evaluations were performed before the administration of antiparkinsonian drugs. In the 55 patients who already had been on antiparkinsonian treatment, the medications were withheld for longer than 24 hours before the evaluation.

2. Clinical evaluation of the patients

In all 128 patients, the clinical severity rating scores were measured using the unified Parkinson's disease rating scale (UPDRS) motor score and Hoehn &Yahr (H&Y) scale for motor function. Items of the UPDR motor scores were grouped into those representing the severity of tremor (item 20 and 21), rigidity (item 22), bradykinesia (item 24, 25, 26 and 31), speech (item 18) and axial motor deficits

(item 27, 28, 29, 30).

3. Statistical analysis of clinical deficits of which severities correlate with age of patient and duration of disease

Statistical analysis was performed with SAS (Statistical Analysis System: SAS Institute, Cary, NC) version 9.1 running in the Window system. To control the effect of duration of disease on the relationship between the age and UPDRS total motor scores or subscores, we used a multiple linear regression model. Same analysis was used to control the effect of the age on the relationship between duration of disease and UPDRS total motor scores or subscores.

4. Brain FDG PET studies

A. Quantitative brain FDG PET study

All 128 patients underwent brain FDG PET studies after agreement to informed consent. The subjects fasted overnight prior to the FDG PET scan. To minimize the environmental stimuli, all the procedures were performed in a quiet and dimly lit room with the subjects' eyes opened. 45 to 55 minutes after the injection of 0.14 mCi/kg of FDG through the antecubital vein, PET scan was performed using Allegro PET scanner (Phillips Medical Systems; gadolinium oxyorthosilicate crystals) for the acquisition of high resolution three dimensional PET images. After 1.5 minute of transmission, 17 minutes of emission and final 1.5 minute of transmission scans, three-dimensional (3D) PET image was reconstructed

using 3D version of the row action maximum likelihood algorithm (3D-RAMLA). The time course of [^{18}F]-radioactivity was obtained with repetitive sampling of radial arterial blood for 40 minutes after the administration of FDG. Finally, 3D parametric PET image representing regional CMRglu was acquired using a software PMOD version 2.61 (PMOD technologies Ltd., Zurich, Switzerland) with FDG-autoradiography method (lump constant=0.437, k1=0.102, k2=0.130, k3=0.062, k4=0.0068).[16]

B. Correction of partial volume effect

On the same day of each FDG PET scan study, about 160 slices of axial T1-weighted brain MR images were obtained with 3D spoiled gradient-recalled sequences (3D-SPGR sequences; repetition time = 6.8 ms, minimum of echo time = 1.6 to 11.0 ms, flip angle = 20°, 256 x 256 matrix, slice thickness = 1 mm) using a 3.0 Tesla MR scanner (Signa EXCITE, GE Medical Systems, Milwaukee, WI). The original brain MR images were reformatted parallel to the anterior and posterior commissure line and resampled with 1 x 1 x 1 mm of voxels.

The PVELab (EU 5th framework program, Enhancement of Clinical Value of Functional Imaging through Automated Removal of Partial Volume Effect, Project #QLG3-CT-2000-000594; http://nru.dk/pveout) software implemented to MATLAB 7.0 (MathWorks, Natick, MA) was used to correct the partial volume effect.[17] Using the Müller-Gärtner method, we obtained partial volume effect-corrected FDG PET

images.

5. Analysis of CMRglc using statistical parametric mapping (SPM)

We used SPM2 (Wellcome Department of Cognitive Neurology, Institute of Neurology, London, UK) software and MATLAB 7.0 (MathWorks, Natick, MA) to statistically analyze the PET data. For the purpose of spatial normalization, the PET images were transformed into the Montreal Neurological Institute-152 (MNI-152) template brain image. An isotropic Gaussian kernel of 10 mm of full width half maximum (FWHM) was applied to improve the signal-to-noise ration. Using multiple regression model covariated with age, we searched for significant brain areas in which CMRglu negatively correlated with disease duration. Conversely, a multiple regression model covariated with disease duration was used to find brain areas in which CMRglu negatively correlated with the age at onset. It was considered statistically significant when the false discovery rate (FDR) corrected *p*-value was less than 0.05.

III. RESULTS

1. Characteristics of subjects

The mean (SD; range) age at examination of 128 patients was 64.6 (8.1; 47-85) years and mean age of PD onset was 60.7 (8.9; 45-84) years. The mean of disease duration was 49.3 (49.7; 1-245) months. The mean UPDRS motor score

was 28.0 (13.6; 6-73). The mean UPDRS motor scores representing the severity of tremors was 3.6 (3.3;0-18), rigidity was 5.3 (3.7;0-17), bradykinesia was 9.5 (4.5;1-21), and axial symptoms was 4.3 (3.2; 0-16). Mean K-MMSE score was 27.9 (1.8; 24-30). Modified H&Y stage was 1 in 15 patients (11.7%), 1.5 in two patients (1.6%), 2 in 37 patients (28.9%), 2.5 in 36 patients (28.1%), 3 in 19 patients (14.8%), 4 in 15 patients (11.7%) and 5 in four patients (3.1%).

2. Clinical deficits of which severities correlate with duration of disease and age of patients

The statistical analysis showed that the disease duration correlated with the total UPDRS [regression coefficient (RC) = 0.177, *p*-value < 0.001)] and all four UPDRS subscores representing tremor (RC = 0.028, *p*-value < 0.001), rigidity (RC = 0.040, *p*-value < 0.001), bradykinesia (RC = 0.048, *p*-value < 0.001), and axial motor deficit (RC = 0.037, *p*-value < 0.001).

However, the current age of patients correlated with total UPDRS motor score (RC = 0.305, *p*-value = 0.012) and the UPDRS scores representing the severity of bradykinesia (RC = 0.091, *p*-value = 0.042) and axial symptoms (RC = 0.101, *p*-value = 0.001), but not with those of tremor (RC = 0.053, *p*-value = 0.137) and rigidity (RC = 0.001, *p*-value = 0.976).

3. Brain regions in which CMRglu correlate with age of patients and disease duration analyzed by SPM2

Multiple regression analysis adjusted for the disease duration demonstrated a negative correlation between current age and whole CMRglc (correlation coefficient=0-0.17, $p<0.05$). CMRglu correlated inversely with current age in the medial prefrontal, lateral prefrontal, orbitofrontal, anterior cingulate, insula, superior and inferior temporal cortices, caudate, thalamus and cerebellar cortex (FDR corrected $P<0.05$). (Figure 1, Table 1)

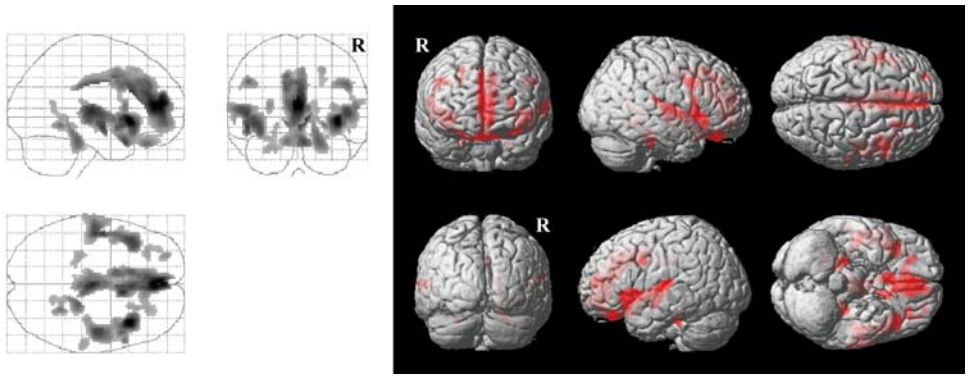

Figure 1. Graphic image of SPM result

The projection view (left) and three-dimensional surface rendering images (right) of statistical parameter mapping (SPM) analysis of [^{18}F]-fluorodeoxy glucose positron emission tomography findings show brain areas in which glucose metabolism correlate with current age of 128 non-demented patients with Parkinson's disease (FDR corrected $p<0.05$)

	BA	x	y	z	T
Rt superior frontal	9	24	40	29	3.02
Rt middle frontal	8, 9	48	13	29	4.96
Rt inferior frontal	11, 44, 47	38	17	-4	7.52
Rt orbitofrontal	11	6	13	-21	5.51
Rt precentral	44	55	14	9	4.57
Lt superior frontal	11	-32	46	-17	3.06
Lt middle frontal	10	-28	53	8	3.93
Lt inferior frontal	9, 47	-42	19	-6	5.78
Lt medial frontal	9, 10, 25	-2	47	11	7.56
Lt orbitofrontal	11	-10	13	-21	4.52
Rt superior temporal	21, 22, 42	48	-11	4	5.75
Lt superior temporal	22	-50	-8	-8	6.07
Rt anterior cingulate	24, 25, 32	2	41	9	7.44
Rt posterior cingulate	23, 30	2	-22	31	5.12
Rt parahippocampal	19, 30, 35	20	-32	-17	5.06
Lt anterior cingulate	24, 25, 32	-1	-10	32	5.26
Lt posterior cingulate	23	-8	-34	27	3.02
Lt parahippocampal	27, 35, 36	-26	-30	-24	3.52
Rt caudate		8	12	-2	6.11
Rt thalamus		2	-17	8	6.35
Lt thalamus		-1	-17	5	6.25

Abbreviations: SPM = statistical parametric mapping; Rt = right, Lt = left, BA = Brodmann's area; x, y, z = Talairach coordinate; T = t-value

Table 1. Results of SPM analysis
This table shows brain areas in which glucose metabolism correlate with age.

Another multiple regression analysis adjusted for the age at examination showed no correlation between disease duration and whole CMRglu. CMRglc correlated inversely with disease duration solely in the occipital cortex (FDR corrected $P<0.05$). (Figure 2)

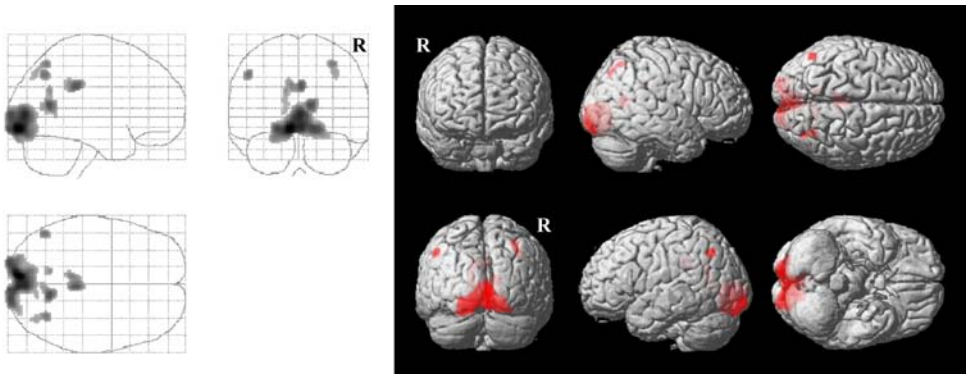

Figure 2. Graphic image of SPM result

The projection view (left) and three-dimensional surface rendering images (right) of statistical parameter mapping (SPM) analysis of [^{18}F]-fluorodeoxy glucose positron emission tomography findings show brain areas in which glucose metabolism correlate with disease duration of 128 non-demented patients with Parkinson's disease (FDR corrected p<0.05)

IV. DISCUSSION

The hypotheses of a role of aging in the development of PD have been countered by various evidences, including fixed incidence rate of PD despite of increased life expectancy,[18] results of pathological studies,[7,19] assays of concentration of dopamine and its metabolites in the striatum.[20] Also, fluorodopa PET studies showed different topographical distribution of nigral dopaminergic neuronal loss between PD patients and normal elderly.[21] These findings represent that aging has little effect on the development of PD. However, age-related negative

motor signs, such as bradykinesia, appear to contribute to the increasing disabilities of elderly PD patients.[22] Indeed, elderly patients with PD had more dopa-resistant axial symptoms than young ones after similar period of evolution,[5,23] and they also have more rapid progression and higher mortality than younger ones, because of frequent dopa-resistant features such as imbalance, falling, dysphagia, dysarthria and dementia.[2]

The present study showed that in patients with PD bradykinesia and axial motor deficits are associated with aging and increasing duration of disease, whereas rigidity and tremor are associated with disease duration but not with age. These findings suggest that aging and disease duration contribute differently to motor deficits in patients with PD. Moreover, aging contributes to reduction of cerebral metabolism rather than disease duration in PD patients.

Clinical deficits of which severities correlate with age of patients and duration of disease

Clinicopathological findings in the elderly individuals who died without PD showed a correlation between degree of neuronal loss in the dorsal substantia nigra and severity of axial motor deficits.[24-26] The severity of axial motor deficits of PD patients also correlates with the degree of nigrostriatal dopamine deficiency.[27] However, such parkinsonian axial motor deficits do not respond to the levodopa

treatment, then, old PD patients mainly suffer from dopa-resistant axial motor deficits.[28-31] To control posture and gait, PD patients need additional attention and executive function because of their basal ganglia dysfunction. Such higher cortical functions are managed by the prefrontal, dorsolateral frontal, inferior frontal and cingulate cortices.[32] In the present study, CMRglu of these brain areas correlated inversely with age of patients. These findings suggest that axial motor deficits seem to occur in association with basal ganglia dysfunction and might deteriorate further by the age-related frontal dysfunction in PD.[33,34]

Among the parkinsonian motor deficits, bradykinesia correlates best with the degree of nigrostriatal dopamine deficiency.[27] In healthy individuals, dopaminergic neurons, transporters, and receptors reduce with age.[7,20,35-40] Therefore, it is tempting to attribute the correlation between the degree of bradykinesia and age of patients to the increasing nigral and striatal dopaminergic dysfunction with age. However, functional and pathological studies of aged individuals showed no age-related nigrostriatal dopaminergic deficit.[41,42] In PD, functional imaging studies could not demonstrate reduction in striatal dopamine transporter density with age.[43,44]

Bradykinesia is not a specific sign for nigrostriatal dopamine deficiency, but may also occur in association with disordered motor set arising from the frontal cortex.[45] A brain PET study showed a significant correlation between the degree of bradykinesia and density of prefrontal presynaptic monoamine reuptake sites.[46] Also,

reduced CMRglu in the lateral frontal area correlates with bradykinesia.[12] Therefore, in PD frontal dysfunction with age may contribute in part to the age-related deterioration of bradykinesia.[47] These findings are concordant with the present study which demonstrated the age-related deterioration in clinical severity of bradykinesia and age-related frontal lobe dysfunction in PD patients.

Although maximal speed of movement decreases with age, normal aged individuals rarely develop positive parkinsonian motor deficits including rigidity and rest tremor.[22,25] In PD, age of patients has little effect on the rate of deterioration of tremor and rigidity.[5] In fact, positive parkinsonian motor deficits might lessen in severity with age.[22] Accordingly, present study showed no correlation between age of patients and severity of rigidity and tremor.

In PD, degree of reduced striatal dopamine transporter correlates with the duration of disease, but not with the age of patients.[44] Also, a postmortem pathological study of PD showed that longer disease duration, adjusted for age, correlates with the reduced number of nigral neurons.[7] Consequently, duration of disease correlates with the severity of parkinsonian motor deficits.[9,29-31,48] The present study also showed that duration of PD correlates with H&Y stage, total UPDRS scores, and UPDRS subgroups representing the severity of rigidity, tremor, bradykinesia and axial motor deficits.

Possible mechanisms responsible for reduced cerebral glucose metabolism with age of patients and disease duration

Our result demonstrated that there was inverse correlation between age at examination and CMRglu of medial and lateral prefrontal, orbitofrontal, anterior cingulate, insular, superior and inferior temporal cortices, caudate, thalamus and cerebellar cortex. Disease duration correlated inversely with CMRglu solely in the occipital cortex. These findings suggest that different brain areas are involved in PD patients according to age of patient and disease duration, furthermore, aging and disease duration contribute differently to cerebral dysfunction resulting in clinical diversity of PD patients.

Possible mechanisms for inverse correlation between age at examination and CMRglu are cerebral cortical neuronal loss, reduced cortical synapses and reduced subcortical afferents including dopaminergic and non-dopaminergic pathways.

Age-related atrophy and neuronal loss are located in the prefrontal and temporal lobes, and parietal and occipital lobes are relatively preserved. [49-51] Correspondingly, our result shows an inverse correlation between age at examination and cerebral activities in the prefrontal, orbitofrontal, anterior cingulate and temporal cortices. Moreover, pathological studies performed in nonhuman animals demonstrate that age-related pathological changes occur in more restricted area e.g. cortical layer I, which gives cortical efferent fibers to caudate nucleus and

cerebellum.[52,53] Decreased CMRglu in caudate and cerebellum may be originated from age-related reduced frontal cortical efferent fibers.

However, there is no significant neuronal loss in the motor and premotor cortices in elderly individuals and PD patients, [49,54] and apart from layer 1, significant numbers of cortical neurons are not lost. Then, other contributing factor may be the changes in nerve fibers such as loss of dendrites and synapses, which results in the reduced cortical activities.[55,56] Age-related reduction in the number of synapses is significant and synaptic balance is also disturbed with age in the frontal lobe of nonhuman primates.[53,57-59] Because the extent of a neuron's dendritic arborization affects integration and process of incoming information and spines are the major site for excitatory synapses, age-related regression of dendritic arborization and spines can have detrimental effects on frontal lobe function.[57] Those ultrastructural morphologic changes and functional disturbance may be a possible mechanism contributing to the decreased CMRglu in the frontotemporal cortex with aging.

Reduced subcortical afferents may be another explanation for cerebral cortical hypometabolism associated with age. In rats, the changes in frontal lobe glucose uptake follow various lesions of ascending catecholaminergic pathways, which include dopaminergic fibers and noradrenergic fibers.[60] In prefrontal cortex of humans and nonhuman animals, layer I has a high integrative potential because

dendrites in layer 1 form synapses with numerous axons from various subcortical sources such as thalamic afferents, basal nucleus of Meynert (nbM), substantia nigra and raphe nuclei.[47,53]

The dopaminergic output displays a decreasing density gradient; ventral motor, premotor and supplementary motor areas are densely innervated, and the parietal, temporal and posterior cingulate cortices are more lightly innervated.[33] However, motor and premotor areas as well as prefrontal cortex display a severe depletion of cortical dopaminergic innervations in PD patients.[47] And there was no correlation with age at examination or disease duration and CMRglu of motor and premotor areas in our result. Therefore, age-related CMRglu change cannot be attributed exclusively to dopaminergic dysfunction.

Layer 1 also receives afferents from the nbM, of which cholinergic neurons project their axons to many cerebral cortices.[61] Cholinergic neuronal abnormalities are present with aging although the distribution of cholinergic projections is dense to the posterior frontal cortex than prefrontal cortex.[62] In a study with baboons, ipsilateral cerebral cortical hypometabolism occurred predominantly in the frontotemporal cortex after an electrical coagulation of the unilateral nbM.[63] These findings support an involvement of loss of cholinergic cortical inputs in the age-related CMRglu change observed in the present study.

In PD patients, locus ceruleus of noradrenergic projections and serotonergic

neurons are substantially damaged.[64] However, inn humans, age-related midbrain catecholamine neuronal loss does not occur.[42] Therefore, loss of noradrenergic and serotonergic cortical inputs does not seem to be a main cause of age-related CMRglu change observed in the present study.

The present study demonstrated an inverse correlation between disease duration and CMRglu of the occipital cortex. PD patients show reduced occipital CMRglu bilaterally, more prominent in contralateral side to the side showing clinically more severe impairment. Regarding the origin of occipital hypometabolism with diseases progression, a pathological change in occipital cortex, nigrostriatal dopaminergic dysfunction and dysfunction of other subcortical neurotransmitters must be considered. However, a pathological change in occipital cortex per se is not plausible for the inverse correlation between the disease duration and occipital CMRglu because cortical Lewy bodies are rarely found in the occipital cortex of non-demented PD patients.[65]

Since a dopaminergic innervation to primary visual cortex was found in cat,[66] a clinical study with PD patients without dementia showed severe glucose metabolic reduction in the primary visual cortex and it correlated with motor impairment, which suggests the association between nigrostriatal dysfunction and the occipital metabolism in PD.[14] However, in vitro study showed that the occipital cortex does not receive dopaminergic input from the mesencephalon.[67] These

findings suggest that occipital hypometabolism is not caused by nigrostriatal deficiency in PD.

In PD patients, choline acetyl transferase activity is significantly decreased in occipital cortex.[68] Recent PET study measuring acetylcholinesterase activity demonstrates that cholinergic dysfunction occurs especially in the medial occipital cortex from early stage of PD.[69] These findings suggest possible contribution of cholinergic innervation to the effect of disease duration on occipital hypometabolism.

V. CONCLUSION

In PD, there is an inverse correlation between age at examination and frontotemporal CMRglu and age-related cortical changes might be the major factor. Disease duration of PD is inversely correlated with occipital CMRglu and subcortical cholinergic dysfunction is probably responsible for this change. In summary, age and disease duration have independent, additive effects on the deterioration of cortical metabolism, which leads to various clinical disabilities in PD patients. Moreover, age-related widespread, particularly frontal, dysfunction may accelerate deterioration of bradykinesia and axial motor deficits.

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Abstract (in Korean)

나이와 유병기간이 파킨슨병 환자들의 뇌 포도당 대사량에 미치는 영향

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서론: 파킨슨병에서 일관되게 흑질 도파민성 세포 소실을 관찰할 수 있는 반면, 임상 양상은 매우 다양하다. 파킨슨병 자체와 관련된 신경퇴행이나 노화에 의한 신경 퇴행이 파킨슨병의 발생과 진행에 여러 양상으로 영향을 미칠 것이다. 또한 이러한 신경퇴행은 임상적 다양성을 설명하는 방편으로 고려되어 왔다 그러나, 아직까지 임상양상과 기능저하를 보이는 뇌 부위 사이의 관계를 환자의 나이와 유병기간을 고려하여 체계적으로 연구된 바 없었다. **방법**: 128명의 치매가 없는 파킨슨병 환자들을 대상으로 하였다. 파킨슨병의 운동 기능 저하는 통합파킨슨척도(UPDRS) 운동 점수를 이용하여 평가하였다. 모든 환자들에게 뇌자기공명영상 및 [^{18}F]-fluorodeoxy glucose 양전자 방출 사진을 촬영하였다. 다중선형회귀분석을 이용하여 파킨슨병 운동증상의 심한 정도와 환자의 나이 및 유병기간을 연관 분석하였다. 또한 환자의 나이 및 유병기간과 연관성이 있는 대뇌 포도당대사를 보이는 뇌부위를 확인하기 위해 다중선형회기분석법을 사용하였다. **결과:** 환자의 평균(표준편차) 나이는 64.6 (8.1) 세로 평균 유병기간은 49.3 (49.7) 개월이었다. 총 UPDRS 운동 점수는 28 (13.6)점 이었다. 진전의 심한 정도를 대표하는 평균 UPDRS 운동 점수는 3.6 (3.3)점, 경직은 5.3 (3.7)점, 서동증은 9.5

(4.5)점 이었고 몸통 증상은 4.3 (3.2)점 이었다. 환자의 나이와 전체 UPDRS 운동 점수는 양의 상관관계를 보였다. 환자의 나이와 서동증, 몸통증상의 심한 정도도 환자의 나이가 증가할수록 증가하였으나 진전과 경직은 환자의 나이와 연관성이 없었다. 유병기간은 총 UPDRS 운동 점수 및 진전, 경직, 서동증, 몸통증상을 대표하는 모든 평균운동점수와 연관성이 있었다. 환자의 나이가 증가할수록 전전두엽, 안와전두엽, 상측두엽, 전-후 대상엽, 해마방회, 미상핵 및 시상의 대뇌 포도당대사량은 감소하였다. 반면, 유병기간은 후두엽 대사와 반비례하는 연관관계를 보였다. **결론**: 파킨슨병에서 나이와 유병기간은 대뇌 포도당대사에 독립적으로 부가 효과를 가지고, 이로 인해 파킨슨병 환자에서 다양한 임상양상을 나타내게 한다. 또한 나이와 연관된 전반적인, 특히 전두엽을 침범하는 기능저하는 환자의 서동증과 몸통증상을 악화시키는 역할을 하는 것으로 사료된다.

핵심되는 말: 파킨슨병, 노화, 유병기간, 양전자방출 단층촬영