Effect of Cigarette Smoking on Disease Progression in Idiopathic Parkinson's Disease Patients

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A Dissertation Submitted to The Graduate School of Ajou University in Partial Fulfillment of the Requirements for the Degree of Master of Medicine

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February, 2010

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December, 21st, 2009

− Abstract −

Effect of cigarette smoking on disease progression in idiopathic Parkinson's disease patients

Introduction: Cigarette smoking is known to have a protective role against the development of idiopathic Parkinson's disease (IPD). Despite this, there have been few studies focusing on whether cigarette smoking is able to slow IPD disease progression. The few that have examined this issue must be regarded with care due to their intrinsic methodological problems which have likely hampered their power to detect any potential neuroprotective effect of cigarette smoking. Given that a relatively small proportion of female IPD patients has a history of smoking it is reasonable to distinguish disease progression relative to gender, or simply to include only male patients, neither of which the previous studies did. We therefore evaluated the neuroprotective role of cigarette smoking in male IPD patients.

Method: A total of 81 male IPD patients, who regularly visited Ajou University hospital neurologic clinic, were enrolled in this study. All patients were evaluated by means of a structured questionnaire. General demographic data and Unified Parkinson's Disease Rating Scale (UPDRS) results were compared for each group in order to determine the effects of smoking on IPD progression.

Results: Among 81 patients, 25 patients (smoker group) were current smokers or stopped smoking only after the IPD symptomatic onset. The remaining 56 patients (non-smoker group) were those who had ceased smoking prior to the onset of IPD symptoms or those who

had never smoked. The age (62.7 yrs Vs. 68.2 yrs, *p*=0.072), disease duration (5.3 yrs Vs. 4.8 yrs, *p*=0.344), and levodopa dosage (616.8 mg Vs. 572.9 mg, *p*=0.583) were similar between the smoker group and non-smoker group. However, the age of IPD onset (57.3 yrs Vs. 63.5 yrs, *p*=0.047*)*, UPDRS motor scores (14.8 Vs. 19.1, *p*=0.034), particularly the akineto-rigid subscores (7.1 point Vs. 9.7 point, *p*=0.022), and the UPDRS motor score progression rates were lower in the smoker group than those in the non-smoker group (3.4 points /year Vs. 5.3 points /year, *p*=0.007). In a Cox regression analysis, the age of IPD onset was the most significant prognostic factor. When 25 patients from the smoker group were matched to the age of IPD onset and onset phenotype matched controls for 25 patients from the non-smoker group, the smoker group still had a lower UPDRS motor score (14.8 points Vs. 20.3 points, *p*=0.032), and a lower UPDRS motor score progression rate than the non-smoker group (3.4 points per year Vs. 5.1 points per year, *p*=0.037).

Conclusion: This study demonstrated that the continuation of cigarette smoking has a protective effect in male IPD, effectively slowing the rate of disease progression. Even after adjusting for the age of IPD onset, smoking was still identified as being able to significantly slow the progression of IPD.

Key words: Parkinson's Disease, Cigarette Smoking, Progression of Parkinson's disease
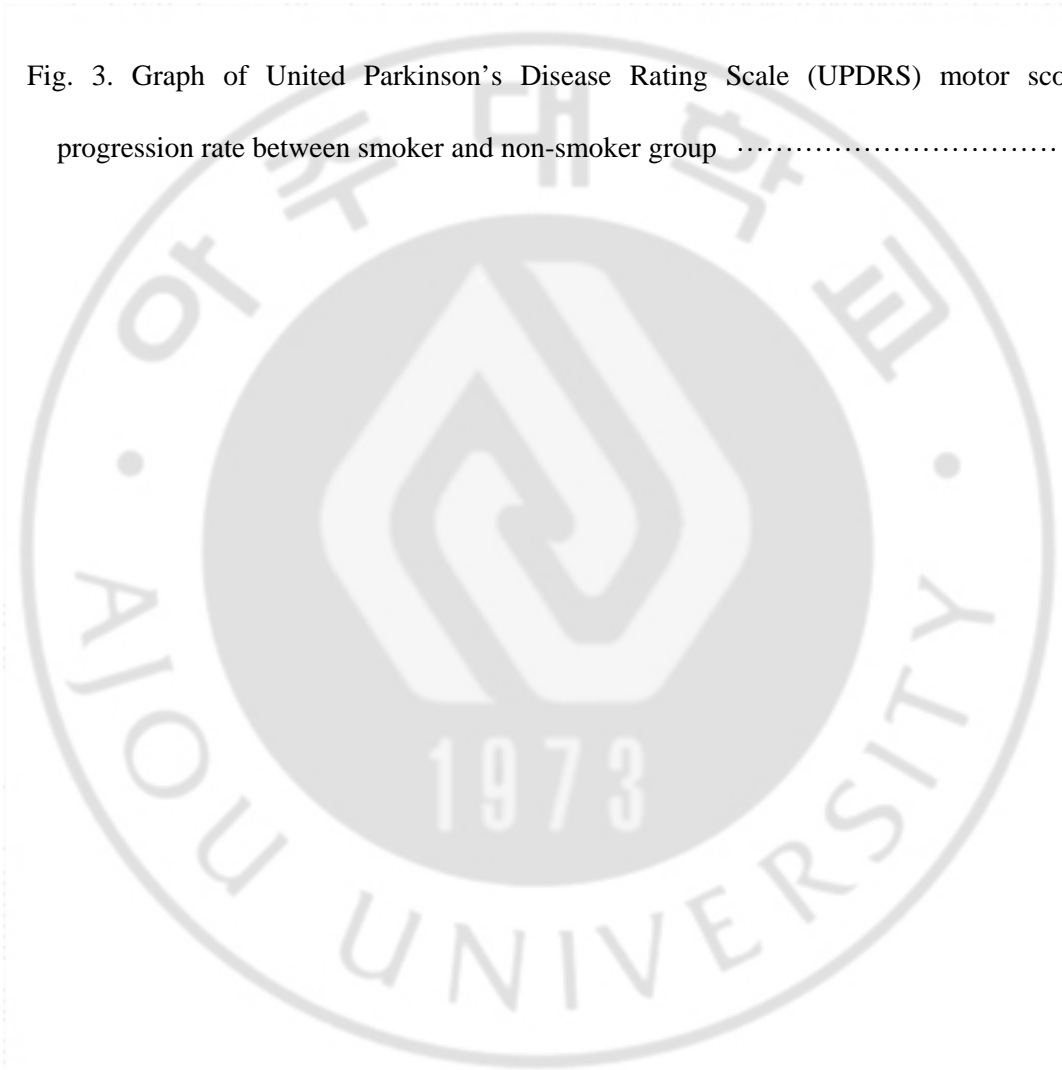
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I. INTRODUCTION

Idiopathic Parkinson's disease (IPD) is a progressive neurodegenerative disorder characterized by tremor, rigidity, bradykinesia, and postural instability. Together with Alzheimer's disease (AD), IPD is one of the most common neurodegenerative diseases, with a lifetime risk of developing IPD at 1.5% (Allam et al., 2005; Brown et al., 2005; de Lau et al., 2004; de Rijk et al., 1995; de Rijk et al., 2000; Gorell et al., 2004). The motor symptoms characteristic of IPD are caused by dopaminergic neuronal loss in the substantia nigra within the midbrain. Although the exact cause of dopaminergic neuronal loss has not been clearly elucidated, genetic factors, infections, oxygen free radicals, or environmental factors have been proposed as possible etiologies (Dick et al., 2007a; Dick et al., 2007b; Doty, 2008). Pathologically, IPD is characterized by the presence of Lewy bodies (Samii et al., 2004), which appear prior to the typical IPD motor phenomena emerge, and which accumulate in the central nervous system, particularly in the olfactory bulb and lower brainstem (Braak et al., 2003; Hawkes, 2008). Overtime, Lewy bodies accumulate beyond the brainstem and eventually reach the cerebral cortex while at the same time, dopaminergic neurons in the substantia nigra gradually disappear (Braak et al., 2003). As neuronal loss and Lewy body accumulation progress, IPD motor phenomena worsen (Alves et al., 2005). Given the understanding of IPD progression, there have been many studies that have attempted to establish factors that influence the speed of IPD progression. It has been demonstrated that gender, age of IPD onset, onset phenotype, and lower Unified Parkinson's Disease Rating Scores (UPDRS) at IPD onset seem to be influential factors in determining IPD progression

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(Alves et al., 2005; Post et al., 2007).

Treatment of IPD is usually symptomatic and relies heavily on the replenishment of dopamine (2004; Fahn et al., 2004; Lees et al., 2009; Samii et al., 2004). However, this form of treatment has its limitations, as over time, adverse effects such as the wearing off of drug efficacy and levodopa-induced dyskinesias occur.

Interesting results can be deduced from epidemiologic studies of IPD. For example, cigarette smoking has repeatedly been shown to have a protective role against the development of IPD (Ritz et al., 2007). In fact, several case-control studies and prospective cohort investigations have supported this observation (Grandinetti et al., 1994; Hellenbrand et al., 1997). It is assumed that the pharmacological activity of several compounds in cigarette smoke has a protective effect against development of IPD.

Given that cigarette smoke has been demonstrated to be protective effect against IPD, one may then hypothesize that cigarette smoke may also slow the rate of disease progression in patients who have already established IPD. Unfortunately, this optimistic hypothesis has not supported by literature related to this matter (Alves et al., 2004; Kandinov et al., 2007; Papapetropoulos et al., 2005). In fact, these studies have claimed that while smoking may protect from the development of IPD, it cannot slow down its progression once it has developed inside the nervous system.

It is possible that these contradictory studies found negative results because of the existence of their intrinsic methodological shortcomings. For example, these studies included both male and female patients together without considering the fact that male patients represent a significantly higher proportion of smokers. As a result, their study populations

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were comprised of significant portions of male smokers and female non-smokers, inherently making them prone to biased observations. In addition, these studies also failed to take into account other factors that influence the rate of disease progression such as age of onset and phenotype of motor symptom (i.e. tremor dominant Vs. akineto-rigid dominant phenotypes).

Based on this discrepancy, in this study we studied the rate of disease progression in male IPD patients while taking into account other factors that have been shown to contribute to IPD progression.

II. METHOD

A. Subject and Evaluation

We enrolled male IPD patients who had visited our Ajou University Hospital neurology clinic for regular follow-ups from Oct. 2008 to Feb. 2009. The diagnosis of IPD was based on the United Kingdom Parkinson's Disease Society Brain Bank (UK PDS Brain Bank) clinical diagnostic criteria (Hughes et al., 1992). The UKPDS diagnostic criteria are composed of three steps, the first of which is characterized by core features of IPD such as bradykinesia, resting tremor, rigidity, and postural instability. The second step is characterized by sixteen exclusion criteria and the third step, by eight supportive criteria.

Out of 83 candidate male patients, two patients were excluded. One patient had undergone previous deep brain stimulation surgery of the subthalamic nucleus, while the other patient had received a secondary diagnosis of severe cerebral amyloid angiopathy (CAA) based on a brain magnetic resonance image (MRI). Exclusion was agreed upon as these conditions were expected to have significantly altered the natural disease course of IPD.

All patients were interviewed by experienced neurologists in order to evaluate their disease history and current Unified Parkinson's Disease Rating Scale (UPDRS) status. The UPDRS is composed of four parts, the first part being of which is mentation, behavior, and mood. The second part measures the patient's activities of daily living, while the third part also known as the UPDRS motor score, measures the motor symptoms of PD, and is thought of as the critical marker in evaluating disease progression. The overall UPDRS motor score

is comprised of several subscores composed of tremor, akineto-rigid, speech, facial expression, posture, and gait subscores. The fourth part measures the complications of drug therapy. Total UPDRS scores are the sum of all four parts of UPDRS.

In this study, motor symptoms were examined while patients were on medication. In addition, smoking histories were taken from patients and their family members using structured questionnaires (Figure 1.). Results from which were grouped into: 1) smoker group for those who were current smokers or those who had quit smoking only after the IPD symptomatic onset or 2) non-smoker group which was composed of two subgroups groups. The first of these were those who quit smoking before IPD symptomatic onset, and the second were those who never smoked. Age of IPD onset was defined as the point in time which the patients or their family members identified for the emergence of parkinsonian motor symptoms such as tremor, rigidity, bradykinesia, or gait difficulty.

Patient age, age of IPD onset, disease duration, medication dosage (calculated as Levodopa equivalent dosage), Total UPDRS scores, UPDRS motor scores, Hoehn and Yahr stages, and onset phenotypes (ie. Tremor dominant versus akineto-rigid dominant type) were taken into account in the analysis. Levodopa equivalent dosages were standardized with the use of a formula following from this equation: 100mg standard levodopa = 125mg sustained-release levodopa, 1.5mg pramipexole, 6mg ropinirole, 10mg bromocriptine or 1mg pergolide (Pahwa et al., 1997; Thobois et al., 2002).

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ID_____

Name_____

Chart Review							
Current age		yrs					
Onset age	year	month	Disease Duration		years		month
Medication start	year	month	Medication Duration		years		month
Onset Type ;	Tremor	/	Akineto-Rigid				
Other Medical problem	;						
Medication	Sinemet ( )		Stalevo ( )		Madopar ( )		Trihexin ( )
	Jumex ( )		Pk-merz ( )		Requip ( )		Mipapex

Patient Interview				
Current Smoker ( )	Pack per day :	Pack-year after IPD		
Ex-smoker after IPD ( )	Previous pack per day :	Pack year after IPD,	Duration after quit smoking yr	
Ex-smoker before IPD ( )	Previous pack per day :		Duration after quit smkoing yr	
Never Smoked ( )	Total			PY

UPDRS			
Total score ( )	UPDRS-III ( )	Tremor subscore ( )	(3~9)
H&Y ( )		Akineto-Rigid subscore ( )	(10~22)

Fig. 1. Structured questionnaire to registry male IPD patients.

B. Statistical analysis

A chi-square test was used for determining differences in proportions for categorical variables and the Student's *t*-test, to compare means for continuous variables. A Pearson's correlation was used for examining the correlation between pack-years after IPD onset and the rate of disease progression in all enrolled patients. The rate of disease progression was deduced using the UPDRS (total scores or motor scores) divided by disease duration in years. A Cox regression model including age of IPD onset, onset subtype, and smoking subgroup was used to calculate the relative risk for disease progression between smokers and ex- or non-smokers. Event in the Cox regression model was defined as UPDRS motor scores being greater than the score of the highest quartile for all enrolled patients' UPDRS part III scores. A *p*-value of less than 0.05 was considered to indicate a statistically significant difference. All statistical analyses were performed using SPSS 13.0 (SPSS, Inc., Chicago, IL).

III. RESULTS

A. General Demographics

(Table 1) summarizes general demographics between the two groups. Among 81 enrolled patients, 25 patients were the smoker group and 56 patients were the non-smoker group. Compared with the non-smoker group, the smoker group showed younger age of disease onset (57.3 yrs Vs. 63.5 yrs, *p=0.047*) and smoker group also showed also younger age trend of disease onset although there was no statistical significance (62.7 yrs Vs. 68.2 yrs, *p=0.072*). While there was slightly longer disease duration and medication duration in smoker group, there was no statistical significance between two groups (5.3 yrs Vs. 4.8 yrs, *p=0.344*, 3.7 yrs Vs. 3.4 yrs, *p=0.687*). All of enrolled patients were treated with levodopa. Levedopa equivalent dosage was also similar between two groups (616.8 mg Vs. 572.9 mg, p=0.583). Use of medication other than levodopa had no difference between two groups. Onset phenotype showed no difference between groups also.

Table 1. General demographics between two groups.

	Smoker group (n=25)	Non-smoker group (n=56)	p value
Current Age (years)	62.7 ± 13.3	68.2 ± 9.8	0.072
Age of Onset (years)	57.3 ± 13.7	63.5 ± 9.4	**0.047***
Disease Duration (years)	5.4 ± 2.7	4.7 ± 3.2	0.344
Levodopa equivalent Dose (mg)	616.8 ± 347.5	572.9 ± 323.1	0.583
Dopamine Duration (years)	3.7 ± 2.7	3.4 ± 2.8	0.687
Onset Type			0.734
Tremor-dominant	16	38	
Akineto-Rigit-dominant	9	18	
Other Medication			
Ropinirole	7	20	0.496
Pramipexole	3	3	0.366
Trihexin	2	10	0.249
Selegiline	6	13	0.939
Amatadine	5	6	0.260

* Statistically Significant ($p<0.05$)

B. Movement Scales

(Table 2) summarizes a comparison of movement scales between the two groups. The smoker group had significantly lower UPDRS motor scores (14.8 Vs. 19.1, p=0.034); however, the total UPDRS score didn't indicated any statistical differences between the two groups (30.2 point Vs. 32.3 point, p=0.587). With respect to the UPDRS motor scores, while tremor subscores between the two groups didn't show a difference (2.4 point Vs. 3.6 point, p=0.09), akineto-rigid subscores did (7.1 point Vs. 9.7 point, p=0.022). Additionally, the total UPDRS progression rate exhibited a lower trend in the smoker group although it did not achieve statistical significance (6.7 points /year Vs. 8.9 points /year, p=0.135). On the contrary, the UPDRS motor progression rate demonstrated a lower progression rate in the smoker group (3.4 points /year Vs. 5.3 points /year, p=0.007). The Hoehn-Yahr stage didn't show a difference between the two groups (2.5 Vs. 2.3, p=0.655). In addition, there was no correlation between post-IPD smoking pack-year and UPDRS motor score or UPDRS progression rate (r2=0.042, p=0.065 in UPDRS progression rate, r^2=0.010, p=0.382 in UPDRS motor scores). In the Cox hazard regression model, which included an adjustment for age of onset, onset subtype, and smoking subtype, patients with an older age of onset had a higher probability of reaching the highest quartile with respect to UPDRS motor scores (more than 22 points) during disease progression (RR: 1.079, 95% CI: 1.020 to 1.141, p=0.008). Also, the smoker group had a tendency to have a lower probability of progressing to a high UPDRS motor score although there was no statistical significance (RR : 0.294, 95% CI: 0.085 to 1.016, p=0.053). Figure 2 illustrates the Cox hazard regression curve

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labeled with the smoker and non-smoker groups

Table 2. Comparison of movement scales between smoker group and non-smoker group.

	Smoker group (n=25)	Non-smoker (n=56)	p value
Total UPDRS (mean)	30.2 ± 14.3	32.3 ± 17.1	0.587
UPDRS motor score (mean)	14.8 ± 7.0	19.1 ± 10.4	0.034*
Tremor Score (mean)	2.4 ± 2.2	3.6 ± 3.3	0.09
AkinetoRigid Score (mean)	7.1 ± 4.0	9.7 ± 5.7	0.022*
H & Y Stage (mean)	2.5 ± 1.8	2.3 ± 1.6	0.655
Total UPDRS progression /year (mean)	6.7 ± 4.2	8.9 ± 6.7	0.135
Motor UPDRS progression /year (mean)	3.4 ± 2.2	5.3 ± 3.9	0.007*

* Statistically Significant ($p<0.05$)

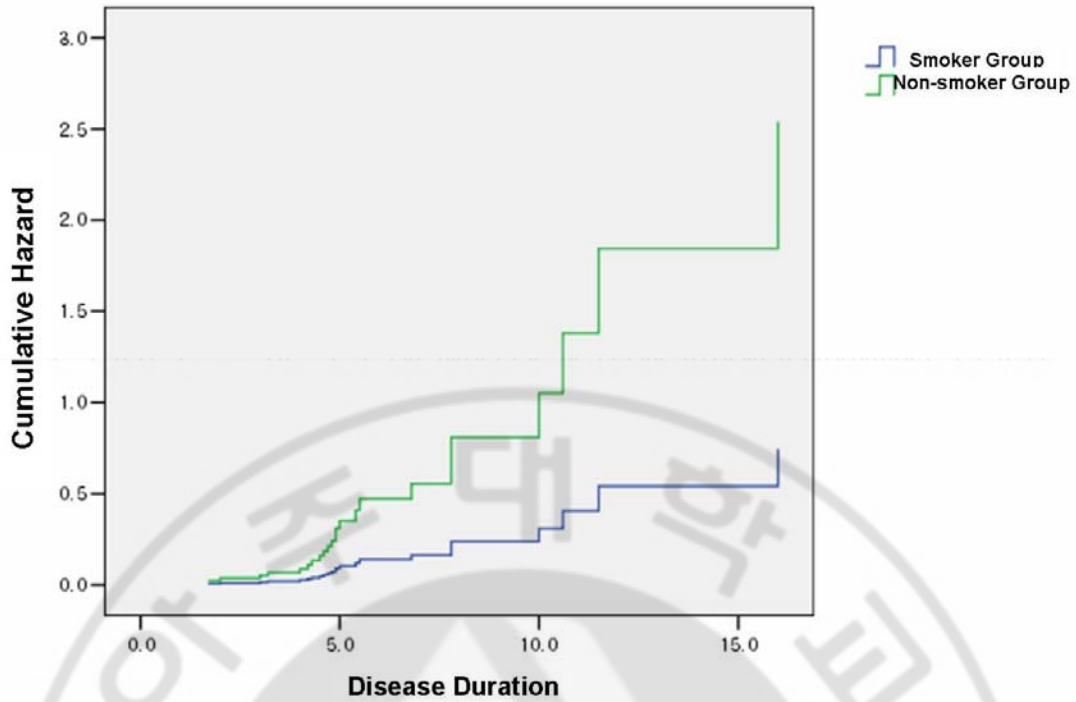UPDRS : Unified Parkinson's Disease Rating Scale

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Fig. 2. Cox regression hazard model between smokers after onset of IPD and ex- or never-smokers. This figure shows continuing smokers after onset of IPD had lower possibility to progress high UPDRS motor score, although there was not statistical significance. (RR : 0.294, 95% CI: 0.085 to 1.016, p=0.053)

IPD : Idiopathic Parkinson's Disease

C. Comparison after controlling for age of onset and onset phenotype

Predefined outcome analysis revealed that age of IPD onset was the most predictive factor of IPD progression while smoking habits also seemed to slow the disease progression as measured by UPDRS III / disease duration. Because age of onset was the only predictive factor of disease progression in the Cox regression model, we re-evaluated the effect of cigarette smoking in the smoker group after adjusting for the age of IPD onset and onset phenotype, both of which are known to be definite factors in the rate of IPD progression. The control group, which was matched for the two aforementioned variables, consisted of 25 patients selected from the non-smoker group.

(Table 3) summarizes general demographics and movement scales of the smoker and control groups. Current age, IPD duration, medication duration, and use of medication other than levodopa were not significantly different between the two groups. Additionally, UPDRS total scores, tremor subscores, Hoehn-Yahr stages, and UPDRS total score progression rates were not different. However, UPRDRS motor scores (14.8 points Vs. 20.3 points, p=0.032), akineto-rigid subscores (7.1 points Vs. 10.5 points, p=0.016), and UPDRS motor score progression rates (3.4 points per year Vs. 5.1 points per year, p=0.037) were statistically different between the two groups. Figure 3 illustrates UPDRS motor scale progression between smoker group and non-smoker group after controlling age of onset.

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Table 3. Comparison of general demographics and movement scale between two groups after age of IPD onset adjustment

	Smoker group (n=25)	Control group (n=25)	p value
General Demographics			
Age (years),	62.7 ± 13.3	64.6 ± 11.3	0.592
Age of Onset (years),	57.3 ± 13.7	59.4 ± 10.7	0.535
Disease Duration (years),	5.4 ± 2.7	5.2 ± 3.5	0.743
L-Dopa equivalent Dose (mg)	616.8 ± 348.0	589.6 ± 355.4	0.786
Dopamine Duration (years),	3.7 ± 2.7	3.8 ± 3.1	0.907
Onset Type			0.765
Tremor	16	17	
Akineto-Rigit	9	8	
Other Medication			
Ropinirole	7	7	0.758
Pramipexole	3	1	0.609
Trihexin	2	5	0.221
Selegiline	6	9	0.355
Amatadine	5	2	0.221
Movement Scale			
Total UPDRS (mean)	30.2 ± 14.3	34.8 ± 17.3	0.31
UPDRS motor score (mean)	14.8 ± 7.0	20.3 ± 10.1	**0.032***
Tremor Score (mean)	2.4 ± 2.2	3.6 ± 2.4	0.083
AkinetoRigid Score (mean)	7.1 ± 4.0	10.5 ± 5.5	**0.016***
H & Y Stage (mean)	2.5 ± 1.8	2.6 ± 2.2	0.918
Total UPDRS progression /year (mean)	6.7 ± 4.2	8.8 ± 5.6	0.15
Motor UPDRS progression /year (mean)	3.4 ± 2.2	5.1 ± 3.4	**0.037***

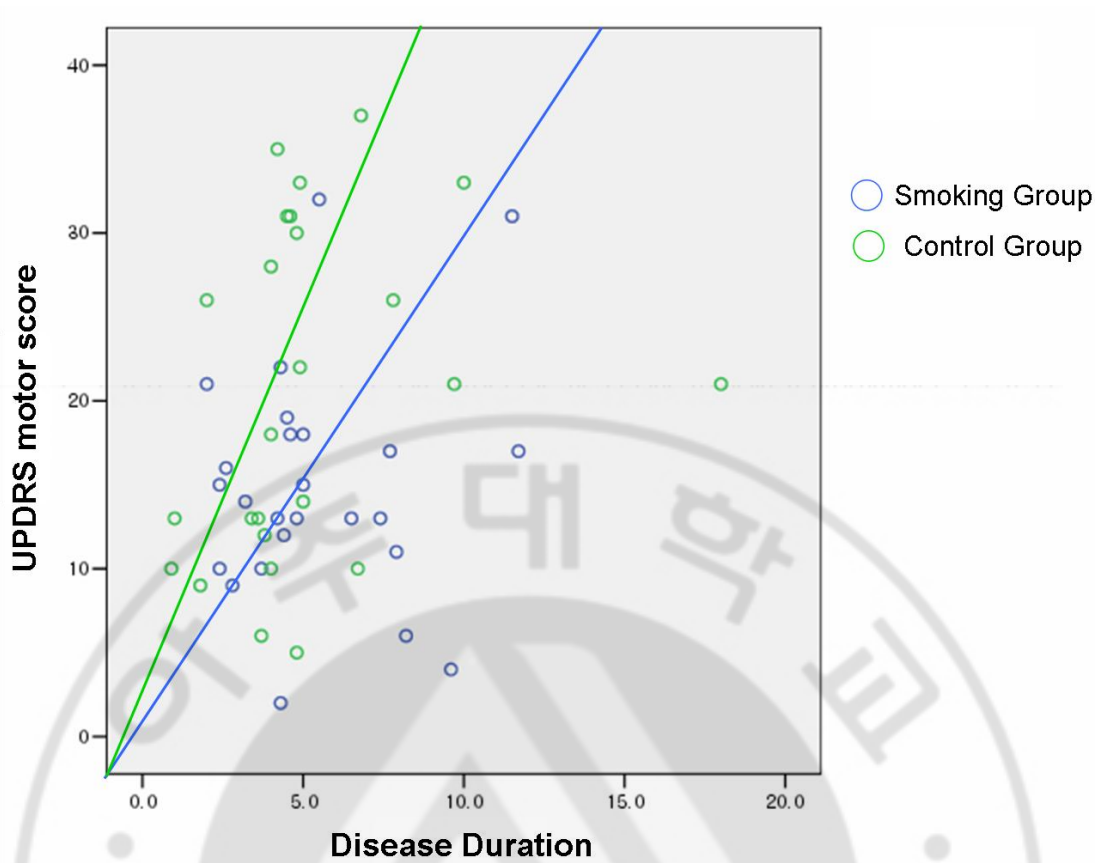* Statistically Significant ($p<0.05$

Figure 3. A scatter plot of disease duration versus UPDRS motor score. Green line represents projected progression slope for the non-smoker group, which is still faster than the smoker group shown in blue line after adjusting for age of onset and onset phenotype. (3.4 scores/year vs. 5.1 scores/year, *p*=0.037)

IV.   DISCUSSION

Our study demonstrates that those who smoked after the onset of IPD symptoms exhibited a slower rate of disease progression, even after an adjustment for the age of onset, the strongest influential factor on disease progression.

Previous studies have been unable to show a protective effect of cigarette smoking (Alves et al., 2004; Papapetropoulos et al., 2005). The main difference between this study and those previous is gender proportion. This study focused only on male IPD patients, while previous studies enrolled both genders. Because male patients make up a much larger portion of smokers than the female patients, comparisons made by these investigators were largely male smoker versus female non-smokers, making them prone to biased results.

Until present, there have been many factors reported to predict IPD progression. Among them, age of onset, subtype according to phenotype, and initial UPDRS motor scores have been well-known to be of prognostic value (Alves et al., 2005; Hely et al., 1999; Post et al., 2007). In this study, of these factors, we found age of IPD onset to be the most important prognostic factor to influence IPD progression, corresponding with previous study results (Alves et al., 2005; Hely et al., 1995). Following from this, those who develop IPD at younger ages may experience a slower disease progression due to the fact that they have more potential to compensate for neurodegenerative changes as well as having fewer of the pathologies usually associated with the aging process (Linazasoro, 2006). Our study was the first to suggest that cigarette smoking had a role in IPD progression after IPD onset as well as in a younger age of disease onset.

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Several compounds in cigarette have being investigated as neuroprotective agents in IPD, of these, nicotine has been studied extensively. In fact, the beneficial effects of nicotine have been demonstrated in animal models (Park et al., 2007; Quik, 2004; Quik and Kulak, 2002). Its neuroprotective role is exerted via activation of nicotinic acetylcholine receptors, and in particular, alpha-6 subreceptors (Quik and McIntosh, 2006). Fibroblast growth factor, which has a neuroprotective effect, was also shown to be activated by nicotinic acetylcholine receptor activation induced by nicotine (Mudo et al., 2007). However, there have been a few studies which evaluated the neuroprotective effect of nicotine in humans as well as previous studies using transdermal nicotine patches, both of which focused on the alleviation of IPD symptoms rather than neuroprotective effect of nicotine (Vieregge et al., 2001). Therefore, the neuroprotective effect of nicotine in humans has not have been clarified and needs to be investigated further. Also other compounds such as pyridines, nitrosamines, quinolines, or indoles representcandidate cigarette chemicals thought to have protective effects against the development of Parkinson's disease (Quik M, 2004).

As described previously, the etiology of IPD has been unclear. Genetic-environmental interaction or a dual hit hypothesis have been the most accepted pathogenetic explanation of IPD until present, even though many IPD-related genes have been discovered (Dick et al., 2007a; Hawkes et al., 2007).

Historically, cigarette smoking has been known to play a protective role against the development of IPD (Grandinetti et al., 1994; Hellenbrand et al., 1997; Liou et al., 1997; Ritz et al., 2007). In our study, the smoker group revealed a younger age of IPD onset than non-smoker group, a finding consistent with similarly designed studies (Alves et al., 2004;

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Papapetropoulos et al., 2005) although this has not been replicated in some other studies. (Boris et al., 2009) It can be assumed that in those cases of individuals developing IPD, despite protective environmental factors (i.e. a smoking habit), there is a greater genetic influence in the disease pathogenesis and thus, these individuals exhibit IPD at much younger ages. Therefore genetic analysis in those who continue to smoke after IPD onset may provide more accurate information about genetic-environmental interaction involved in developing IPD.

This study bears several limitations. The number of included patients is too small to make generalizations. Despite this, we did control for gender and age of IPD onset, both of which are influential factors to IPD progression. Second, this study was not done in a prospective manner and therefore, selection bias may exist in the enrolled patients despite efforts to enroll only capable patients. There is also a chance that recruitment was biased by not including those who has already expired, even though smoking in those with IPD had no additional risk to mortality (Chen et al., 2006). A further limitation is that we didn't examine other potentially influencing environmental factors such as drinking coffee or tea, both of which are well-known influencing factors in IPD development (Hu et al., 2007). We also didn't obtain initial UPDRS scores and therefore, the neuroprotective role of cigarette smoking after IPD onset as demonstrated in this study may be simply one of many influencing environmental factors. Finally, we didn't examine patients during their medication off states although examination during medication off state is usually accepted manner to exactly evaluate IPD progression. Because to make medication off state needed drug wash out period at least about 12 hours and medication off state can develop dopamine

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withdrawal akinetic crisis. Because of these, the present findings must be interpreted with caution and this study should be understood as an one of exploration study. Large prospective, thoroughly evaluated studies are needed in the future to clarify the neuroprotective effect of cigarette smoking and/or nicotine in IPD.

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파킨슨 병 환자에서 흡연이 파킨슨 병의 진행에 미치는 영향

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서론: 흡연은 파킨슨 병의 발생을 막는 역할을 하는 것으로 알려져 있다. 하지만 이미 파킨슨 병이 발생한 환자에서 흡연이 파킨슨 병의 진행에 미치는 영향에 대해서는 몇 개의 연구만이 이루어졌다. 이전에 진행되었던 흡연과 파킨슨 병의 진행에 대한 연구는 흡연의 신경 보호작용을 파악하기에는 방법적인 문제들이 있었다. 따라서 여성 환자의 경우 흡연자의 비율이 적었기 때문에 성별을 나누어 흡연과 파킨슨 병의 진행에 대하여 파악하거나, 남성 환자만을 대상으로 하는 것이 흡연이 파킨슨 병의 진행에 미치는 영향을 파악하기에 더 적합하다고 할 수 있다. 따라서 이 연구에서는 남성 파킨슨 병 환자에서 흡연이 파킨슨 병의 진행에 미치는 영향을 알아보고자 한다.

연구대상 및 방법: 아주대학교 병원 신경과 외래에서 주기적으로 추적 관찰하고 있는 81명의 남성 파킨슨 병 환자를 모집하였다. 모집된 모든 환자들에 대하여 신경과 의사가 설문지를 통하여 파킨슨 병 및 환자의 흡연력을 조사하였다. 이를 바탕으로 파킨슨 병이 발병한 후에도 지속적으로 흡연을 하였던 환자 군과

그렇지 않는 군 간의 인구통계학적인 특성과 파킨슨 병 점수를 비교하였다.

결과: 81명의 환자 중 25명이 파킨슨 병 발병 후에도 지속적으로 흡연을 하는 환자들이었고, 나머지 56명은 파킨슨 발병 전에 금연하였거나 흡연을 전혀 하지 않은 환자였다. 현재 나이 (62.7세 Vs. 68.2세, *p=0.072*), 파킨슨 병의 기간 (5.3년 Vs. 4.8년, *p=0.344*), 사용하고 있는 도파민의 용량 (616.8 mg Vs. 572.9 mg, *p=0.583*)은 두 군간의 차이가 없었다. 하지만, 파킨슨 병 발생 나이 (57.3세 Vs. 63.5세, *p=0.047*)와 파킨슨 병 운동 점수 (14.8점 Vs. 19.1점, *p=0.034*) 특히 운동완서와 강직 점수 (7.1점 Vs. 9.7점, *p=0.022*) 그리고 파킨슨 병 운동 점수의 진행 정도 (3.4점/년 Vs. 5.3점/년, *p=0.007*)는 파킨슨 발병 후에도 흡연을 한 군에서 유의하게 낮았다. 콕스 상관 분석 (Cox regression analysis)에서 파킨슨 병의 발생 나이가 가장 중요한 예후 인자였다. 25명의 흡연 군과 발병 나이와 발병 유형을 보정한 25명의 비흡연군을 비교하였을 때, 파킨슨 병 운동 점수 (14.8점 Vs. 20.3점, *p=0.032*)와 파킨슨 병 운동 점수의 진행 정도 (3.4점/년Vs. 5.1점/년, *p=0.037*)는 지속적으로 흡연 군이 비흡연군보다 유의하게 낮음을 알 수 있었다.

결론: 본 연구는 남성 파킨슨 병 환자에서 파킨슨 병의 발병 이후의 지속적인 흡연이 파킨슨 병의 진행을 늦출 수 있다는 것을 보였으며, 파킨슨 병의 발병 나이 역시 중요한 인자였다. 발병 연령의 보정 이후에도 지속적으로 흡연은 파킨슨 병의 진행을 늦추어 주었다.

핵심어: 파킨슨 병, 흡연, 파킨슨 병의 진행