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Smoking and Cognitive Function in Parkinson's Disease

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Abstract: The risk of dementia among Parkinson's disease (PD) patients is greatly elevated compared to controls, yet little is known about determinants of cognitive function among PD patients. We assessed the relation between cigarette smoking prior to disease onset and later cognitive function among PD patients (n = 286) and age- and sex-matched controls (n = 1144) participating in the Nurses' Health Study and Health Professionals Follow-up Study. Both groups completed telephone-administered assessments of cognitive function. We used linear regression to calculate mean differences in cognitive test scores across smoking categories, adjusted for age, education, sex, age at onset of PD, and years since diagnosis. PD patients scored significantly worse on all tests than their matched controls. In analyses only among PD cases, but not among controls, current smokers at PD onset scored worse than never smokers on the Telephone Interview for Cognitive Status (difference = −0.82, 95% CI: −1.33, −0.30, $P = 0.002$) as well as on a global score combining results of all tests (difference = −0.36, 95% CI: −0.72, 0.01, $P = 0.06$). This difference was equivalent to the difference in global score observed among controls ~10 years apart in age. Analyses of pack-years of smoking prior to disease onset gave similar results. These findings, nested in prospective cohort studies, suggest that cigarette smoking prior to disease onset is associated with worse cognitive function in PD. © 2007 Movement Disorder Society

Key words: Parkinson's disease; cognitive function; smoking; prospective studies; epidemiology; risk factors.

The risk of dementia among Parkinson's disease (PD) patients is up to 6 times greater than in healthy controls[1-3] with accompanying increased risk for institutionalization, mortality, and caregiver distress.[4-6] Nonetheless, research into risk factors for dementia or cognitive impairment in PD has been relatively limited.[7,8]

There are several reasons to believe that cigarette smoking may impact cognitive function in PD. Nicotine is neuroprotective in many in vitro and in vivo experimental settings, and in animal experiments has been found to improve performance in learning and memory tasks.[9] Cigarette smoking is also the most consistent risk factor other than age for PD, with regular long time smokers having less than one third the risk of PD as never smokers.[10,11] Although early studies were somewhat inconclusive as to the association between cigarette smoking and risk of Alzheimer's disease (AD),[12] more recent cohort studies suggest that smoking increases the risk of AD.[13-15] Smoking also increases inflammation, thrombosis, and oxidative stress and as a result is strongly associated with cardiovascular damage[16]; substantial data indicate that vascular disease is related to cognitive impairment. Studies of nondemented elderly have had somewhat inconsistent results, although the more recent large studies suggest a slightly greater cognitive decline among smokers.[17-22] Two early case-control studies did not find an association between cigarette smoking and dementia in PD, although two subsequent longitudinal studies did.[23-26] Both of the longitudinal studies enrolled prevalent cases, which can influence study results depending on survival patterns of individuals with PD. Since cognitive impairment is a strong

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predictor of dementia risk, the aim of our study was to assess the association between cigarette smoking prior to PD and cognitive function among PD patients in the Nurses' Health Study (NHS) and Health Professionals Follow-Up Study (HPFS), in which we had identified incident cases of PD.

PATIENTS AND METHODS

Study Population

The NHS was established in 1976 when 121,700 female registered nurses, aged 30 to 55 years and from 11 US states, responded to a mailed questionnaire about disease history and lifestyle. The HPFS was established in 1986, when 51,529 male health professionals (dentists, optometrists, pharmacists, osteopaths, podiatrists, and veterinarians), aged 40 to 75 years and from all US states, responded to a similar questionnaire. Follow-up questionnaires are mailed to participants every two years to update information on potential risk factors for chronic diseases and to ascertain whether major medical events have occurred. All incident PD cases identified through the 2000 (NHS) and 2002 (HPFS) questionnaires who had no cancer at the cohort baseline nor history of stroke at any time and were still alive were considered eligible for the study. For each confirmed case of PD, we randomly selected four controls among members of the two cohorts who had no report of PD and met the same inclusion criteria as the cases. The controls were matched on year of birth and sex.

We selected 215 cases and 901 controls from the NHS into our cognitive study. Of these, 16 cases and 20 controls were either too sick or deceased by the time we attempted to reach them or we were unable to reach them by phone (n = 19 cases and 74 controls). Of the remaining 180 cases and 807 controls, 149 (82.8%) and 678 (84.0%), respectively, participated in the telephone cognitive interviews. We selected 225 cases and 732 controls from the HPFS into our cognitive study. Of these, 29 cases and 35 controls were either too sick or deceased by the time we attempted to reach them or we were unable to reach them by phone (n = 35 cases and 89 controls). Of the remaining 161 cases and 608 controls, 137 (85.1%) and 466 (76.6%), respectively, participated in the telephone cognitive interviews. All interviewed participants gave consent to participate.

PD Case Ascertainment

Ascertainment of the PD cases in this cohort has been described previously.[27] In brief, for cohort participants who reported a new diagnosis of PD we obtained permission to contact their treating neurologist (or internist if the neurologist did not respond). We asked the contacted physician to complete a questionnaire to confirm the diagnosis of PD and the certainty of the diagnosis, or to send a copy of the medical record. A case was confirmed if a diagnosis of PD was considered definite or probable by the treating neurologist (82%) or internist (15%), or if the medical record included either a final diagnosis of PD made by a neurologist, or evidence at a neurological examination of at least two of the three cardinal signs (rest tremor, rigidity, bradykinesia) in the absence of features suggesting other diagnoses (3%). The review of medical records was conducted by the investigators, blind to the exposure status. Deaths in the cohort were reported by family members, coworkers or postal authorities, or were identified by searching the National Death Index. If PD was listed as a cause of death on the death certificate, we requested permission from the family to contact the treating neurologist or physician and followed the same procedure as for the nonfatal cases.

Assessment of Cognitive Function

As part of a separate investigation of cognitive function among NHS participants, ~20,000 healthy NHS participants over the age of 70 have been interviewed over the telephone by nurses trained to conduct these interviews. As part of the current study, we used, if available, the results of the cognitive testing that had already been done (between 1995 and 2002). Cases and controls who had not already been tested, were contacted by telephone and tested in the same manner. The interview included the following cognitive tests: Telephone Interview for Cognitive Status[28] (TICS), delayed recall of a 10-word list, the East Boston Memory Test[29] (EBMT, immediate and delayed recall), digit span backwards,[30] and verbal fluency.[31]

The TICS is modeled on the Mini-Mental State Examination[32] (MMSE) and a strong linear relation has been shown between performance on the two (Pearson correlation = 0.94).[28] Scores on the TICS can range from 0 to 42. For the EBMT, a short story is read to the respondent. Twelve key elements must be repeated immediately and scores range from 0 to 12; a test of delayed recall is given 15 min later also scored 0 to 12. To further assess verbal memory, we included a delayed recall of a 10-word list, scored 0 to 10. For the digit span backwards test, sequences of digits are read to the respondent who must recall them in backward order. Digit span backwards scores range from 0 to 12. In the test of verbal fluency, participants name as many animals as they can during 1 min, and their score is the number of animals named.

Substantial data support the validity of telephone tests of cognitive function. The test-retest reliability on the TICS is 0.97,[28] and reported correlations are 0.85 to 0.96 for comparison of telephone and in-person administrations.[33,34] In a validation study we conducted among 61 nuns from the Rush Religious Orders Study, women of similar age and educational status as the NHS participants, a correlation of 0.81 was found when comparing the global score from the telephone-administered interview to the global score from an in-person interview.[35]

Statistical Analyses

Our primary outcome was a global score of cognitive function calculated for those participants who completed all tests. This global score was calculated by converting results from each test to z scores, defined as the difference between the participant's score on that test and the mean score among all participants, divided by the standard deviation. The z scores corresponding to each test were then added together and the total was divided by the number of tests to calculate a global score for each participant. In addition, each of the cognitive tests was examined separately. Multiple factors are likely to be related to cognitive function, including age at cognitive interview, age at PD diagnosis, and duration of PD. Because these variables are collinear, it is not possible to fit regression models to estimate the independent association between each variable and cognitive function. Therefore, we calculated an age-adjusted score on each test (and the global score) for all subjects by taking the difference between a subject's actual score and the predicted score based on an ordinary least squares regression of cognitive score as a function of age at interview among the controls. Differences in scores between cases and controls were assessed with random effects models to account for the matching between cases and controls. Ordinary least squares regression was then used to examine the association between smoking variables and continuous age-adjusted cognitive test scores first among the cases only, adjusted for sex, education (RN, BA, or postgraduate degree), age of onset of PD (in years), and duration (in years) of PD (for interviewed cases this was the time between onset and the cognitive interview). Additional analyses were run also adjusting for alcohol consumption (none, <5 g/day, 5–10 g/day, and >10 g/day) from the most recent NHS and HPFS data (1998) and physical activity (quartiles of mets/day) from the 1986 questionnaires. We also ran logistic regression models for the odds of scoring in the lowest 10% of the global score and each individual test. Such a population-based 10% cutpoint is a valid predictor of cognitive impairment. The same covariates as mentioned earlier were included in these models. For women, we ran additional analyses adjusting for the highest educational attainment of their spouses (high school or less, college, graduate school, or missing), since spouses' education is likely a reasonable marker of their socioeconomic status. Smoking was considered as never, past or current smoker at the time of onset of PD, or lifetime pack-years of smoking at that time. There was little change in this status after PD onset: among all never smokers at PD onset, 1 case reported smoking 10 years later; among all past smokers at PD onset, only 2 cases subsequently reported smoking (2 and 8 years later); and among all current smokers at PD onset, 5 cases reported quitting by 2 years later, and 1 case reported quitting 8 years later. To test for a difference in this association between male and female PD cases, interaction terms between sex and the smoking variables were added to the models. To test for a difference between cases and controls, we ran models with all subjects that included a term for case control status and an interaction term between the smoking variables and case-control status.

RESULTS

Among NHS and HPFS participants selected into our study, those cases and controls who were interviewed for cognitive testing and those who were not had similar smoking history and caffeine intake, although cases who were not interviewed were slightly older and had a slightly longer duration of PD (Table 1). As expected, among participants cases smoked less than controls. Characteristics of interviewed cases by smoking status are shown in Table 2.

The difference in cognitive performance between PD cases and their matched controls was highly significant ($P < 0.0001$) for all tests (Fig. 1). Among the cases, the mean difference compared with never smokers in global score was -0.09 for past smokers [95% confidence interval (CI): -0.26, 0.07; $P = 0.26$] and -0.36 for current smokers (95% CI: -0.72, 0.01, $P = 0.06$) (Fig. 2). The difference in global score between current smokers and never smokers with PD was approximately equivalent to the average difference in global score between study controls 10 years apart in age. Current smokers performed worse than never smokers on all tests, most significantly on the TICS (difference $= -0.82$, 95% CI: -1.33, -0.30, $P = 0.002$). Scores of past smokers were also worse than never smokers, but not to the extent of current smokers (Fig. 2). Additionally adjusting for alcohol and physical activity did not markedly change results. Results using continuous pack-years as the smoking variable were similar: the effect estimate

TABLE 1. *Baseline characteristics[a] by case and participation status among all subjects selected into study*

	Interviewed			
	Cases		Control	
	Yes (n = 286)	No (n = 154)	Yes (n = 1144)	No (n = 489)
Male (% of all men)	47.9	57.1	40.7	54.4
Smoking (%)				
Never smoker	53.8	54.5	43.6	43.7
Past smoker	38.9	41.2	42.1	42.8
Current	5.6	4.0	12.6	11.7
Missing	1.7	0.4	1.7	1.8
Pack-years (mean)	22.5	19.0	26.1	27.7
Caffeine intake (mean mg/day)	187	180	225	225
Education,[b] highest degree attained (%)				
RN	71.5	71.5	69.6	61.4
BA	19.2	14.5	21.5	13.2
Postgraduate	9.3	2.8	8.6	5.0
Missing	0	11.2	0	20.5
PD duration[c] (yr)	6.4	8.0	–	–
Mean age in 2000 (yr) (SD)	71.9 (6.5)	74.4 (7.7)	72.2 (6.5)	72.1 (8.3)

[a]At time of PD onset or equivalent year for matched controls. All variables, except age and sex, are age-adjusted by direct standardization to all participants.

[b]Among women only. There is more missing data among noninterviewed women because we collected extra education data at the time of the interview. All men had postgraduate degrees.

[c]From onset of PD to the time the letter of invitation into study was sent.

for the global score per 10 pack-years of smoking was −0.05 (95% CI: −0.09, 0.00).

The results for the global score were effectively unchanged when the verbal fluency score was excluded, which relies on speed of word production and therefore could be affected by bradykinesia. In addition, there was no significant interaction between smoking status and sex among PD cases, and in analyses among women only, additional adjustment for spousal education level had almost no effect on the smoking estimates. In logistic regression models, current smokers had an odds ratio (OR) of 3.3 (95% CI: 1.1–10.4; $P = 0.04$) for cognitive impairment on the global score. These results for odds of cognitive impairment showed overall a similar pattern of results as those for mean differences in cognitive function. The association between current smoking and cognitive test results among PD cases was significantly different from that among PD controls for TICS ($P = 0.0004$) and the immediate EBMT ($P = 0.05$), and approached a significant difference for the global score ($P = 0.07$) and the delayed EBMT ($P = 0.12$).

DISCUSSION

In this study of incident PD cases within two large prospective cohort studies we found that current smokers at PD onset had a markedly worse global cognitive

TABLE 2. *Characteristics[a] of interviewed cases by smoking status*

	Smoking Status		
	Never (n = 153)	Past (n = 112)	Current (n = 16)
Male (%)	50.3	45.5	25.0
Age at onset of PD (yr) (SD)	66.7 (7.6)	67.1 (7.9)	65.3 (7.8)
Age at interview (yr) (SD)	74.1 (6.3)	73.9 (6.0)	73.1 (6.5)
PD duration[b] (mean yr) (SD)	7.3 (4.1)	6.8 (4.2)	8.0 (4.7)
Education,[c] highest degree attained (%)			
RN	75.5	68.2	50.9
BA	15.7	21.9	39.0
Postgraduate	8.8	10.0	10.1
Pack-years of smoking	0	20.2	37.8
Caffeine (mg/day)	179	209	256

[a]Education, smoking, and caffeine variables are from the time of PD onset. Education, smoking, and caffeine variables are age adjusted by direct standardization to all cases.

[b]From onset of PD to the time of cognitive testing.

[c]Among women only. All men had postgraduate degrees.

function score about 6 years after PD onset than never smokers. The difference in cognitive function between smokers and never smokers was approximately equivalent to the difference in cognitive function that we observed in our healthy participants who were 10 years apart in age; that is, cigarette smoking among PD patients appeared to be cognitively equivalent to 10 more years of age among our controls. These results are not likely the result of motor speed impairment as the only test with significant motor speed demands was the verbal fluency test and the results were virtually the same for the global score when this test was removed from analysis.

Because the NHS and HPFS are comprised of people from across the US, we assessed participants' cognitive function with telephone interviews. We found high correlation between telephone and in-person cognitive testing.[35] Nonetheless, telephone cognitive assessment does not allow for the testing of some cognitive domains, such as visual information processing. Visuospatial deficits have been commonly reported in PD patients, although these may be secondary to executive function deficits, which are perhaps the most frequently reported deficit among PD patients.[7] However, executive function deficits would also be expected to affect performance in other cognitive domains, such as the verbal fluency task and the digit span backwards test we administered. The assessment of cognitive function by telephone also meant that we did not have data on other symptoms of PD nor neuroimaging data that might be related to cognitive function. We were also limited by the inability to obtain cognitive data on all incident cases in the cohorts because of death or other nonparticipation. However, there was little difference in smoking characteristics between participating and nonparticipating PD cases. Lastly, we had only a single assessment of cognition, thus we could not determine whether smoking may be related to change in cognitive function over time. Because of this, we cannot determine whether the difference in cognitive function between smokers and nonsmokers is already present at the time of diagnosis or occurs as a result of more rapid decline in cognitive function after PD onset.

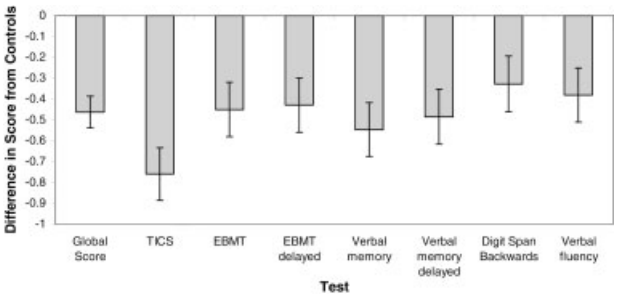

FIG. 1. Age-adjusted global score and standardized age-adjusted individual test scores among all interviewed Parkinson's disease cases relative to their matched controls. Standardization was done by dividing a subject's score on a given test by the standard deviation of scores on that test among all participants. All differences were significant at $P < 0.0001$. TICS, Telephone Interview for Cognitive Status; EBMT, East Boston Memory Test. Mean raw scores on the TICS, EBMT, delayed EBMT, delayed word recall, digit span backwards, and verbal fluency for cases/controls were 31.7/33.8, 8.8/9.6, 8.2/9.1, 1.4/2.3, 5.7/6.3, and 16.2/18.1, respectively.

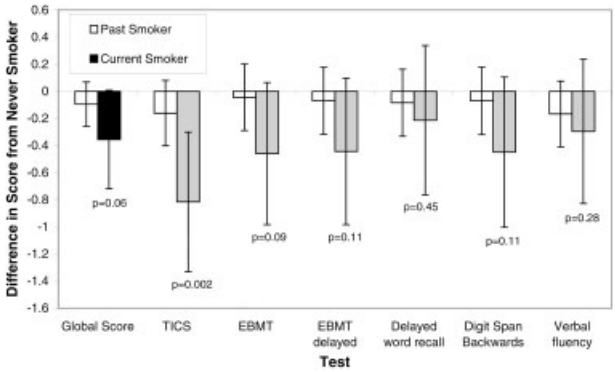

FIG. 2. Age-adjusted global score and standardized age-adjusted individual test scores among all interviewed Parkinson's disease (PD) cases relative to never smokers for past (open bars) and current (stippled bars) smokers at the time of PD onset, adjusted for sex, education, age at onset of PD, and duration of PD. Standardization was done by dividing a subject's score on a given test by the standard deviation of scores on that test among all cases. TICS, Telephone Interview of Cognitive Status; EBMT, East Boston Memory Test.

Although no previous studies have examined cognition, the association between smoking and risk of dementia among PD patients has been examined in two previous studies. In the first of these,[23] which included 100 PD patients, the OR for dementia was 4.0 (95% CI: 1.4–12.0) for smokers compared with nonsmokers (asked as a yes/no question). In a more recent study,[25] among 180 nondemented PD patients followed for an average of 3.6 years, the risk ratio was 2.0 (95% CI: 1.0–3.9) for ever smokers compared with never smokers, adjusting for age at baseline, gender, years of education, duration of PD, and total UPDRS motor score; the multivariate risk ratio for current smokers compared with never smokers was 4.5 (95% CI: 1.2–16.4). The opposite association of smoking and cognitive function in PD than of smoking and risk of developing PD itself is intriguing. A possible interpretation is that the onset of PD renders patients more susceptible to some adverse effects of smoking. This could be related to vascular complications and subclinical brain infarcts,[16] or increased oxidative stress in the central nervous system (CNS).[36] Another possibility is that smoking exerts selective neuroprotective effects on the dopaminergic neurons in the substan-

tia nigra without protecting other areas of the CNS that are more directly involved in cognitive function. Because the diagnosis of PD relies on the motor manifestations, by the time of diagnosis smokers could have more widespread nonmotor signs of disease. Finally, because PD is rare among smokers, the positive predictive value of a diagnosis of PD among smokers is probably lower than among nonsmokers. Some smokers with PD could in fact have other neurodegenerative conditions with a more pronounced cognitive component than PD, and thus contribute to lower the global cognitive score in this group. In summary, these findings, nested in prospective cohort studies, suggest that cigarette smoking prior to disease onset is associated with worse cognitive function at older ages in PD.

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REFERENCES

1. Aarsland D, Andersen K, Larsen JP, Lolk A, Nielsen H, Kragh-Sorensen P. Risk of dementia in Parkinson's disease: a community-based, prospective study. Neurology 2001;56:730-736.
2. Marder K, Tang MX, Cote L, Stern Y, Mayeux R. The frequency and associated risk factors for dementia in patients with Parkinson's disease. Arch Neurol 1995;52:695-701.
3. Mayeux R, Chen J, Mirabello E, et al. An estimate of the incidence of dementia in idiopathic Parkinson's disease. Neurology 1990;40: 1513-1517.
4. Aarsland D, Larsen JP, Karlsen K, Lim NG, Tandberg E. Mental symptoms in Parkinson's disease are important contributors to caregiver distress. Int J Geriatr Psychiatry 1999;14:866-874.
5. Aarsland D, Larsen JP, Tandberg E, Laake K. Predictors of nursing home placement in Parkinson's disease: a population-based, prospective study. J Am Geriatr Soc 2000;48:938-942.
6. Louis ED, Marder K, Cote L, Tang M, Mayeux R. Mortality from Parkinson disease. Arch Neurol 1997;54:260-264.
7. Levin BE, Katzen HL. Early cognitive changes and nondementing behavioral abnormalities in Parkinson's disease. Adv Neurol 2005; 96:84-94.
8. Rippon GA, Marder KS. Dementia in Parkinson's disease. Adv Neurol 2005;96:95-113.
9. Picciotto MR, Zoli M. Nicotinic receptors in aging and dementia. J Neurobiol 2002;53:641-655.
10. Grandinetti A, Morens DM, Reed D, MacEachern D. Prospective study of cigarette smoking and the risk of developing idiopathic Parkinson's disease. Am J Epidemiol 1994;139:1129-1138.
11. Hernan MA, Zhang SM, Rueda-deCastro AM, Colditz GA, Speizer FE, Ascherio A. Cigarette smoking and the incidence of Parkinson's disease in two prospective studies. Ann Neurol 2001;50:780-786.
12. Almeida OP, Hulse GK, Lawrence D, Flicker L. Smoking as a risk factor for Alzheimer's disease: contrasting evidence from a systematic review of case-control and cohort studies. Addiction 2002; 97:15-28.
13. Launer LJ, Andersen K, Dewey ME, et al. Rates and risk factors for dementia and Alzheimer's disease: results from EURODEM pooled analyses. EURODEM Incidence Research Group and Work Groups. European Studies of Dementia. Neurology 1999;52:78-84.
14. Merchant C, Tang MX, Albert S, Manly J, Stern Y, Mayeux R. The influence of smoking on the risk of Alzheimer's disease. Neurology 1999;52:1408-1412.
15. Ott A, Slooter AJ, Hofman A, et al. Smoking and risk of dementia and Alzheimer's disease in a population-based cohort study: the Rotterdam Study. Lancet 1998;351:1840-1843.
16. Ambrose JA, Barua RS. The pathophysiology of cigarette smoking and cardiovascular disease: an update. J Am Coll Cardiol 2004; 43:1731-1737.
17. Ford AB, Mefrouche Z, Friedland RP, Debanne SM. Smoking and cognitive impairment: a population-based study. J Am Geriatr Soc 1996;44:905-909.
18. Galanis DJ, Petrovitch H, Launer LJ, Harris TB, Foley DJ, White LR. Smoking history in middle age and subsequent cognitive performance in elderly Japanese-American men. The Honolulu-Asia Aging Study. Am J Epidemiol 1997;145:507-515.
19. Hebert LE, Scherr PA, Beckett LA, et al. Relation of smoking and low-to-moderate alcohol consumption to change in cognitive function: a longitudinal study in a defined community of older persons. Am J Epidemiol 1993;137:881-891.
20. Kalmijn S, van Boxtel MP, Verschuren MW, Jolles J, Launer LJ. Cigarette smoking and alcohol consumption in relation to cognitive performance in middle age. Am J Epidemiol 2002;156:936-944.
21. Launer LJ, Feskens EJ, Kalmijn S, Kromhout D. Smoking, drinking, and thinking. The Zutphen Elderly Study. Am J Epidemiol 1996;143:219-227.
22. Ott A, Andersen K, Dewey ME, et al. Effect of smoking on global cognitive function in nondemented elderly. Neurology 2004;62: 920-924.
23. Ebmeier KP, Calder SA, Crawford JR, Stewart L, Besson JA, Mutch WJ. Clinical features predicting dementia in idiopathic Parkinson's disease: a follow-up study. Neurology 1990;40:1222-1224.
24. Glatt SL, Hubble JP, Lyons K, et al. Risk factors for dementia in Parkinson's disease: effect of education. Neuroepidemiology 1996; 15:20-25.
25. Levy G, Tang MX, Cote LJ, et al. Do risk factors for Alzheimer's disease predict dementia in Parkinson's disease? An exploratory study. Mov Disord 2002;17:250-257.
26. Marder K, Flood P, Cote L, Mayeux R. A pilot study of risk factors for dementia in Parkinson's disease. Mov Disord 1990;5:156-161.
27. Ascherio A, Zhang SM, Hernan MA, et al. Prospective study of caffeine consumption and risk of Parkinson's disease in men and women. Ann Neurol 2001;50:56-63.
28. Brandt J, Spencer M, Folstein M. The telephone interview for cognitive status. Neuropsychiatry Neuropsychol Behav Neurol 1988;1:111-117.
29. Albert M, Smith LA, Scherr PA, Taylor JO, Evans DA, Funkenstein HH. Use of brief cognitive tests to identify individuals in the community with clinically diagnosed Alzheimer's disease. Int J Neurosci 1991;57:167-178.
30. Lezak M. Neuropsychological assessment, 3rd ed. New York: Oxford University Press; 1995.
31. Morris JC, Heyman A, Mohs RC, et al. The Consortium to Establish a Registry for Alzheimer's Disease (CERAD). I. Clinical and neuropsychological assessment of Alzheimer's disease. Neurology 1989;39:1159-1165.
32. Folstein MF, Folstein SE, McHugh PR. "Mini-Mental State". A practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res 1975;12:189-198.
33. Kawas C, Karagiozis H, Resau L, Corrada M, Brookmeyer R. Reliability of the Blessed Telephone Information-Memory-Concentration Test. J Geriatr Psychiatry Neurol 1995;8:238-242.
34. Roccaforte WH, Burke WJ, Bayer BL, Wengel SP. Validation of a telephone version of the mini-mental state examination. J Am Geriatr Soc 1992;40:697-702.
35. Stampfer MJ, Kang JH, Chen J, Cherry R, Grodstein F. Effects of moderate alcohol consumption on cognitive function in women. N Engl J Med 2005;352:245-253.
36. Jenner P. Oxidative stress in Parkinson's disease. Ann Neurol 2003;53 (Suppl 3):S26–S36, discussion S36–S28.