Intake of Japanese and Chinese teas reduces risk of Parkinson's disease

Keiko Tanaka a,*, Yoshihiro Miyake a, Wakaba Fukushima b, Satoshi Sasaki c, Chikako Kiyo-hara d, Yoshio Tsuboi e, Tatsuo Yamada e, Tomoko Oeda f, Takami Miki g, Nobutoshi Kawamura h, Nobutaka Sakae h, Hidenao Fukuyama i, Yoshio Hirot a b, Masaki Nagai j, the Fukuoka Kinki Parkinson's Disease Study Group 1

a Department of Public Health, Faculty of Medicine, Fukuoka University, Fukuoka 814-0180, Japan
b Department of Public Health, Osaka City University Graduate School of Medicine, Osaka, Japan
c Department of Social and Preventive Epidemiology, School of Public Health, The University of Tokyo, Tokyo, Japan
d Department of Preventive Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
e Department of Neurology, Faculty of Medicine, Fukuoka University, Fukuoka, Japan
f Department of Neurology, Utano National Hospital, Kyoto, Japan
g Department of Geriatric Medicine, Osaka City University Graduate School of Medicine, Osaka, Japan
h Department of Neurology, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
i Human Brain Research Center, Kyoto University Graduate School of Medicine, Kyoto, Japan
j Department of Preventive Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan
1 Department of Public Health, Saitama Medical University, Faculty of Medicine, Saitama, Japan

ARTICLE INFO

Article history:
Received 24 December 2010
Received in revised form 25 February 2011
Accepted 25 February 2011

Keywords:
Caffeine
Case-control studies
Coffee
Japan
Parkinson's disease

ABSTRACT

Studies that have addressed the association between the intake of coffee or caffeine and Parkinson's disease (PD) were conducted mainly in Western countries. Little is known about this relationship in an Asian population. Therefore, we performed an assessment of the association of the intake of coffee, other caffeine-containing beverages, and caffeine with the risk of PD in Japan. The study involved 249 PD cases and 368 control subjects. Information on dietary factors was obtained through a self-administered diet history questionnaire. Adjustment was made for sex, age, region of residence, educational level, pack-years of smoking, body mass index, the dietary glycemic index, and intake of cholesterol, vitamin E, β-carotene, vitamin B6, alcohol, and iron. Intake of coffee, black tea, and Japanese and Chinese teas was significantly inversely associated with the risk of PD: the adjusted odds ratios in comparison of the highest with the lowest quartile were 0.52, 0.58, and 0.59, respectively (95% confidence intervals = 0.30–0.90, 0.35–0.97, and 0.35–0.995, respectively). A clear inverse dose–response relationship between total caffeine intake and PD risk was observed. We confirmed that the intake of coffee and caffeine reduced the risk of PD. Furthermore, this is the first study to show a significant inverse relationship between the intake of Japanese and Chinese teas and the risk of PD.

© 2011 Elsevier Ltd. All rights reserved.

1. Introduction

The causes of Parkinson’s disease (PD) are unknown. But both genetic and environmental factors with complex interactions are thought to be responsible for the development and progression of the disease [1,2]. The results of studies of twins suggested that genetic factors are important in early-onset PD cases while environmental factors play a predominant etiologic role in late-onset PD patients [3,4]. There has been increasing evidence of a reduced risk of PD among coffee drinkers [5–11]. A meta-analysis by Hernán et al. showed that the risk of PD is about 30% lower among coffee drinkers than among non-coffee drinkers [12]. The most recent meta-analysis based on 26 studies also showed an inverse association between caffeine intake and the risk of PD (pooled relative risk = 0.75) [13]. Investigations on the association between intake of coffee or caffeine and PD were conducted mainly in the USA and in Europe [5–9,11,14–17]. Relatively little is known about such relationships in Asian populations [10,18,19]. It is necessary to accumulate further evidence of the influence of the intake of coffee and caffeine on PD among Asian populations. In addition, investigations of the association between caffeine-containing beverage other than coffee, such as black tea and green tea, and the risk of PD are sparse, and what information is available has been conflicting [5,9,10,14,15,18,19]. In the Singapore Chinese Health study, a prospective cohort study, consumption of black tea and daily drinks reduces the risk of PD [17].
were within 6 years of the onset of PD whereas no association between consumption of coffee and green tea and PD risk was observed [18]. A case-control study in France showed that tea consumption was a risk factor for PD [14]. In the present case-control study of PD among Japanese, we investigated the association between the consumption of coffee, other caffeine-containing beverages, and caffeine and the risk of PD.

2. Methods

2.1. Study subjects

Patients with PD were recruited at 3 university hospitals and 1 national hospital in Fukuoka Prefecture, a metropolitan area of Kyushu Island in southern Japan, and in 3 university hospitals, 1 national hospital and 1 municipal hospital in Osaka, Kyoto, and Wakayama Prefectures, which are part of the Kinki region, which is located in the midwestern part of the mainland. Eligible cases were patients who were within 6 years of the onset of PD and who had been diagnosed by the collaborating neurologists according to the United Kingdom Parkinson’s Disease Society Brain Bank clinical diagnostic criteria (steps 1 and 2) [20]. The neurologists in charge asked eligible PD patients to take part in our case-control study. Of 298 eligible PD patients identified during the period from 1 April 2006 to 31 March 2008, 250 agreed to participate in the study (response rate: 84%).

During the same period, control subjects, without a previous diagnosis of a neurodegenerative disease, were recruited from departments other than the department of neurology in 3 of the 11 collaborating hospitals: 1 university hospital in Fukuoka Prefecture and 1 university hospital and 1 national hospital in the Kinki region (orthopedic surgery, ophthalmology, otorhinolaryngology, plastic surgery, and oral surgery). Control subjects were not, individually or in larger groups, matched to cases. When a potential control subject was seen as an outpatient or was hospitalized in any of these 3 hospitals, that individual was asked by an attending doctor or one of our research nurses to participate in our case-control study as a control subject. Finally, 372 of the potential control subjects participated in our study whereas 156 refused (response rate: 70%).

Excluded were 1 case and 4 control subjects because of missing data on the factors under investigation, leaving data on 249 cases and 368 control subjects available for analysis. The ethics committees of the 11 collaborating hospitals approved our case–control study (Faculty of Medicine, Fukuoka University; Utano National Hospital; Osaka City University Graduate School of Medicine; Graduate School of Medical Sciences, Kyushu University; Wakayama Medical University; Kyoto University Graduate School of Medicine; Kurume University School of Medicine; Minami-Kyoto National Hospital; Toneyama National Hospital; Kyoto City Hospital; and National Omuta Hospital). Written informed consent was obtained from all subjects.

2.2. Data collection

Participants filled out a set of 2 self-administered questionnaires and mailed these materials to the data management center or handed them to research nurses. Our research technicians completed missing answers and/or illlogical data by telephone or direct interview.

Dietary habits during the preceding month were assessed using a self-administered, semi-quantitative, comprehensive, diet history questionnaire (DHQ). Estimates of daily intake of foods (150 items in total), energy, and selected nutrients were calculated using an ad hoc computer algorithm for the DHQ based on the Standard Tables of Food Composition in Japan [21,22]. In the current study, coffee, black tea, and Japanese and Chinese teas, including green tea and oolong tea, were used for estimation of total caffeine intake because the major contributors to total caffeine intake in the diet of Japanese subjects was shown to be coffee (women: 46.7%, men: 47.1%), Japanese and Chinese teas (women: 47.1%, men: 47.4%), and black tea (women: 4.3%, men: 3.0%) [23]. In a validation study of 92 Japanese women and 92 Japanese men, Pearson’s correlation coefficients between the DHQ and 16-dietary recall dietary records were 0.43 and 0.38 for caffeine, 0.43 and 0.51 for cholesterol, 0.50 and 0.58 for the dietary glycemic index, 0.39 and 0.50 for vitamin E, 0.64 and 0.38 for β-carotene, 0.66 and 0.56 for vitamin B₆, 0.64 and 0.82 for alcohol, and 0.65 and 0.47 for iron, respectively (S Sasaki, unpublished observations, 2006). Energy-adjusted intake by the residual method was used for the analyses except for the dietary glycemic index [24]. Body mass index was calculated as weight (kg) divided by the square of height (m)².

A second questionnaire elicited information on sex, age, educational level, and smoking habits. This questionnaire was developed for this survey based on a comprehensive literature review of epidemiological studies on risk factors for PD, and its validity has not been investigated.

2.3. Statistical analysis

Intake of coffee, other caffeine-containing beverages, and caffeine was categorized at quartile points based on the distribution of intake among control subjects.

### Table 1

#### Characteristics of Parkinson’s disease cases and control subjects.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases, n = 249</th>
<th>Controls, n = 368</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male)</td>
<td>93 (37.4)</td>
<td>141 (38.2)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>68.5 (8.6)</td>
<td>66.6 (8.5)</td>
</tr>
<tr>
<td>Region of residence</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KinKi</td>
<td>160 (64.3)</td>
<td>214 (58.2)</td>
</tr>
<tr>
<td>Fukuoka</td>
<td>89 (35.7)</td>
<td>154 (41.9)</td>
</tr>
<tr>
<td>Educational level (years)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;10</td>
<td>51 (20.5)</td>
<td>77 (20.9)</td>
</tr>
<tr>
<td>10–12</td>
<td>122 (49.0)</td>
<td>171 (46.5)</td>
</tr>
<tr>
<td>≥13</td>
<td>76 (30.5)</td>
<td>120 (32.6)</td>
</tr>
<tr>
<td>Pack-years of smoking</td>
<td></td>
<td></td>
</tr>
<tr>
<td>None</td>
<td>185 (74.3)</td>
<td>222 (60.3)</td>
</tr>
<tr>
<td>0.1–29.9</td>
<td>37 (14.9)</td>
<td>65 (17.7)</td>
</tr>
<tr>
<td>30.0+</td>
<td>27 (10.8)</td>
<td>81 (22.0)</td>
</tr>
<tr>
<td>Daily intake*</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total energy (kcal)</td>
<td>2016.1 (630.2)</td>
<td>1995.4 (733.2)</td>
</tr>
<tr>
<td>Coffee (g)</td>
<td>119.0 (138.8)</td>
<td>172.7 (207.7)</td>
</tr>
<tr>
<td>Black tea (g)</td>
<td>23.8 (95.3)</td>
<td>27.8 (81.5)</td>
</tr>
<tr>
<td>Japanese and Chinese teas (g)</td>
<td>507.2 (407.1)</td>
<td>591.8 (452.0)</td>
</tr>
<tr>
<td>Caffeine (mg)</td>
<td>287.2 (193.8)</td>
<td>358.7 (224.0)</td>
</tr>
<tr>
<td>Dietary glycemic index</td>
<td>65.1 (4.7)</td>
<td>65.4 (5.3)</td>
</tr>
<tr>
<td>Cholesterol (mg)</td>
<td>331.3 (129.5)</td>
<td>300.9 (132.5)</td>
</tr>
<tr>
<td>Vitamin E (mg)</td>
<td>8.5 (2.4)</td>
<td>8.4 (2.9)</td>
</tr>
<tr>
<td>β-carotene (mg)</td>
<td>3021.7 (1630.9)</td>
<td>3126.0 (2024.7)</td>
</tr>
<tr>
<td>Vitamin B₆ (mg)</td>
<td>1.3 (0.4)</td>
<td>1.3 (0.4)</td>
</tr>
<tr>
<td>Alcohol (g)</td>
<td>5.5 (15.4)</td>
<td>10.0 (25.8)</td>
</tr>
<tr>
<td>Iron (mg)</td>
<td>7.5 (1.9)</td>
<td>7.6 (2.2)</td>
</tr>
</tbody>
</table>

* Nutrient and food intake were adjusted for total energy intake using the residual method except for the dietary glycemic index.

Logistic regression analysis was used to estimate crude odds ratios (ORs) and 95% confidence intervals (CIs) for PD relative to the quartile of dietary exposure variables under study, with the lowest quartile as the reference. Multiple logistic regression analysis was used to control for confounding factors. Sex, age, region of residence, educational level, pack-years of smoking, body mass index, glycemic index, and intake of cholesterol, vitamin E, β-carotene, vitamin B₆, alcohol, and iron were used as confounding variables. Smoking, intake of cholesterol, vitamin E, β-carotene, and vitamin B₆ and the dietary glycemic index were significantly associated with PD in this population. The following factors were classified: region of residence (Fukuoka and KinKi); educational level (<10, 10–12, ≥13 years); and pack-years of smoking (0, 0.1–9.9, and ≥10.0). Age, body mass index, the dietary glycemic index, and intake of cholesterol, vitamin E, β-carotene, vitamin B₆, alcohol, and iron were used as continuous variables. The trend of association was assessed by a logistic regression model assigning ordinal scores to the quartile of the exposure variables. Two-sided P values less than 0.05 were considered statistically significant. All analyses were performed using the SAS software package version 9.2 (SAS Institute, Inc., Cary, NC, USA).

3. Results

The mean age of the 249 PD cases at onset was 65.3 years (standard deviation, 8.7 years), and the mean duration of PD was 3.2 years (standard deviation, 1.5 years). About 66% of cases (n = 164) were in modified Hoehn and Yahr (H&Y) stages 1–2.5. The characteristics of cases and control subjects are shown in Table 1. Cases and control subjects had a similar sex distribution.

Cases were more likely to be older, report never having smoked, have a lower body mass index, and have a higher intake of cholesterol and a lower intake of coffee, black tea, Japanese and Chinese teas, caffeine, and alcohol than control subjects. Region of residence, educational level, and other dietary variables were similar in the two groups.

Compared with the intake of coffee in the lowest quartile, its consumption in the highest quartile was significantly inversely associated with the risk of PD, showing a clear inverse dose–response relationship (Table 2). Although adjustment for sex, age, region of residence, educational level, pack-years of smoking, body mass...
index, the dietary glycemic index, and intake of cholesterol, vitamin E, β-carotene, vitamin B₆, alcohol, and iron.

index, the dietary glycemic index, and intake of cholesterol, vitamin E, β-carotene, vitamin B₆, alcohol, and iron attenuated the inverse association, it remained statistically significant (adjusted OR for the highest quartile = 0.52, 95% CI: 0.30–0.90, P for trend = 0.02). An independent inverse association was also observed between black tea consumption and the risk of PD (adjusted OR for the highest quartile = 0.58, 95% CI: 0.35–0.97, P for trend = 0.005). For consumption of Japanese and Chinese teas, the multivariate OR for the highest quartile compared with the first quartile was statistically significant (adjusted OR = 0.59, 95% CI: 0.35–0.995); however, the dose–response inverse association between Japanese and Chinese tea consumption and the risk of PD was of borderline significance (P for trend = 0.08). In addition, total caffeine intake was inversely associated with the risk of PD (adjusted OR in the highest quartile = 0.46, 95% CI: 0.27–0.78, P for trend = 0.003).

To examine whether the association of the intake of coffee, black tea, and Japanese and Chinese teas with PD risk could be attributed to caffeine intake, we conducted further analyses in which we adjusted for total caffeine intake as a continuous variable. After such an analysis, the significant inverse association between the intake of coffee and Japanese and Chinese teas in the highest quartile and the risk of PD disappeared: additional adjusted ORs were 0.74 (95% CI: 0.39–1.41, P for trend = 0.38) and 1.38 (95% CI: 0.62–3.01, P for trend = 0.39), respectively. Conversely, the inverse association of black tea with the risk of PD was essentially unaltered after further adjustment for total caffeine intake: an additional adjusted OR for PD in the fourth quartile of black tea consumption was 0.58 (95% CI: 0.35–0.97, P for trend = 0.005).

Among PD patients, intake of coffee and caffeine was inversely correlated with the severity of PD as evaluated by the modified H&Y scale, with Spearman’s correlation coefficients of −0.17 (P = 0.006) and −0.18 (P = 0.004), respectively. The adjusted ORs from the lowest to the highest category of coffee intake in patients with 2.5–5 H&Y stage PD compared to those with 1–2 H&Y stage PD were 1.00, 0.80 (95% CI: 0.40–1.61), 0.52 (95% CI: 0.29–1.28), and 0.30 (95% CI: 0.11–0.76), respectively. Corresponding figures for caffeine intake were 1.00, 0.80 (95% CI: 0.40–1.60), 0.77 (95% CI: 0.36–1.65), and 0.22 (95% CI: 0.08–0.58), respectively.

4. Discussion

The present case–control study in Japan showed that intake of coffee, black tea, Japanese and Chinese teas, and caffeine was significantly inversely associated with the risk of PD. Our results are in agreement with the majority of the previous epidemiological studies that found an association between the intake of coffee and caffeine and a reduced risk of PD [5–11]. A meta-analysis based on 7 cohort studies, 2 nested case-control studies, 16 case-control studies, and 1 cross-sectional study showed a 25% reduction in the risk of PD among caffeine consumers [13]. Although this association has turned up repeatedly in epidemiological studies, a clear biological basis for this phenomenon has yet to be identified. Further control for caffeine intake removed the inverse association between the intake of coffee and Japanese and Chinese teas and the risk of PD. Therefore, the beneficial association with the intake of Japanese and Chinese teas may be ascribed to some extent to caffeine intake or unmeasured constituents in relation to caffeine. Caffeine has antagonistic actions at adenosine A₂A receptors [25]. Results of an animal study showed that adenosine A₂A receptor antagonists improved motor deficits in marmosets treated with 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine (MPTP), a neurotoxin that selectively destroys dopaminergic neurons in the substantia nigra [26]. Caffeine was shown to reduce dopaminergic cell destruction by MPTP in experiments on mice [27]. The beneficial effect of caffeine on the development of PD might be attributed to blockage of adenosine A₂A receptors.

In the current study, the risk reduction associated with the intake of black tea did not appear to be confounded by caffeine intake. Our results were in agreement with the results of the Singapore Chinese Health Study that found that the significant inverse association
between black tea consumption and PD risk was independent of caffeine intake [18]. Components of black tea other than caffeine might be responsible for its protective effect against PD [18].

Our study had some strengths. All patients were diagnosed by a neurologist according to established criteria. There is little reason to suspect that there was a serious misdiagnosis of PD. The response rate among cases was relatively high (84%). We took into consideration comprehensive information on potential non-dietary and dietary confounders. However, residual confounding effects could not be ruled out.

Our study has, however, a number of limitations. Our DHQ could only approximate consumption although the correlation between the DHQ and dietary records was reasonable, as described above. The possibility of non-differential exposure misclassification might have biased the magnitude of the observed associations toward the null. Our DHQ was designed to assess dietary intake for 1 month prior to completing the questionnaire. Current rather than past dietary habits were assessed because retrospective estimation of past dietary consumption is generally difficult and the utility of our DHQ for dietary intake in the past is unknown. Therefore, the current study was inevitably based on the assumption that the patterns of relative food intake of cases and control subjects remained fairly stable over time. In Japan, there seems to be no special diet for PD patients. Nevertheless, the dopamine deficiency in PD patients might affect their food preferences in the preclinical stage [28]. Moreover, some of the non-motor symptoms, such as constipation and hyposmia, might precede the onset of overt motor signs [29,30]. Such symptoms might also affect food choices. Thus, pre-symptomatic and/or post-symptomatic PD could influence dietary habits in some cases, which would lead to misclassification of their true long-term dietary exposure. In some PD patients, intake of coffee might have decreased after the diagnosis of PD. The results of a sensitivity analysis restricted to cases less than 3 years from onset (n = 109, 43.8% of cases) were similar to those of the overall analysis: the adjusted OR in the multivariate model in the highest quartile was 0.83 (95% CI: 0.40–1.70, P for trend = 0.84) for coffee, 0.89 (95% CI: 0.44–1.80, P for trend = 0.24) for black tea, 0.68 (95% CI: 0.33–1.38, P for trend = 0.62) for Japanese and Chinese teas, and 0.66 (95% CI: 0.32–1.32, P for trend = 0.23) for caffeine.

Recruitment of cases was conducted in 11 collaborating hospitals, whereas control subjects were selected from 1 university hospital in Fukuoka Prefecture and 1 university hospital and 1 national hospital in the Kinki region. There is a possibility that control subjects did not entirely represent the population from which cases were drawn. When restricting analysis to cases that had been recruited in the 3 hospitals from which control subjects were recruited (n = 153, 62% of cases), results were similar to those in the overall analysis: the adjusted OR in the multivariate model in the highest quartile was 0.59 (95% CI: 0.30–1.12, P for trend = 0.14) for coffee, 0.65 (95% CI: 0.35–1.20, P for trend = 0.03) for black tea, 0.67 (95% CI: 0.37–1.21, P for trend = 0.29) for Japanese and Chinese teas, and 0.52 (95% CI: 0.27–0.97, P for trend = 0.04) for caffeine.

The current study might not have substantial statistical power, although significant inverse associations were detected.

This is the first epidemiological study to find beneficial effects of the intake of Japanese and Chinese teas, including green tea and oolong tea, on the risk of PD. Furthermore, we confirmed an inverse association between coffee and caffeine intake and the risk of PD in Japanese subjects. Because the Japanese culture is distinct from that in the West, this consistency in results between studies of Western populations and those of our study further strengthens the notion that caffeine intake is associated with a decrease in the risk of PD.

Acknowledgments

None of the authors had any personal or financial conflict of interest. This study was supported by Health and Labour Sciences Research Grants, Research on Intractable Diseases, Research Committee on Epidemiology of Intractable Diseases from the Ministry of Health, Labour, and Welfare, Japan.

Appendix

Other members of the Fukuoka Kinki Parkinson’s Disease Study Group are as follows: Yasuhiko Baba and Tomonori Kobayashi (Department of Neurology, Faculty of Medicine, Fukuoka University); Hideyuki Sawada, Eiji Mizuta, and Nagako Murase (Clinical Research Institute and Department of Neurology, Utano National Hospital); Tsuyoshi Tsutada and Hiroiyuki Shimada (Department of Geriatrics and Neurology, Osaka City University Graduate School of Medicine); Jun-ichi Kira (Department of Neurology, Neurological Institute, Graduate School of Medical Sciences, Kyushu University); Tameko Kihira and Tomoyoshi Kondo (Department of Neurology, Wakayama Medical University); Hidekazu Tomimoto (Department of Neurology, Kyoto University Graduate School of Medicine); Takayuki Taniwaki (Division of Respirology, Neurology, and Rheumatology, Department of Medicine, Kurume University School of Medicine); Hiroshi Sugiyama and Sonoyo Yoshida (Department of Neurology, Minami-Kyoto National Hospital); Harutoshi Fujimura and Tomoko Saito (Department of Neurology, Toneyama National Hospital); Kyoko Saida and Junko Fujikata (Department of Neurology, Kyoto City Hospital); Naoki Fujii (Department of Neurology, Neuro-Muscular Center, National Omuta Hospital); Masatoshi Naito and Jun Arimizu (Department of Orthopaedic Surgery, Faculty of Medicine, Fukuoka University); Takashi Nakagawa, Hiromi Harada, and Takayuki Sueta (Department of Otorhinolaryngology, Faculty of Medicine, Fukuoka University); Toshihiro Kikuta and George Umemoto (Department of Oral and Maxillofacial Surgery, Faculty of Medicine, Fukuoka University); Eichi Uchio and Hiroshi Mitigita (Department of Ophthalmology, Faculty of Medicine, Fukuoka University); Kenichi Kazuki, Yoichi Ito, and Hiroyoshi Iwaki (Department of Orthopaedic Surgery, Osaka City University Graduate School of Medicine); Kunihiko Siraki and Shin-suke Ataka (Department of Ophthalmology and Visual Sciences, Osaka City University Graduate School of Medicine); Hidey Yamane and Rie Tochino (Department of Otolaryngology and Head and Neck Surgery, Osaka City University Graduate School of Medicine); Teruichi Harada (Department of Plastic and Reconstructive Surgery, Osaka City University Graduate School of Medicine); Yasushi Iwashita, Motoyuki Shimizu, Kenji Seki, and Keiji Ando (Department of Orthopedic Surgery, Utano National Hospital).

References


