Studies on drinking behavior, personality and L-dopa induced hallucination of idiopathic Parkinson's disease patients

Fujii Chieko

Thesis (Ph. D. in Medical Sciences)—University of Tsukuba, (A), no. 2426, 2000.3.24

Includes supplementary treatises

Includes bibliographical references

URL http://hdl.handle.net/2241/6117

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<th>著者</th>
<th>藤井 千枝子</th>
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<td>著者別名</td>
<td>島田 千枝子</td>
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<td>内容記述</td>
<td>研究は、アルコール摂取とパーキンソン病との関係、パーキンソン病患者の性格特性、L-ドパ誘発性幻覚に関する研究</td>
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<td>発行年</td>
<td>2000年</td>
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<td>その他のタイトル</td>
<td>弧発性パーキンソン病患者の飲酒様態、パーソナリティおよびL-ドパ誘発性幻覚に関する研究</td>
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この研究は、パーキンソン病患者の飲酒様態、性格特性、L-ドパ誘発性幻覚の関係を明らかにするために行われました。
Abstract

The etiology of idiopathic Parkinson's disease (PD) remains unknown although it has been suggested that PD is a multifactorial disease caused by environmental and genetic risk factors. A number of studies have characterized life styles, psychological traits and clinical symptoms for idiopathic PD. Especially, the tendency to dislike alcohol, the low score of the novelty seeking (NS) and the high score of the harm avoidance (HA) in Tridimensional Personality Questionnaire (TPQ), and individual difference of the occurrence of L-dopa induced hallucination in PD may involve the genetic backgrounds.

This study was carried out to confirm the personality characteristic of Caucasian patients by using Japanese patients, and to elucidate the genetic background with specific reference with polymorphism of the ALDH2 and cholecystokinin (CCK) genes.

A total of 116 Japanese outpatients with PD diagnosed by three neurologists from 4 hospitals in Kanto area were analyzed for these studies. Among them 93 patients with PD were analyzed for ALDH2 genotypes and alcohol consumption, and 67 Japanese PD patients were used for TPQ assessments. All patients (116) were analyzed in order to investigate the role of polymorphism of the CCK gene. Age matched control groups (297 subjects for ALDH2 genotyping and alcohol consumption, 69 subjects for TPQ, and 95 subjects for the CCK gene polymorphism) were analyzed.

PCR-SSCP (polymerase chain reaction-single strand conformational change polymorphism) analysis was used to determine ALDH2 and CCK genotypes. Mean values of alcohol consumption (ethanol g/month/person) and TPQ from patients with PD were estimated by direct interview, and those from controls were obtained by questionnaire. The comparison between PD patients and control subjects were analyzed using a chi-square
test, or alternatively, by a one-way analysis of variance (ANOVA) test (P values less than 0.05 were considered statistically significant). Analysis of linkage disequilibrium between two given loci were performed by using the ASSOCIAT (version 2.32) software in conjugation with the LINKAGE UTILITY programs (Terwillinger JD et al., 1994). D’ values for linkage disequilibrium were also calculated according to the previous report (Chen et al., 1997).

Distributions of the three genotypes and the allele frequencies of ALDH2 were not significantly different between patients and control subjects; however, the PD patients consumed significantly less alcohol than control subjects with the same ALDH2 genotype. These data suggest that the lower values of alcohol consumption among PD patients of all ALDH2 genotypic subgroups may be caused by factors such as the premorbid personality rather than ALDH2 polymorphism.

Japanese PD patients have significantly lower scores in the NS dimension of the TPQ, as well as significantly higher HA scores, compared with matched control subjects. These results suggest that the high HA score, and the low NS score in the TPQ test observed in patients with PD is a cross-cultural phenomenon, although the influence of depression, long-term treatment and premorbid gene/environmental interactions may also effect these personality traits.

Four polymorphic sites of the CCK gene, in both the coding and promoter region, (-196G→A, -45C→T, 1270C→G, 6662C→T) were found in PD patients and controls. A significant difference was found in the distributions of three identified genotypes at the -45 locus between PD patients and age-matched control subjects ($\chi^2$=7.95, p=0.018, Bonferroni correction; p=0.054). In addition, a significant difference at the -45 locus was obtained amongst the three genotypic groups when compared between
PD patients that experienced hallucinations and those who did not ($\chi^2=8.08$, $p=0.018$, Bonferroni correction; $p=0.144$). These data suggested that mutations at the -45 locus in the promoter region of the CCK gene may influence vulnerability to hallucination in PD patients treated with L-dopa.

However, the analysis concerning hallucination is limited by the small sample size. Future investigations, involving larger number of patients demonstrating hallucinations, will be necessary to explore this finding further.

Key words: Polymorphism, Cholecystokinin gene, ALDH2 gene, Tridimensional Personality Questionnaire, Association study