

Cross-Cultural Differences in Patient Perceptions of Dyskinesia in Parkinson's Disease

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ABSTRACT: Background: The prevalence of levodopa-induced dyskinesia (LID) in Parkinson's disease (PD) varies among geographical regions. Cultural differences in patient-based perceptions of LID have not been studied.

Objective: We compared patient and clinician evaluations of LID severity across multiple cultures in patients with PD.

Methods: The data set included the Unified Dyskinesia Rating (UDysRS) scores from 16 language translation programs (3566 patients). We defined the Perception Severity Index (PSI) as the ratio between normalized patient-based subjective ratings (UDysRS Part 1B) and normalized clinician examination (Parts 3 and 4) scores (Part 1B/Parts 3 + 4) and compared the PSI across languages.

Results: The mean PSI for the Chinese language (2.16) was higher than those of all other languages, whereas the ratio for the Korean language (0.73) was lower than those for Japanese, German, Turkish, Greek, Polish, and Finnish languages (corrected *P* values <0.05).

Conclusions: Culture, as represented by language, affects the subjective perception of LID and needs to be considered in multinational clinical PD trials on dyskinesia. © 2023 International Parkinson and Movement Disorder Society.

Key Words: dyskinesia; culture; Parkinson's disease

Introduction

Cultural factors may affect the personal experience of medical symptoms together with genetic and environmental factors. Studies across cultures have demonstrated differences in the personality characteristics of populations, such as lower levels of extroversion in East Asian countries compared with northern European countries.¹ These differences can be associated with regional gene pools or cultural differences (ie, the shared set of beliefs, norms, and values of a group). They have been used to explain the reported lower prevalence of depression and anxiety disorders in Asia than in American and European countries,^{2,3} although differences in health care systems and diagnostic criteria are also likely involved. In Parkinson's disease (PD), there are clinically relevant differences in the presentation of symptoms across disparate geographical regions,⁴ clearly documented in the realm of nonmotor symptoms in patients from different ethnic backgrounds and Eastern and Western cultures.⁵⁻⁹

PD is frequently associated with levodopa-induced dyskinesia (LID). The prevalence of LID has been estimated to be 50% to 75% after 10 years,¹⁰ 61% to 96% after 9 to 15 years,¹¹ and 68% after 6 years of treatment with levodopa.¹² In addition, once present, dyskinesia is often pragmatically divided into troublesome and nontroublesome forms, with the distinction largely determined by the impact of dyskinesia on the individual patient. It is possible that the prevalence of troublesome dyskinesia is decreasing as a result of improved knowledge of levodopa-induced complications and better individual optimization of treatment, but it is also possible that different cultures view dyskinesia as having very different impacts on functioning.^{13,14} Asian patients have generally been reported to be particularly prone to LID,⁴ but this observation is not universal, and the prevalence of LID in Japan and China has also been reported to be lower than seen in European PD patients.¹⁵ Possible explanations for these differences include regionally different pharmacogenetics, management strategies, and cultural differences. Several studies have evaluated the contribution of genetic factors in PD patients on the development of adverse effects attributed to treatment with catechol-O-methyltransferase inhibitors, dopamine agonists, and monoamine oxidase B inhibitors. However, the majority of studies have reported relatively

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TABLE 1 Demographic characteristics and ICCs for subjective and objective ratings of dyskinesia severity based on the UDysRS

Demographics		
N		3566
Age, y, mean (SD)		65.6 (9.8)
PD duration, y, mean (SD)		5.9 (5.5)
Sex, percentage male		51.4
Race, percentage Caucasian		76.9
Language	Frequency	ICC
Greek	250	0.85
Polish	245	0.80
Slovakian	244	0.78
Japanese	241	0.73
German	169	0.70
Turkish	217	0.69
Spanish	211	0.67
Russian	194	0.67
Finnish	202	0.67
Hungarian	240	0.66
Hebrew	226	0.61
Portuguese	199	0.61
Korean	250	0.61
French	230	0.59
Italian	239	0.47
Chinese	209	0.36
Total	3566	0.73

Abbreviations: ICC, intraclass correlation coefficient; UDysRS, Unified Dyskinesia Rating Scale; SD, standard deviation; PD, Parkinson's disease.

small pharmacogenetic effects, suggesting that other factors, such as cultural issues, may be involved.¹⁶ From the perspective of multinational clinical PD therapeutic trials, possible cultural differences in the presentation of dyskinesia are of relevance, as they would induce noise in the data and compromise study designs. From the viewpoint of the patient, differences would underline the importance of individualized patient-centered treatment that takes into account culturally dependent issues impacting well-being.

In the present study, we focused on LID in PD patients from various cultures. We accessed the large, international dataset of the Unified Dyskinesia Rating Scale (UDysRS) owned by the International Parkinson and Movement Disorder Society.¹⁷ Importantly, the UDysRS collects LID information from both the patients and the investigators, and it has now been

translated and validated for several languages from different geographical regions, enabling cross-cultural comparisons among language areas. Therefore, to uncover possible cultural differences in the perception of LID in PD patients, we investigated the ratios of subjective patient evaluations to objective investigator evaluations of the UDysRS.

Patients and Methods

The UDysRS, originally developed in the English language, provides a comprehensive rating tool of dyskinesia in PD.^{17,18} For the present study, we used the International Parkinson and Movement Disorder Society (MDS)-based Clinical Outcome Assessment Program Translation dataset, which included 4134 complete ratings and 16 different languages. Each language had contributed a minimum of 250 cases to the database. Data from 14 languages were collected from individual countries (eg, Spanish, Spain; French, France), and two languages were collected from more than one country (German, Germany and Austria; Portuguese, Portugal and Brazil). All raters were required to complete a UDysRS online training module to ensure uniform application of scoring.

The ratio of the normalized subjective score (UDysRS Part 1B) to the normalized objective score (Parts 3 and 4) was calculated. This ratio was termed the Perception Severity Index (PSI). Given that the objective severity scores differed across cultures, the ratio of subjective/objective scores provided an index for how perceptions differed across an equalized severity. As such, $PSI = 1$ ideally indicates a perfect match between objective observation and patient perceptions, whereas scores of greater than or less than one indicate more subjective or objective ratings, respectively. Intraclass correlation coefficients were calculated to assess the rate of agreement between subjective and objective scores for each language. Comparisons across the languages were conducted using an analysis of variance model. Post hoc comparisons were performed using a Scheffé correction for multiple comparisons. We included only patients with objective scores (Parts 3 and 4) greater than zero (a clinician evaluated that dyskinesias were present), resulting in 3566 subjects for analysis (Table 1). All analyses were conducted using SPSS (version 28; IBM Corp., Armonk, NY).

Results

The demographic characteristics of the studied patients are presented in Table 1. The intraclass correlation coefficients between subjective and objective scores ranged from a low of 0.36 for Chinese to a high of 0.85 for Greek.

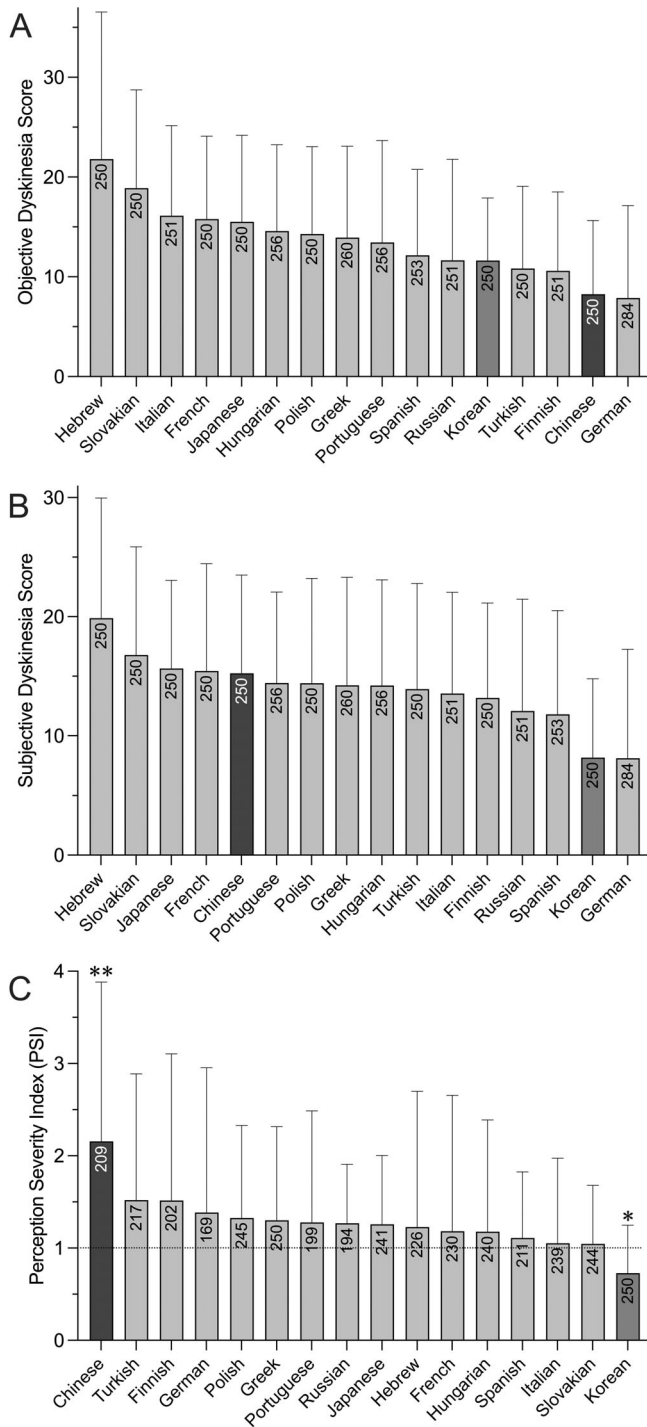


FIG. 1. Mean (standard deviation) objective scores (A), subjective scores (B), and Perception Severity Indexes (PSIs) (C) (subjective to objective ratios) for each language. Values within bars denote sample sizes. The Chinese PSI was higher than other languages (**, all corrected *P* values of <0.008). The Korean ratio was lower than the Turkish, Finnish, German, Polish, Greek, and Japanese ratios (*, all corrected *P* values of <0.011).

Objective dyskinesia scores were different across languages ($F[15:3363] = 39.4; P < 0.001$; Fig. 1A). Objective scores for Hebrew were higher than for all other languages (all *P* values <0.001). Slovakian scores were

higher than those for Spanish, Turkish, Greek, Korean, Russian, Polish, Finnish, Chinese, and German (all *P* values ≤ 0.027). Italian scores were higher than Turkish scores ($P = 0.008$). Turkish scores were lower than French and Portuguese scores (all *P* values ≤ 0.004). Chinese scores were lower than those for Japanese, Italian, Spanish, French, Hungarian, Greek, Portuguese, Russian, and Polish (all *P* values ≤ 0.016). Korean scores were lower than those for Portuguese, Italian, French, and Hungarian (all *P* values ≤ 0.036).

Similarly, subjective dyskinesia scores differed across languages ($F[15:2177] = 29.3; P < 0.001$; Fig. 1B). Korean subjective scores were lower than those of all other languages (all *P* values <0.001). Hebrew subjective scores were higher than those of all other languages (all *P* values ≤ 0.014), except Slovakian, for which no difference was found.

The normalized mean PSI ranged from a high of 2.16 for the Chinese language to a low of 0.73 for the Korean sample (Fig. 1C). Overall, across the gamut of languages, the PSI varied ($F[15:3550] = 14.91; P < 0.0005$). Post hoc comparisons of PSIs for individual languages revealed specific differences. PSIs were higher in the Chinese language cohort than for all other languages (all *P* values <0.008, corrected). PSIs were lower in the Korean language cohort than in the Japanese, German, Turkish, Greek, Polish, and Finnish cohorts (all *P* values <0.011).

Discussion

The present study demonstrates differences between countries with regard to the personal experience of dyskinesias in PD. In the absence of a better explanation, these differences could be attributable to the intrinsic cultural peculiarities of each country/language. The PSIs in Chinese-speaking PD patients were considerably higher than those of any other language/culture. An opposite effect was observed for the Korean language, for which objective scores were higher than subjective scores compared with several other language areas. It is noteworthy that opposite differences were seen in two Asian languages/cultures, which underlines the trend being present even between geographical regions that are relatively close. This finding emphasizes the importance of cultural sensitivity and the high risk of coalescing cultures simply based on global location or broad racial assumptions.

The term *troublesome dyskinesia*, a key concept in PD clinical trials, was introduced in 2000, when discomforting or disturbing *on* dyskinesias (bad time) were separated from milder forms of *on* dyskinesias (good time) in patient home diaries.¹⁹ Before the description, a common and often the only end point had been the reduction of *off* time, with only minor

consideration for possible subjective harm induced by dyskinesia. With respect to the patient-centered and culturally valid perspective, it is important to note that the troublesomeness of a symptom refers only to the subjective rating given by the patient. According to our results, the subjective experience of LID is modulated by culture as represented by language. The UDysRS does not specifically use the terminology of troublesome and nontroublesome dyskinesia, so we cannot comment on any threshold or minimal clinical severity based on the UDysRS that corresponds to troublesomeness across or within given cultures.

Our results also showed differences in objective clinician-observed and subjective patient-reported levels of dyskinesia between language areas. However, these differences are mostly likely related to general sampling differences. For instance, Hebrew and Slovakian languages scored significantly higher than other languages on both objective and subjective ratings, suggesting that the patient samples for these regions included higher numbers of severely dyskinetic patients than those for other languages (eg, German). There were no systematic differences between large geographical regions, such as intercontinental differences between Western and Eastern cultures, previously reported for nonmotor symptoms of PD.^{5,6} Instead, we observed opposite subjective perceptions of LID in two East Asian countries in relatively close proximity. The reason for this difference is unclear, but one relevant factor may be the difference in language structure. There is a specific structure in the Korean language that may predispose speakers to pay more attention to certain information compared with Chinese (ground information to figure information).²⁰ It is possible that this could lead to some attentional bias relative to Chinese speakers.²⁰ The structure of languages can be important together with cultural differences and can lead to different interpretations of politeness, impatience, and rudeness.²¹ Therefore, although translations between languages may per se be accurate and validated, important intrinsic qualities of languages and cultural differences may lead to attentional biases between languages. Apart from the UDysRS, the linguistic and cultural differences may extend to other multilingual clinical validated scales that include patients' subjective ratings, such as the MDS–Unified Parkinson's Disease Rating Scale. Further studies are therefore needed specifically to focus on culturally dependent differences in caregiver perceptions of symptoms and links to regional drug-prescribing practices and regional educational levels (eg, recognition of LID vs. tremor).

To summarize, LID, an important clinical issue and an end point in many clinical trials, is associated with cultural differences. The impact of culture and language structure on subjective ratings requires attention and controlling for in PD clinical trials. To improve the

external validity of trials, it may be necessary to understand troublesome dyskinesia as a culturally dependent issue and to separately investigate subjective and objective LID when possible. This should also be recognized in the clinical evaluation of the treatment response of PD patients from different cultural and linguistic backgrounds. ■

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Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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V.K.: 1A, 1B, 1C, 2C, 3A

S.L.: 1A, 1B, 2C, 3B

P.M.-M.: 1A, 1B, 2C, 3B

C.G.G.: 1A, 1B, 2C, 3B

G.T.S.: 1A, 1B, 1C, 2A, 2B, 3B

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