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A Cross-Cultural Validation of the Filipino and Hiligaynon Versions of the Parts IIIB (Non-Motor Features) and IV (Activities of Daily Living) of the X-Linked Dystonia-Parkinsonism– MDSP Rating Scale

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ABSTRACT

Introduction: X-linked dystonia-parkinsonism (XDP) is a progressive movement disorder which also encompasses non-motor features and alterations in activities of daily living. The study aims to translate the Parts IIIB (Non-Motor Features) and IV (Activities of Daily Living) of the XDP-Movement Disorder Society of Philippines Rating Scale to Filipino and Hiligaynon and subsequently validate these versions, which are more understandable to the natives given that XDP originated from the Panay Islands in the Philippines.

Methods: This is a cross-cultural, cross-sectional validation study, composed of the following steps: forward translation, backward translation, panel reconciliation, pretesting, and field testing. Two sets of 10 XDP patients were recruited to the Filipino and Hiligaynon groups for pretesting and cognitive debriefing while another 2 sets of 50 XDP patients were assigned for field testing.

Results: The Filipino version had a good internal consistency with a Cronbach's alpha of 0.951 during the pretesting and 0.886 during the field testing. Similar results were seen in the Hiligaynon version (0.837; 0.900). Both also had good conceptual equivalence as demonstrated by significant Pearson r values of 0.384 to 0.814 for the Filipino and 0.355 to 0.800 for the Hiligaynon versions.

Conclusion: The Filipino and Hiligaynon versions of the Parts IIIB and IV of the XDP–MDSP scale are internally valid and reliable. These scales are considered acceptable to assess the severity of the non-motor features and difficulties in activities of daily living among XDP patients.

1. Introduction

X-linked dystonia parkinsonism (XDP) or *"Lubag"* is a progressive, degenerative movement disorder first reported in adult Filipino males [1,2]. The prevalence rate of XDP in the Philippines is 0.31 per 100,000, mostly originating from the Panay Islands [2]. Based on the available data, there are 810 recorded cases of XDP, of which 300 have had genetic testing [3]. Of the reported cases, there are 14 diagnosed female patients [3,4]. However, the current prevalence needs to be established. The age at onset of the disease is in the late 30s to early 40s (12–64 years) [4,5], which was also documented in a recent review wherein the median age at onset was 40 years [6]. XDP presents with focal dystonia during the early stage of the disease [7,8], and becoming generalized within 2 to 5 years [1]. It may also initially manifest with parkinsonism [7] which has a better prognosis but early diagnosis of XDP in such cases may be ignored if family history of XDP is unknown [9]. Parkinsonism was also documented to develop later in the disease [1,8,10,11]. With XDP as case example, a recent large MDSGene Database extraction study that screened 233 citations and curated phenotypic and genotypic data for 414 cases, indicated that dystonia was the initial presenting symptom in 82% of cases compared to the 14% with parkinsonism as initial presentation [6]. Female XDP carriers are mostly asymptomatic but may display non-progressive focal dystonia, chorea, focal tremor, or mild parkinsonism [4].

The X-Linked Dystonia-Parkinsonism–Movement Disorder Society of Philippines (XDP–MDSP) Rating Scale was developed to evaluate the

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severity of symptoms, functionality, and treatment response of these patients [12]. It is composed of 5 parts namely: I-dystonia, II-parkinsonism, III-non-motor features, IV-ADL, and V-global impression [12]. Non-motor symptoms have contributed to the quality of life and disability in patients with movement disorders [13].

Pain has been experienced by 80% of individuals with oro-mandibular dystonia, 75% with truncal–axial dystonia [4], 70% with cervical dystonia, and 30% with focal hand dystonia and writer's cramp [14]. Impaired sleep quality and efficiency [14,15], reduced REM sleep, and increased awakenings have been reported and associated in patients with dystonia [14]. Aside from insomnia, fatigue was also reported in 51% of 102 patients with cervical dystonia, using the NMSQuest questionnaire [16]. In a pilot study comparing eight genetically confirmed XDP patients with their age-matched controls, changes in sympathetic skin response (SSR) amplitudes were recorded among XDP patients [17]. However, there was no significant association found between their SSR findings and autonomic dysfunction symptoms [17].

Aside from the non-motor aspects, the functional impairment caused by severe dystonia and parkinsonism usually leads to great disability in activities of daily living [4]. In the phenomenological study by Lee, et al. in 2011, out of 312 XDP survivors, only 19 patients (6%) were still working, 209 patients (69%) were still ambulatory but were no longer employed, 7 patients (2%) were no longer ambulatory but still able to care for themselves, and 72 patients (23%) were either wheelchair-bound or bedbound [2]. Depression also contributes to the incapability of XDP patients to work thus leading to unemployment and eventual loss of financial stability and independence [18]. Dystonia patients exhibited lower quality of life on all subscales of the Medical Outcomes Study Short Form 36 (SF-36) compared to healthy controls [19].

In light of the paucity of data regarding the non-motor features and activities of daily living among XDP patients who ancestrally originated from the Philippines with a dense population coming from Panay Islands, the primary aim of this study is to do a cross-cultural validation of the Filipino and Hiligaynon versions of the self-administered Parts IIIB (Non-Motor Features) and IV (Activities of Daily Living) of the XDP–MDSP rating scale. The authors believe that it is also important to translate this rating scale to Hiligaynon since it is the most widely used spoken dialect in the Panay Islands and there are some expressed terms in Hiligaynon that could not be accurately translated to Filipino or English. Secondarily, the authors wish to determine the reliability of the Filipino and Hiligaynon versions of Parts IIIB (Non-Motor Features) and IV (Activities of Daily Living) of the XDP – MDSP rating scale and establish its conceptual equivalence. This cross-cultural validation of the XDP–MDSP rating scale into Filipino and Hiligaynon versions is relevant too in the light of the recent publication on the Hiligaynon version of Montreal Cognitive Assessment (MoCA-Hil) as applied among XDP patients [20].

2. Materials and methods

This is a cross-cultural, cross-sectional validation study of the Parts IIIB (Non-Motor Features) and IV (Activities of Daily Living) of the XDP–MDSP rating scale - Filipino and Hiligaynon Versions involving adult Filipinos genetically diagnosed with XDP who can speak and understand the Filipino and/or Hiligaynon language. The validity study of the instruments was conducted in the Neurology Ambulatory Care Service of the University of Santo Tomas Hospital, Manila, Philippines. The patients recruited were from the investigators' clinics and referrals from other neurology consultants.

A purposive, convenience sampling technique was used. For pretesting of the questionnaire, at least 12 to 50 respondents are required [21]. For field testing, the rule of thumb in terms of respondent-to-item ratio varies among different studies and ranges from 2 to 20 subjects per item, but with a minimum of 100 to 250 subjects [22]. Considering the rarity of XDP, a total of 20 patients was assigned for the pretesting and cognitive debriefing phase, with 10 patients each in the Filipino and Hiligaynon groups. Another 2 groups of 50 patients each, were included for the field testing. Patients who are only able to speak Filipino were assigned to the Filipino group while patients who are bilingual (Filipino and/or Hiligaynon), were assigned to either Filipino or Hiligaynon group.

Professionals with experience in translation and cultural adaptation measures, were involved in the construction of the questionnaires. The professors who independently took part in the forward and backward translation of the questionnaire from English to Filipino and vice versa are from the Center for Translation and Translation Studies of the University of Santo Tomas. On the other hand, the professor who assisted in the forward translation of the questionnaire from English to Hiligaynon is associated with The Bienvenido N. Santos Creative Writing Center of the De La Salle University while a clinician who is a translator and is fluent in Hiligaynon, Filipino and English, helped in the backward translation from Hiligaynon to English.

The translators were assisted by the authors for concepts or terms that were not familiar. The authors compared, agreed on the construct of questions and response choices to obtain a unique final version in the local language by consensus. The final Filipino and Hiligaynon versions of the questionnaire were back-translated by different bilingual professionals, blind to the wording of the original English version. There was a qualitative assessment of the instruments involving 2 groups of 10 XDP patients who answered either the Filipino or Hiligaynon version of the XDP–MDSP rating scale. The acceptability of the Parts IIIB and IV of the XDP–MDSP rating scale Filipino and Hiligaynon versions was evaluated using a semi-structured questionnaire in cognitive interviews with XDP patients. Sixteen (26.67%) patients in the Filipino and 19 (31.67%) patients in the Hiligaynon groups allowed a family member or legal representative answer the informed consent form and the questionnaire on the their behalf because of motor symptoms, pain, difficulty speaking and writing. If the caregiver was unsure of an answer, the patient was asked and would respond through hand gestures. When individually interviewed and asked if they had any difficulty understanding the questions, or if the questions were displeasing, all of the participants answered none. They further added that all of the questions were relevant to their condition. Field testing of the final Filipino and Hiligaynon versions involved 2 groups with 50 XDP patients each. The average time spent completing the scale was 20 min.

Content validity of each of the items in the Filipino and Hiligaynon questionnaires was no longer done, as the original English version of the XDP–MDSP rating scale was already validated by a panel of experts.

For this present study, we applied the proposed XDP staging by Lee, et al. [2] which relies on the clinical presentation and severity of functional impairment in performing activities of daily living. The stages are: I - focal dystonia or one parkinsonian trait but without impairment of function, II - segmental dystonia or two parkinsonian traits and minimal impairment of function, III - multifocal dystonia or/and more than two parkinsonian traits and some impairment of function, IV - generalized dystonia or/and moderate to severe parkinsonian trait and moderate to severe impairment of function, and V - any combination of dystonia and parkinsonism and totally dependent for activities of daily living [2].

2.1. Statistical/data analysis

Statistical analyses were done using the Stata Statistical Software, Version 13, College Station, TX: StataCorp LP. Descriptive statistics included mean, frequency, and percentage. A p-value of ≤ 0.05 was considered significant. To evaluate conceptual equivalence and determine the correlation of each item to the scale for either the Filipino or Hiligaynon version, Pearson correlation coefficient was utilized. For this study, a correlation coefficient of 0.235 denotes that an item is consistent with the content of the scale. Internal consistency of both versions was assessed using Cronbach's alpha with a cut-off score of ≥ 0.70.

2.2. Ethics

The permission to develop the Filipino and Hiligaynon versions of the Parts IIIB and IV of the XDP–MDSP rating scale was granted by the co-author (RLR), who was part of the team that developed the original scale written in English. The use of the said rating scale was also given free of charge for academic purposes. Informed consent was secured from the patients and/or caregivers by the authors before their participation. There was no psychological discomfort documented among the patients during testing. This study was approved by the Research Ethics Committee of the hospital.

3. Results

A total of 120 patients, genetically diagnosed with XDP, were enrolled in this study. The mean age of the participants was 48.03 years. Out of 120 participants, only four were female. The majority of the patients reached tertiary level of education (45%), are unemployed (88.3%), and have a mean duration of disease of 7.5 years. Most of the patients predominantly present with dystonia (F: 71.67%; H: 73.33%). Majority of the patients were classified under Stage III (F: 38.33% ; H: 46.67%) and minority consists of stages I (F; H: 5%) and V (F: 8.33%; H: 11.67%). In terms of on board therapeutic regimen during the present testing, the most widely taken oral medication was biperiden in both the Filipino (48.33%) and Hiligaynon (50%) tested groups. This was followed by clonazepam (46.67%) in the Filipino group and levodopa/carbidopa (43.33%) in the Hiligaynon group. Less than to almost half of the participants receive botulinum toxin injection as adjunct to oral medications for both groups (F: 36.67%; H: 48.33%). Only one participant was recorded to have underwent deep brain stimulation (esupp Table 1).

The Filipino translated instrument had a good internal consistency with a Cronbach's alpha of 0.951 during the pretesting. A similar result was seen during the field testing, with Cronbach's alpha of 0.886. (esupp Table 2) The Hiligaynon translated instrument also had a good internal consistency with a Cronbach's alpha of 0.837 during the pretesting and 0.900 during the field testing (esupp Table 3).

The correlation of each item to the scale measuring the non-motor symptoms and activities of daily living was acceptable and significant with Pearson r values of 0.384 to 0.814 for the Filipino version. The same result was observed for the Hiligaynon version, with values that range from 0.355 to 0.800 (esupp Table 4).

4. Discussion

This has been the first linguistic and cross-cultural validation study that translated the Parts IIIB and IV sections of the XDP–MDSP rating scale to Filipino and Hiligaynon, which are the most commonly used languages of XDP patients. Based on this study, the Filipino and Hiligaynon versions of the questionnaire were shown to have good internal consistency and high conceptual equivalence.

Considering most of the patients and their families are more troubled on the motor symptoms that the patient is presenting and likewise are focused on the improvement of these symptoms, the non-motor features and difficulties in activities of daily living are usually taken for granted. Since Parts IIIB and IV of the XDP–MDSP rating scale are patient or caregiver administered, it is essential that they fully understand the contents of each item for them to accurately convey the symptoms of the patient. Although the Parts IIIB and IV of the XDP–MDSP rating scale take on average 20 minutes to complete, it would give us an overview of what the patient is experiencing.

Other non-motor features to be taken into account are the impact on cognition and mood, which are not part of the scope of this study. In an article which reported on the cognition in XDP patients, utilizing Mini-Mental State Examination (MMSE), Clock Drawing Test (CDT), and Frontal Assessment Battery (FAB), 16/21 (76%) patients have cognitive impairment in at least one of the tests administered [13]. Among patients with young-onset generalized and adult-onset focal and segmental dystonia, 14 patients had an attention-executive cognitive deficit on the Cambridge Neuropsychological Test Automated Battery [14].

Psychiatric disorders were also recorded among XDP patients with 14.3% having major depression and 35.7% having anxiety disorders, such as social phobia (28.6%), agoraphobia (21.4%) [4,23], and panic disorder (7.1%) [4]. Suicide rate of 10.8% among XDP patients with a mean age of 44 years was also documented [13].

Future translation and validation studies on the clinician-administered parts of the scale - I (Dystonia), II (Parkinsonism), and IIIA (Non-Motor Features) may also aid in the clinical care of these patients. The limitations and caveats to this present study include: (1) low regard to the representativeness of the sample population per disease stage since XDP is considered to be a rare disease endemic to the Panay Islands and it is arduous to enroll genetically diagnosed patients; (2) treatment given to the patients, such as botulinum toxin injection and deep brain stimulation, which potentially affects their responses. Intake of oral medications such as anticholinergics, antihistamines, sedatives and benzodiazepines [10,24], as well as levodopa/carbidopa [25] have inconsistent to no benefits for XDP; (3) non consideration of the preferred language of bilingual participants since the study utilized purposive, convenience sampling; and (4) patients' verification of answers with the caregiver. However for patients who have difficulty communicating, a primary caregiver may provide answers for them.

5. Conclusion

The Filipino and Hiligaynon versions of the Parts IIIB and IV of the XDP–MDSP scale are internally valid and reliable. These scales are considered acceptable to assess the severity of the non-motor features and disturbances in activities of daily living among XDP patients, based on either the patient's or caregiver's perspective. These scales will be more convenient for the patients and families to use in relaying the symptoms the patients are manifesting and would also assist the physicians in monitoring the progression of the disease and effectiveness of treatment. Lastly, these validated scales will be of great benefit in future clinical trials on disease-modifying agents for this debilitating genetic disorder.

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Ethical approval

The study was approved by the Research Ethics Committee (REC) at the University of Santo Tomas Hospital, Manila, Philippines.

Data availability

The raw data that support the results of this study are available from the corresponding author on reasonable request.

CRediT authorship contribution statement

Richelle Ann S. Santiano: Conceptualization, Methodology, Software, Validation, Formal analysis, Investigation, Data curation, Writing - original draft, Visualization, Project administration. **Raymond L. Rosales:** Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing - original draft, Supervision, Project administration.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.prdoa.2021.100100.

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