Movement Disorders
CLINICAL PRACTICE

RESEARCH ARTICLE

Cognitive Functional Abilities in Parkinson's Disease: Agreement Between Patients and Informants

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ABSTRACT: Background: The Penn Parkinson's Daily Activities Questionnaire-15 (PDAQ-15) assesses cognition-related instrumental activities of daily living (IADL) in Parkinson's disease (PD).
Objectives: To assess the degree and predictors of disagreement between patients (PT) and knowledgeable informants (KI) on the PDAQ-15.
Methods: We recruited 254 PT and KI pairs (PT-KI), determined predictors of agreement, and compared scores to a performance-based functional measure (Direct Assessment of Functional Status [DAFS]; N = 61).
Results: PT and KI total score (intraclass correlation = 0.57) and individual item (Cohen's kappa = 0.46–0.62) agreement were moderate. Patient depression, global cognition, and caregiver burden (all $P < 0.05$), predicted PT-KI discrepancy. PT-KI discrepancy was highest in patients with a dementia diagnosis, followed by mild cognitive impairment and then normal cognition (all $P < 0.01$), with PT rating themselves relatively more functionally intact as cognition worsened. DAFS performance was more highly correlated with KI (r = 0.82; $P < 0.001$) than PT (r = 0.62; $P < 0.001$) PDAQ-15 score.
Conclusions: Our results support using KI as proxies when assessing cognitive IADLs in PD PTs, particularly in cases of more advanced cognitive decline.

Parkinson's disease (PD) is a neurodegenerative disorder effecting motor, cognitive, and neuropsychiatric function and instrumental activities of daily living (IADL).[1] Whereas most IADL scales used in PD were designed to measure functional deficits in Alzheimer's disease, and are often correlated with motor scores, the Penn Parkinson's Daily Activity Questionnaire-15 (PDAQ-15) was created specifically to assess cognition-related functional abilities in PD patients (PT) without a motor function confound.[2–4]

PT with and without PD may be unable to give valid self-assessments of their cognitive deficits, tending to rate their disability as less severe than knowledgeable informants (KI).[5–7] It has been shown that even mildly cognitively impaired PD PT can misrepresent performance on IADLs, leading to disagreement with KI.[8–10] Similarly, PT and KI discrepancy has been found to increase as PT depression worsens, leading PD PT to underestimate their cognitive limitations.[11–15] KI depression, burden, and stress can also lead to an underestimation of PT's functional status and an overestimation of their disabilities.[16–19]

Accurate appraisal of disease progression is a vital endpoint in PD research when both functional and cognitive abilities are measured in targeted therapeutic trials. The purpose of this study was to measure agreement between PT and KI assessment of cognitive functional status by the PDAQ-15, examine factors that predict disagreement, and determine which group

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Keywords: Parkinson's disease, cognitive function, activities of daily living.
Relevant disclosures and conflicts of interest are listed at the end of this article.
Received 22 March 2019; revised 19 April 2019; accepted 22 April 2019.
Published online 17 May 2019 in Wiley Online Library (wileyonlinelibrary.com). DOI: 10.1002/mdc3.12781

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was more accurate using a gold-standard performance-based assessment of cognitive function.

Patients and Methods

Two hundred fifty-four PD PT and their KI were enrolled at the University of Pennsylvania (Philadelphia, PA). PT were diagnosed with PD based on the UK Brain Bank criteria.[20] KI and PT separately and independently completed the PDAQ-15. The PDAQ-15 is a 15-question scale, with each question scored 0 to 4 on a Likert scale with a total range of 0 to 60 points (higher score indicates better cognition-related functional abilities). In-depth overviews of the original PDAQ and the abbreviated PDAQ-15 have been described previously.[2,21]

The 15-item Geriatric Depression Scale (GDS-15) was used to assess patient mood.[22] Clinical examinations performed included the Motor Subscale (Part III) of the UPDRS and KI burden.[23,24]

Neuropsychological Assessment

Neuropsychological tests: global cognition (Dementia Rating Scale-2 [DRS-2] and Montreal Cognitive Assessment [MoCA])[25,26]; executive/working memory (Letter Number Sequencing[27]), phonemic fluency [FAS],[28] and Trails B[29]); attention and psychomotor speed (Symbol Digit Modalities Test[30] and Trails A[29]); visuospatial (Judgment of Line Orientation[31] and clock drawing[32]); language (short Boston Naming Test[33] and semantic verbal fluency [animals][28]); and memory (Hopkins Verbal Learning Test-Revised[34]).

Consensus Cognitive Diagnosis

All participants were diagnosed as cognitively normal, mild cognitive impairment (MCI), or PD dementia (PDD) after completion of their annual (up to year 4 of study participation) or biannual (after year 4) assessment by expert consensus process, as previously described.[35–37]

PDAQ-15 Discrepancy

We measured discrepancy between PT and KI PDAQ-15 by subtracting the PT score from the KI score. We used both the raw score, that is, RAW PDAQ-15 discrepancy (a positive [+] score indicating that KI rated PT higher than PT rated themselves, whereas a negative [–] score indicated that PT rated themselves better than did KI) and absolute value (ABS) discrepancy (directionality of discrepancy not taken into account, e.g., | KI PDAQ-15 total score (–) PT PDAQ-15 total score | = |ABS|) in our analyses.

Direct Assessment of Functional Status Subgroup

A subset (N = 61) of PT was also assessed using the Direct Assessment of Functional Status (DAFS), a performance-based assessment of cognitive function. The DAFS was completed within 1 year of completing the PDAQ-15. The DAFS assesses standard instrumental IADLs and includes props such as a telephone, checkbook, grocery boxes, and a pillbox. The assessment is divided into several subcategories—communication, financial, shopping, and medication—which assess PT ability to navigate each of the tasks.[36] Each task is scored on a binary scale based on whether the patient correctly completed the task, for a maximum score of 57.

Statistical Analyses

Intraclass correlation (ICC) was calculated to examine the level of agreement between PT and KI PDAQ-15 total raw scores. Cohen's weighted kappa was used to determine degree of agreement at the individual item level. Univariate regression models were used to determine predictors of both ABS and RAW PDAQ-15 discrepancy. A predictor was included in subsequent regression models if it predicted discrepancy at $P < 0.10$. Linear regression models analyzed significant predictors of ABS and RAW discrepancy. Pearson partial correlation was used to assess correlation between PDAQ-15 and DAFS scores adjusting for covariates (PT age, GDS-15 total, DRS-2 total, and KI burden). A linear regression model was constructed to predict DAFS score. All statistical tests are two-sided. Bonferroni correction for multiple testing was used to compare PDAQ-15 discrepancy based on consensus cognitive diagnosis. Bonferroni-corrected P values are reported in Supporting Information Table S1. Statistical significance was set at <0.05 for all analyses. Statistical analyses were conducted using R programming software (R Foundation for Statistical Computing, Vienna, Austria).

Results

Demographic and Clinical Variables

Demographic and clinical characteristics are summarized in Table 1.

Agreement Between Patient and Knowledgeable Informant

PT and KI showed moderate agreement on the total PDAQ-15 (ICC = 0.57).[37] Cohen's weighted kappa for each item (range, 0.46–0.62) also indicated moderate agreement between PT and KI at the individual item level[38] (Supporting Information Table S4). Of the 254 PT and KI pairs, 98 (38.6%) had an ABS discrepancy of ≥6 points, which is >10% of total score range for the instrument. PT and KI groups had the greatest discrepancy on questions about the PT's ability to use household machines, with 45 (17.7%) groups differing by ≥2 points on this item. The least discrepancy was generated on questions about the PT's abilities to remember the date and maintaining a train of thought (only 22 [8.7%] groups differed by ≥2 points).

TABLE 1 *Demographic, clinical, and psychiatric/cognitive characteristics*

Variables (N = 254)	Percentage or Mean (SD)	Min	Max	DAFS Subgroup (N = 61)
Sex	67.7% male			86.7% male
Age, years	70.1 (8.1)	50.0	91.0	73.1 (7.7)
Education	16.2 (2.5)	10.0	21.0	15.9 (2.6)
PD duration	7.9 (5.5)	0.7	26.6	10.2 (5.8)
UPDRS Part III Total[a]	26.3 (13.8)	2.0	71.0	33.3 (14.6)
KI Burden Total	16.3 (14.4)	0.0	70.0	20.0 (15.5)
KI PDAQ-15 Total	47.6 (14.1)	3.0	60.0	39.8 (17.3)
PT PDAQ-15 Total	47.4 (11.7)	14.0	60.0	41.6 (11.7)
Raw PDAQ-15 Discrepancy[b]	0.2 (10.2)	−40.0	38.0	1.8 (13.5)
ABS PDAQ-15 Discrepancy[c]	6.5 (7.9)	0.0	40.0	9.3 (9.9)
DAFS total (N = 61)[d]	38.4 (14.0)	6.0	55.0	38.4 (14.0)
GDS-15 Total[e]	2.8 (3.0)	0.0	13.0	2.8 (3.2)
DRS-2 Total[f]	134.1 (12.2)	69.0	144.0	124.1 (17.3)
MoCA Total (N = 251)[g]	24.4 (4.7)	6.0	30.0	20.9 (6.0)
Subgroup (N = 58)				

[a]Unified Parkinson's Disease Rating Scale Part III (motor task).
[b]Raw Discrepancy (KI PDAQ-15 total (-) PT PDAQ-15 total).
[c]Absolute Value discrepancy (| KI PDAQ-15 total (-) PT PDAQ-15 total |).
[d]Direct Assessment of Function Scale.
[e]Geriatric Depression Scale 15-item version total.
[f]Mattis Dementia Rating Scale version 2.
[g]Montreal Cognitive Assessment total.

Factors Contributing to PDAQ Disagreement

Linear regression models showed that the significant predictors of increasing ABS PDAQ discrepancy between PT and KI were lower DRS-2 score ($F_{(3,\ 250)} = 17.45$; $P = 0.03$), higher GDS-15 score ($P = 0.002$), and increasing KI burden ($P = 0.05$).

Significant predictors of increasing RAW PDAQ-15 discrepancy in direction of higher KI relative to PT rating were increasing DRS-2 score ($F_{(3,\ 250)} = 28.84$; $P = 0.004$), higher GDS-15 score ($P < 0.001$), and lower KI burden ($P < 0.001$).

The RAW PDAQ-15 discrepancy was minimal as patient cognition approached normal, and grew as PT cognition declined, with PT estimating their cognitive functional abilities better than did KI as actual cognitive performance declined (see Supporting Information Fig. S1).

Stratifying the pairs of KI and PT into three groups based on PT consensus cognitive diagnosis (normal cognition [NC] = 121; MCI = 72; PDD = 61), we found that ABS discrepancy was significantly lower between NC (mean = 4.30; SD = 5.38) and MCI (7.24, 7.84; $P = 0.03$) and between NC and PDD (10.18, 10.27; $P < 0.001$). Similarly, RAW discrepancy was significantly different between NC (1.98, 6.60) and PDD (−4.02, 13.94; $P < 0.001$) and between MCI (0.74, 10.68; $P = 0.02$) and PDD (Table 2 and Supporting Table S1), where, in both cases, PT rated themselves higher than did KI.

Patient and Knowledgeable Informant Perception of Cognition Compared to a Performance-Based Measure

The subgroup completing the DAFS was significantly older ($t_{(94.9)} = -2.7$; $P = 0.008$), had a significantly longer disease duration ($t_{(87.5)} = 2.8$; $P = 0.006$), had significantly greater ABS discrepancy ($t_{(79.1)} = 2.05$; $P = 0.04$), significantly lower PT ($t_{(84.6)} = -3.36$; $P = 0.002$), and KI ($t_{(80.0)} = 3.29$; $P = 0.001$) raw PDAQ-15 scores, and had significantly lower DRS-2 scores ($t_{(74.8)} = 4.27$; $P < 0.001$) than those participants who did not complete the DAFS (Supporting Information Table S2).

TABLE 2 *Predictors of PDAQ-15 discrepancy*

Predictors	Coefficient Estimate	Std Error	*t* Value (DF)	*P* Value
ABS discrepancy				
Intercept	14.72	5.54	2.66 (7.19, 249)	0.008**
DRS-2 total	−0.09	0.04	−2.18	0.03*
GDS-15 total	0.54	0.17	3.20	0.002**
KI Burden Total	0.11	0.04	3.09	0.002**
Raw discrepancy				
Intercept	−15.90	6.84	−2.32 (8.87, 250)	0.02*
DRS-2 total	0.14	0.05	2.90	0.004*
GDS-15 total	0.96	0.21	4.58	7.37e-06***
KI Burden Total	−0.35	0.05	−7.57	7.04e-13***

*Significance at 0.05; **significance at 0.01; ***significance at 0.001.

Pearson's partial correlation determined that the KI (r = 0.82; $P < 0.001$) PDAQ-15 total score compared to PT (r = 0.62; $P < 0.001$) was more strongly correlated with DAFS performance. A linear regression model determined that higher DRS-2 score ($F_{(7,53)} = 53.61$; $P < 0.001$), lower age ($P = 0.01$), and higher KI PDAQ-15 total raw score ($P < 0.001$) were independent predictors of better DAFS performance, but PT PDAQ-15 score was not (Supporting Information Table S3).

Discussion

Agreement between PT and KI rating of PT cognition-based functional abilities is moderate, based on both total PDAQ-15 score and at the individual item level. Increasing KI burden and PT depression, and a decrease in global PT cognitive abilities, predict greater disagreement. In addition, KI ratings of cognitive function more accurately predicted performance-based cognitive function than did PT ratings.

Our results indicate that the KI PDAQ was more strongly associated with the gold-standard performance-based measures of cognitive functioning than was the PT PDAQ, which is consistent with previous studies,[8–11] showing that as PD patients decline cognitively from NC to MCI to PDD, they become less accurate in assessing their functional abilities.

Similarly, our findings are in agreement with other studies that show that PT who are depressed have greater disagreement with KI rating. Specifically, we found that increasing PT depression was associated with PT rating their abilities better compared to KI. This finding is consistent with some,[13–16] but not all, previous findings.[4,16,39,40]

Increasing KI burden was also a predictor of PDAQ-15 discrepancy, with higher burden associated with KI rating PT cognition function lower compared with PT rating. KI burden has been previously linked to anxiety and depression and correlated with PT disease stage and depression.[16,19]

These results show that similar total PDAQ-15 scores are obtained when a patient and his or her knowledgeable informant complete the instrument, with the discrepancy decreasing as PT cognition improves. However, as PD progresses and cognition and depression worsen, PT may not be as well suited as their KI to judge their cognitive function. It is also possible that increasing caregiver burden may lead knowledgeable informants to underestimate patient abilities. Assessing functional abilities specific to cognition is necessary to diagnose either PD-MCI or PDD based on International Parkinson and Movement Disorder Society (MDS) recommended criteria, and assessment instruments include self-reported rating scales and a performance-based measure. Our data were not longitudinal and thus further research should build on these cross-sectional findings to determine whether patient and knowledgeable informant ratings of patient cognitive function converge or diverge over time, and which is more sensitive to predicting future cognitive decline and improvement with therapeutic interventions. Additionally, the DAFS was only performed in a subset of PD individuals, most of whom had significant cognitive impairment, and therefore it is unclear whether our results would hold true in a younger, less-impaired cohort. However, if our findings are confirmed in follow-up longitudinal analyses, then it suggests that KI are suitable, and maybe preferred, proxies for assessing cognitive functional abilities of PT in PD.

Acknowledgments

Data contributed to this project by NIA grant AG09215 at the Perelman School of Medicine at the University of Pennsylvania (Trojanowski JQ-PI).

Author Roles

(1) Research Project: A. Conception, B. Organization, C. Execution; (2) Statistical Analysis: A. Design, B. Execution, C. Review and Critique; (3) Manuscript Preparation: A. Writing of the First Draft, B. Review and Critique.

B.L.D.: 1A, 1B, 1C, 2A, 2B, 3A
S.X.X.: 1A, 1B, 1C, 2A, 2B, 3A
G.C.: 1A, 1B, 1C, 2A, 2B, 3B
J.R.: 1A, 1B, 1C, 2A, 2B, 3A
A.S.: 1A, 3B
S.R.: 1C, 2A, 3B
A.C.-P.: 3B
J.E.D.: 3B
J.F.M.: 3B
N.D.: 3B
J.Q.T.: 3B
D.W.: 1A, 2A, 3A

Disclosures

Ethical Compliance Statement: Informed consent was obtained from all PT and KI pairs. Consenting process was approved by the Institutional Review Board at the Perelman School of Medicine at the University of Pennsylvania (Reference: 820710). We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this work is consistent with those guidelines.

Funding Sources and Conflicts of Interest: This study was supported by the NIA. The authors report no conflicts of interest.

Financial Disclosures for previous 12 months: Dr. Xie has received research funding or support from National Institutes of Health (NIH); payments for consulting services related to cancer from F. Hoffman-La Roche Ltd. Dr. Siderowf is supported by the Michael J. Fox foundation, NINDS, and received honoraria for consultancy from Biogen, Voyager Therapeutics, Merck, and Denali and serves on the data safety monitoring board (DSMB) for Wave Life Sciences and Prilenia Therapeutics. Dr. Chen-Plotkin is supported by the NIH (RO1 NS082265

and UO1 NS082134), the Burroughs Wellcome Fund, the Benaroya Fund, the Alzheimer's Association//Michael J. Fox Foundation/Weston Brain Institute, and the Pechenik Montague Award Fund. Dr. Morley receives research funding from the Department of Veteran Affairs and GE Healthcare. Dr. Dahodwala receives grant funding from NIH, Parkinson's Foundation, Michael J. Fox Foundation, Parkinson's Council, AbbVie, Biotie, and Medtronic. Dr. Trojanowski may accrue revenue in the future on patents submitted by the University of Pennsylvania wherein he is co-inventor and he received revenue from the sale of Avid to Eli Lily as co-inventor on imaging related patents submitted by the University of Pennsylvania. Dr. Weintraub has received research funding or support from Michael J. Fox Foundation for Parkinson's Research, National Institutes of Health (NINDS), Department of Veterans Affairs, Alzheimer's Disease Cooperative Study, and the MDS; honoraria for consultancy from Acadia, Biogen, Biotie (Acorda), Bracket, Clintrex LLC, Eisai Inc., and the CHDI Foundation; license fee payments from the University of Pennsylvania for the QUIP and QUIP-RS; royalties from Wolters Kluweland; and fees for legal consultation for lawsuits related to medication prescribing in patients with PD.

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Supporting Information

Supporting information may be found in the online version of this article.

Table S1. Bonferroni post-hoc test by consensus diagnosis predicting PDAQ-15 discrepancy.

Table S2. Subgroup of participants who completed the DAFS within 1 year of the PDAQ-15.

Table S3. Linear regression model predicting DAFS performance.

Table S4. Weighted Cohen's kappa statistic per PDAQ-15 question.

Figure S1. Scatter plot showing raw DRS-2 Total Raw score by PDAQ-15 Raw discrepancy.