

## Modernizing Daily Function Assessment in Parkinson's Disease Using Capacity, Perception, and Performance Measures

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**ABSTRACT:** Many disease symptoms restrict the quality of life of the affected. This usually occurs indirectly, at least in most neurological diseases. Here, impaired daily function is interposed between the symptoms and the reduced quality of life. This is reflected in the International Classification of Function, Disability and Health model published by the World Health Organization in 2001. This correlation between symptom, daily function, and quality of life makes it clear that to evaluate the success of a therapy and develop new therapies, daily function must also be evaluated as accurately as possible. However, daily function is a complex construct and therefore difficult to quantify. To date, daily function has been measured primarily by capacity (clinical assessments) and perception (surveys and patient-reported

outcomes) assessment approaches. Now, daily function can be captured in a new dimension, that is, performance, through new digital technologies that can be used in the home environment of patients. This viewpoint discusses the differences and interdependencies of capacity, perception, and performance assessment types using the example of Parkinson's disease. Options regarding how future study protocols should be designed to get the most comprehensive and validated picture of daily function in patients are presented. © 2020 The Authors. *Movement Disorders* published by Wiley Periodicals LLC on behalf of International Parkinson and Movement Disorder Society

**Key Words:** activities of daily living; digital technologies; ICF model; perception

The International Classification of Function, Disability and Health<sup>1</sup> (ICF) model of the World Health Organization is a classification of health and health-related domains. These domains help us to describe changes in body function and structure, what persons with a health condition can do in a standard environment (their level

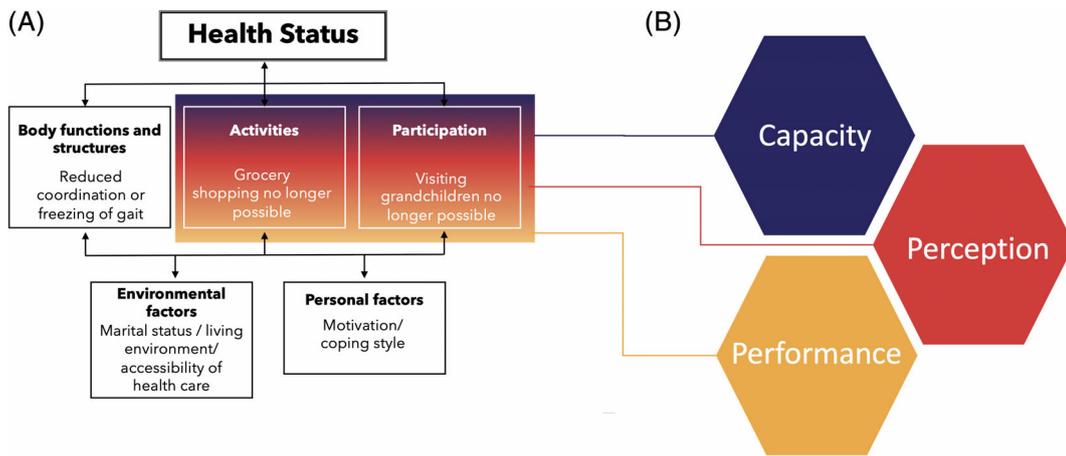
of capacity), and what they actually do in their usual environment (their performance level). This ICF model also provides a definition of daily function, *performance of physical, behavioral, and cognitive activities and their individualized interaction with the environment*. Patients, health-care professionals, health-care industry, and regulatory agencies are increasingly interested in outcome measures that quantify changes in daily function. This is because clinical routine management and clinical trials almost always focus on symptomatic (ie, improvement in symptoms, which belong to the body structure and function domain of the ICF model, Fig. 1A) treatment effects, and they frequently fail to show any relevant effect on daily function at an individual level. However, an increasing body of literature supports that daily function is more closely associated with quality of life<sup>2</sup> compared to any blood-based laboratory value or

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**FIG. 1.** (A) The International Classification of Function, Disability and Health (ICF) model of the World Health Organization, with the 5 domains (in bold) and gait disabilities as an example (plain text) of how a specifically reduced health status can be reflected in, or affect, the different domains. Daily function is represented by the activities of daily living and the participation in societal roles domains (colored area) and influenced by the 3 other domains. (B) Daily function can be measured with different assessment types that measure—at least partly—different facets of daily function. Here, capacity (blue), perception (red) and performance measures (yellow) are shown. [Color figure can be viewed at [wileyonlinelibrary.com](http://wileyonlinelibrary.com)]

image finding.<sup>2-5</sup> We must thus, in regulatory language, substantially improve our knowledge of how our management of diseases and treatment development changes the way a person “feels, functions or survives” in daily life, with a special emphasis on daily function.<sup>6</sup> This interest is also shared by the patients, and there is no reason to believe that health-care professionals also have, or at least should have,<sup>7</sup> great interest in including daily function as a relevant measure for determining the success of therapy.

However, assessment of daily function is challenging, and there is no agreed method to do this. The assessment of daily function is further complicated by the different approaches used to capture it, such as supervised clinical tests and questionnaires given to patients. These are briefly summarized together with the proposal for a new approach.

### Capacity

Until recently, daily function was mainly assessed using tests or observations of the health-care team in the clinical environment by applying, for example, the motor part of the Movement Disorder Society-sponsored Unified Parkinson’s Disease Rating Scale (MDS-UPDRS, Part III) for patients with Parkinson’s disease (PD). Such clinical tests are usually instructed, supervised, observed, and without any definite intention on the part of the person under investigation. They are thought to assess mainly the capacity aspects of function (How good is your [maximal] function?).<sup>8</sup> Capacity-based tests tell us about what someone can do when asked. However, this is not necessarily what this person will do in the context of everyday life. Patients may prefer to carry out daily activities with minimum effort and will not be challenged to maximum capacity during daily activities. Moreover, this assessment approach does not tell us anything about how well and in

what quantity people perform actions (eg, steps, sports activities, and social interactions) in everyday life. Capacity assessments are also not suitable to inform about symptoms that are usually occurring only in daily life (and not in the doctor’s office), such as motor and non-motor fluctuations; early morning dystonia; and gastrointestinal, urogenital, and sleep problems.

### Perception

Another commonly used approach to assess daily function is to ask patients to complete patient-reported outcomes (PROs), that is, questionnaires and diaries. PROs mainly capture the perception of daily function. (How do you rate your function?). PROs are capable of providing information about the understanding, interpretation, and expectation of the patients regarding their disease and treatment. These assessments, however, are prone to (recall) bias<sup>9</sup> and may depend on the current mood of the patients.<sup>10</sup> PROs suffer also from testing bias. Perceived social and emotional support from assessors may “positively” influence results.<sup>10</sup> On the contrary, repetitive testing (as usual for PROs) can lead to bias due to change in behavior, mood, and awareness.<sup>10</sup> PROs can also be influenced by cultural background, knowledge, beliefs, and misinterpretations of standardized questions and physical symptoms and reactions.<sup>11</sup>

### Performance

To complement both clinical (capacity) and patient-reported (perception) assessment approaches, digital technologies offer a new dimension of measuring daily function, that is, performance. Performance is usually uninstructed, unsupervised, and unobserved, and serves an intention. Digital technologies allow an objective impression of how patients function in everyday life

and their ability to routinely perform everyday activities.<sup>12</sup> An example of a digital performance measure validated in the home environment to monitor performance (ie, typing)<sup>13</sup> and that has started its clearance process by the Food and Drug Administration (FDA) is the neuroQWERTY software. This technology monitors psychomotor performance and fine motor function unobserved and in the background while the user is operating on his or her computer or smartphone. Recently, the European Medicines Agency (EMA) approved the continuous measurement of the 95th percentile of stride velocity in the home environment as a secondary endpoint for baseline assessment and for exploratory drug therapeutic studies in Duchenne muscular dystrophy.<sup>14</sup> Other performance parameters are increasingly well understood and may soon be available to provide clinical advice and support clinical decisions. For example, a recent study<sup>15</sup> reporting about 4840 US adults with a mean age of 57 years who wore accelerometers on the hip for a mean of 5.7 days demonstrates that the number of steps performed per day is negatively associated with mortality, but the number of steps per time (cadence, a capacity measure, assessed in this study with accelerometer-measured peak cadence) is not. Digital technologies can also unravel patient's nighttime performance, which may not be very well reflected by any assessments that determine capacity or perception. A plethora of projects and initiatives are currently underway to test the potential of digital assessments to complement current disease management and as endpoints in clinical trials.

In summary, capacity, perception, and performance assessment probably measure different aspects of the daily function.<sup>1</sup> This idea is shown in Figure 1.

The conundrum now is which assessment approach—capacity, perception, and performance—is able to provide insights into aspects of daily function that are relevant to patients, medical professionals, health-care industry, and regulatory agencies. To move this question forward, we need to define or develop promising measures of daily function in each of the 3 aforementioned assessment types. We then need to evaluate how they relate to each other and in which way they independently and collectively provide insights into daily function. This viewpoint will use PD as a disease model, because the differences between the capacity, perception, and performance assessments and the associations between daily function<sup>4,16</sup> (especially mobility<sup>17-19</sup>) and quality of life<sup>2</sup> have already been investigated.

## Current State of Assessments of Daily Function

Recommendations for the development and validation of PROs, clinical scales, and digital measures are

available.<sup>20-24</sup> However, these ways of developing assessments are not designed to solve complex problems such as capturing daily function (see also Fig. 1). We need to better understand what constructs of daily function these assessments represent and how the different assessments are related or complementary.

Different parameters of daily function have been collected in the same cohorts with assessments that capture the different constructs of daily function (ie, capacity, perception, and performance).<sup>8</sup> If these assessments measure similar aspects of daily function, they should be strongly associated with each other (eg, have a high correlation between the respective assessments).

Table 1 provides an overview of studies investigating and reporting on the associations between assessments of daily function in older adults and PD. The table highlights that only a small bandwidth of daily function parameters has been investigated using measures from all 3 types of assessments. Interestingly, these few results suggest that daily function can yield different outcomes, depending on whether the assessment was performed with a capacity, perception, or performance assessment. Gait speed as assessed in the lab on a 10-m pressure sensor mat (capacity) explained only 25% of how mild-to-moderate PD patients perceived their daily function assessed using the “Walk-12G” questionnaire<sup>18</sup> (perception). The gait speed of older adults measured in the lab (capacity) explained only 46% of the variance of usual gait speed assessed over a period of 3 days<sup>26</sup> (performance). In mild-to-moderate PD patients, the Walk-12G questionnaire (perception) correlated only moderately ( $r = -0.46$ ) with mean steps per day and poorly with time spent in brisk walking ( $r = -0.35$ ) in free-living conditions assessed over a period of 7 days<sup>18</sup> (performance). A preliminary analysis comparing sensor data with perceived off medication state showed an area under the curve of maximum 0.73.<sup>28</sup> Moreover, the severity of motor fluctuations (as measured using MDS-UPDRS, Part IV, item 4, a perception measure) was poorly associated with changes in real-life walking patterns (performance) in mildly to moderately affected PD patients.<sup>29</sup> In line with these observations, a recent systematic review—collecting information about the association between subjective and mobile health technology-derived evaluation of freezing of gait and falls<sup>30</sup>—reported significant variability in outcomes measured and results reported.

Moreover, it is relatively unclear to date how far our already-available and validated capacity and perception measures are measuring relevant constructs of daily function at all. According to Deal and colleagues,<sup>31</sup> the following 5 capabilities are most relevant for moderate-to-advanced PD patients: core physical actions, basic self-care activities, other daily activities, social impact, and emotional impact. This work strongly suggests that (1) our capacity measures currently used in clinical management do not capture a relevant proportion of

**TABLE 1.** Low-to-moderate associations between relevant parameters for daily function that measure different constructs (capacity, perception, and performance) in healthy older adults and patients with Parkinson’s disease

Author	Aim	Cohort	Assessment tools	Correlation
Leavy et al (2018) <sup>18</sup>	Investigate the relationship between patient-reported walking difficulties and performance-based walking in laboratory and free-living conditions in mild-to-moderate PD patients	47 HCs (aged >60) 49 mild-to-moderate PD (aged >60) Excluding participants with coexisting neurological conditions affecting balance; cognitive function: MMSE <24	Perception: Walk-12G  Capacity: 10-m pressure walkway Performance: accelerometers 4–7 days	Perception vs. capacity: Walk-12G vs. step velocity: rho = -0.46, R <sup>2</sup> = 0.25, Walk-12G vs. step length: rho = -0.36, R <sup>2</sup> = 0.12 Perception vs. performance: Walk-12G vs. steps/day: rho = -0.46
Hubble et al (2016) <sup>25</sup>	Investigate the relationship between accelerometer-derived measures of movement rhythmicity and clinical measures of mobility, balance confidence, and gait difficulty in PD patients	30 PD patients Included: patients with a history of 2 or more near-misses and/or at least 1 fall in the previous 12 months Excluded: unable to stand and walk independently; cognitive function: Addenbrooke <82	Perception: 1. freezing of gait questionnaire 2. gait and falls questionnaire 3. activities-specific balance confidence scale Capacity: 1. 6-minute walk test 2. timed-up-and-go test 3. retropulsion test	Perception vs. capacity: 1. activities-specific balance confidence scale vs. timed-up-and-go test: rho = -0.52 2. gait and falls questionnaire vs. retropulsion test: rho = 0.43 3. activities-specific balance confidence scale vs. retropulsion test: rho = -0.60 4. gait and falls questionnaire vs. harmonic ratio trunk: rho = -0.43
Hillel et al (2019) <sup>26</sup>	Is daily gait comparable to gait in the lab either in single tasking or dual tasking in healthy elderly?	150 HCs, aged 60–90 Included: able to walk for at least 5 minutes unassisted and had at least 2 falls in the previous 6 months Excluded: cognitive function: MMSE <21	Capacity: 1. single tasking: accelerometer in 15-m corridor 2. dual tasking: accelerometer in 15-m corridor  Performance: free-living: accelerometers for 7 days	Capacity vs. performance: gait parameters measured in single task/dual task vs. free-living Single task (ICC) Dual task (ICC)  step length 0.76 0.68 gait speed 0.66 0.63 step regularity 0.56 0.60 stride regularity 0.35 0.36 step time 0.39 0.26
Brodie et al (2016) <sup>27</sup>	Investigate the relationship between walking during daily activities and laboratory assessed gait in healthy older adults	51 HCs. Participants were able to walk with or without the walking aid	Capacity: 4.6-m GaitRite, 3 walks on normal pace Performance: semi-structured free-living activities, 1 accelerometer	Capacity vs. performance: 1. cadence: lower median cadence in free-living conditions (r = 0.69) 2. step time variability: higher in free-living conditions (r = 0.27)
Del Din (2016) <sup>19</sup>	Explore the impact of environment and pathology by analyzing differences between PD patients and controls in the laboratory and free-living environment (Student’s <i>T</i> or Mann-Whitney <i>U</i> test)	50 HCs (aged >60, cognitive function: MMSE >24) 47 mild-to-moderate PD patients (aged >60, cognitive function: MMSE >24) Any orthopedic or cardiothoracic conditions that may have markedly affected walking or safety during the testing sessions	Capacity: 10-m walkway with accelerometer at the lower back Performance: accelerometer at lower back for 1 week	Capacity vs. performance in both PD patients and HCs: In free-living conditions decreased pace, increased rhythm, higher variability, and asymmetry ( <i>P</i> < 0.001) Moderate correlations between lab and free-living circumstances (r < 0.45)

Overview of the moderate-to-poor correlations between different domains—capacity, performance, and perception—of gait parameters measured in healthy controls (HCs) and patients with Parkinson’s disease (PD).  
Abbreviations: ICC, intraclass correlation coefficients; MMSE, Mini-Mental State Examination; r, Pearson’s correlation; rho, Spearman’s rho; R<sup>2</sup>, coefficient of variation; Walk-12G, patient-reported outcome with 12 questions about perceived walking difficulties.

the daily function that is perceived as most critical to this group of patients; (2) for most of these daily functions it is completely unclear to date how individual PD-specific symptoms (motor and non-motor, as singular symptoms and in interaction with other PD-relevant symptoms as well as comorbidities) contribute to them; (3) it is very unlikely that the aspects of daily function, most relevant for moderate-to-advanced PD patients, are also relevant for early PD; and (4) only those capacity and perception assessments that do capture daily function constraints at an individual level can adequately reflect the complexity and individual relevance of the latter. Moreover, how daily function and underlying disease processes are interlinked is often difficult to determine only with capacity and perception assessments (eg, whether there is a direct link between a symptom and a change in daily function or whether the latter is indirectly influenced by reduced activity and disuse).

## How to Best Assess Daily Function?

Based on the existing need to assess daily function more accurately, the entirely new options that digitalization of health care opens up for assessment development, and the observed increasingly intense networking of different stakeholders, we propose to test daily function using assessment batteries that capture capacity, perception, and performance aspects; include gold standard assessments; and evaluate the interplay between the different assessment types critically. This requires the cooperation of different stakeholders, with patients in the focus and core of the projects. It is therefore imperative to strengthen the role of patients in particular. For PD patients, a deeper understanding of their own specific PD manifestations and contribution of the novel assessment to a more effective decision-making regarding their own self-care has been reported to be a particular motivation for participation in more complex studies.<sup>32</sup> Ideas that lead to the empowerment of patients are presented and discussed in detail in a recent publication.<sup>33</sup> One possible way in which cooperation between different stakeholders could be implemented in practice is illustrated in Serrano et al.<sup>34</sup> Here, PD patients and health-care professionals have used a Delphi process and focus groups to create a prioritized list of symptoms and everyday restrictions that are relevant to daily function for patients and that can be assessed using not only currently validated but also new assessment instruments. In this process, the point that different stakeholders often use a different language to describe symptoms and deficits in daily function was also addressed. A similar approach in a large cohort showed similar results.<sup>35</sup>

Although work as mentioned earlier can be helpful for a basic understanding of what daily function means, for

example, patients with PD,<sup>31,34</sup> we must strive for a consensus definition of the term. We propose here the WHO definition mentioned in the beginning of this article. In any case, this consensus process must include definitions of physiological ranges of daily function and deficits thereof. Only then can a far-reaching conceptualization of the term take place. It seems likely that this process will have to be carried out separately for different diseases, because (1) daily function may differ substantially between individuals at different ages and with different diseases and (2) deficits of daily function as well as the weighting of these deficits may not be comparable across different diseases. It may even be necessary to generate independent concepts for subgroups of diseases, such as early PD versus moderate/advanced PD<sup>31</sup> and dyskinetic versus non-dyskinetic patients.<sup>36,37</sup> Approaches such as biomarker-driven phenotyping may also be helpful.<sup>38</sup>

We further argue that for the development of promising daily function-relevant parameters, we must evaluate new ways of validation. To date, we have mainly used gold standards from the identical assessment type (eg, a capacity measure) for the validation of new (again capacity-assessing) instruments and parameters. A new option could be the use of gold standards from assessment types that differ from the assessment type under investigation.<sup>8</sup> This approach must cover all validation aspects that are expected from conventional validation, that is, construct validity (including convergent validity, discriminate known groups, and discriminant validity), predictive capacity, ability to detect change (including longitudinal validity and minimal important difference), and responsiveness. As in Table 1, only moderate correlations are often to be expected when comparing parameters across different assessment types. These could be predefined by the study team and should be accepted by regulatory bodies. The very positive signals and recommendations of the EMA<sup>39</sup> and the FDA<sup>23</sup> to include performance instruments on an exploratory level in the assessment panels of clinical trials support this proposal by producing data sets that can be analyzed accordingly. Still, only one-third of clinical trials on movement disorders that are actually registered in ClinicalTrials.gov include such performance instruments in their assessment panels.<sup>43</sup> This approach has to be extended to observational studies.

Another possibility for the validation of daily function parameters on a very detailed level provides the ICF model.<sup>44</sup> It enables the evaluation of the following daily function domains: learning and knowledge application; general tasks and demands; communication; mobility; self-care; domestic life; interactions and relationships; important areas of life; and community, social, and civic life. Information may be obtained from the person experiencing disabilities and from other data sources (eg, from the health-care team). The rating is done using a combination

of codes and qualifiers. Codes provide descriptions of specific aspects of functioning, and qualifiers indicate the extent of functioning (rated with a “+”) or disability (rated with a “-”). This model is primarily used in rehabilitation medicine and has unfortunately not yet found its way into many other areas of medicine.<sup>40</sup> However, current developments in the recording of disease symptoms with novel technology and in the nonhospital environment could accelerate the widespread use of this tediously developed tool, which was endorsed by all 191 WHO countries at the time. It may ultimately be required that none of the measures of capacity, perception, and performance will be equally generalizable or have a similar value across large diverse populations.<sup>8</sup> As such, a digital “anchor” to the individual will be required. To that end, the Task Force of Technology and the Rating Scales Program of the International Parkinson and Movement Disorders Society are developing an e-diary<sup>41</sup> whose output could be connected to attribute whether any of the aforementioned measures explain changes that are meaningful to those from whom the measures are collected. Such an e-diary also has the advantage that recall bias can be avoided. Furthermore, it can represent a further milestone in the development of comprehensive daily function parameters: although e-diaries primarily measure perception, capacity and performance assessments can also be recorded relatively easily. Capacity can be measured by instructed tests that are, for example, performed on a smartphone, and performance can be determined by co-using (mobile) technologies that are synchronized to the e-diary. This allows a simultaneous recording of all 3 constructs discussed here, which can be particularly helpful in understanding the interaction of capacity, perception, and performance. This approach may not cover all aspects of daily function. For example, it does not comprehensively cover functional capacity aspects in the domestic environment (which can be collected with instruments such as the University of California San Diego Performance-based Skills Assessment<sup>45</sup>). The e-diary may still be a relevant step forward in the direction of a comprehensive (and potentially much more personalized) daily function assessment, particularly in movement disorders.

The complex collection and validation of daily function also requires aligning of data collection protocols<sup>42</sup> and an active data sharing policy.<sup>8</sup> Eventually, for the evaluation of these data sets, intensive cooperation between the various stakeholders (including patient and clinical specialists) is necessary to interpret the data adequately.

## Conclusion

It seems no surprise that the rapid development in the field of mobile health technologies-based assessment (self-assessment, eg, in the home environment) and the demand of patients and regulatory bodies such as the

EMA and FDA for a more detailed assessment of daily function coincide. This is a valuable development toward “daily relevant medicine.” A clear, conceptualizable, and widely accepted definition of daily function is provided by the WHO-developed ICF model. With novel technologies, the assessment of daily function becomes more complex but also more comprehensive, and therefore possibly more “correct.” Therefore, daily function should be covered by several constructs, for example, by capacity, perception, and performance assessments. A high correlation between the measures from the different assessment types is not always expected, and the level of correlation will broadly be dependent on the constructs and types of measurements being compared. How the individual assessment types collectively contribute to the understanding of the overall concept of “daily function” is currently not well understood, and further research and clinical implementation of these issues require intensive cooperation between patients, health-care professionals, regulatory bodies, and health-care industry. ■

## Conflict of Interest

All authors declare no conflict of interest or have no affiliation with or involvement in any organization or entity with any financial interest or nonfinancial interest in the subject matter discussed in this manuscript.

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