



SHANNON D. DONOFRY, CLAIRE E. O'HANLON

# Measuring Cognition in Clinical Trials in Parkinson's Disease, Dementia with Lewy Bodies, and Related Disorders

---

Annex for Roundtable Proceedings and Roadmap for  
Research

For more information on this publication, visit [www.rand.org/t/CFA3210-1](http://www.rand.org/t/CFA3210-1).

#### **About RAND**

RAND is a research organization that develops solutions to public policy challenges to help make communities throughout the world safer and more secure, healthier and more prosperous. RAND is nonprofit, nonpartisan, and committed to the public interest. To learn more about RAND, visit [www.rand.org](http://www.rand.org).

#### **Research Integrity**

Our mission to help improve policy and decisionmaking through research and analysis is enabled through our core values of quality and objectivity and our unwavering commitment to the highest level of integrity and ethical behavior. To help ensure our research and analysis are rigorous, objective, and nonpartisan, we subject our research publications to a robust and exacting quality-assurance process; avoid both the appearance and reality of financial and other conflicts of interest through staff training, project screening, and a policy of mandatory disclosure; and pursue transparency in our research engagements through our commitment to the open publication of our research findings and recommendations, disclosure of the source of funding of published research, and policies to ensure intellectual independence. For more information, visit [www.rand.org/about/research-integrity](http://www.rand.org/about/research-integrity).

RAND's publications do not necessarily reflect the opinions of its research clients and sponsors.

Published by the RAND Corporation, Santa Monica, Calif.

© 2024 RAND Corporation

RAND® is a registered trademark.

#### **Limited Print and Electronic Distribution Rights**

This publication and trademark(s) contained herein are protected by law. This representation of RAND intellectual property is provided for noncommercial use only. Unauthorized posting of this publication online is prohibited; linking directly to its webpage on [rand.org](http://rand.org) is encouraged. Permission is required from RAND to reproduce, or reuse in another form, any of its research products for commercial purposes. For information on reprint and reuse permissions, please visit [www.rand.org/pubs/permissions](http://www.rand.org/pubs/permissions).

## About This Annex

---

This annex summarizes the cognitive measures evaluated at and participants in the Parkinson’s Disease/Dementia with Lewy Bodies (PD/DLB) Cognition Measures Roundtable, which was held in Washington, D.C., on January 10–11, 2024. This event was hosted by the Critical Path for Parkinson’s Consortium, Cure Parkinson’s, Lewy Body Dementia Association, The Michael J. Fox Foundation for Parkinson’s Research (MJFF), Parkinson Canada, Parkinson’s UK, and Shake It Up Australia Foundation. This event brought together representatives from academia and industry with those from regulatory agencies, community partners, and research funders to discuss challenges in developing clinical outcome assessments for cognitive impairment in PD and DLB and identify priorities for the field and opportunities for collaboration.

This annex of the roundtable proceedings was funded by MJFF and produced within the Quality Measurement and Improvement Program in RAND Health Care.

RAND Health Care, a division of RAND, promotes healthier societies by improving health care systems in the United States and other countries. We do this by providing health care decisionmakers, practitioners, and consumers with actionable, rigorous, objective evidence to support their most complex decisions. For more information, see [www.rand.org/health-care](http://www.rand.org/health-care), or contact

### **RAND Health Care Communications**

1776 Main Street

P.O. Box 2138

Santa Monica, CA 90407-2138

(310) 393-0411, ext. 7775

[RAND\\_Health-Care@rand.org](mailto:RAND_Health-Care@rand.org)

# Contents

---

About This Annex ..... iii

Appendix A. Additional Details on Cognitive Measures ..... 1

Appendix B. Roundtable Attendees ..... 11

Abbreviations ..... 13

References ..... 14

## Appendix A. Additional Details on Cognitive Measures

---

**Addenbrooke’s Cognitive Examination-III (ACE-III).** The Addenbrooke’s Cognitive Examination-III (ACE-III)<sup>1</sup> is a cognitive screening measure that was developed to aid in identification of dementias characterized by more-severe deficits in attention and visuospatial functioning than is typical of Alzheimer’s disease (AD),<sup>2</sup> including Parkinson’s disease dementia (PDD) and dementia with Lewy bodies (DLB). It is composed of tests of attention, orientation, memory, language, and visuospatial skills. The ACE has been shown to detect mild cognitive impairment (MCI) in the context of Parkinson’s disease (PD) and to differentiate individuals with Parkinson’s disease–mild cognitive impairment (PD-MCI) and PDD from those who have AD and frontotemporal dementia.<sup>3</sup>

**Alzheimer’s Disease Assessment Scale-Cognitive.** The Alzheimer’s Disease Assessment Scale-Cognitive (ADAS-Cog)<sup>4</sup> is a subscale of the ADAS that was developed to assess cognitive impairment in AD and is considered the gold standard of measurement in trials evaluating the effects of therapeutics on cognitive outcomes among patients with AD.<sup>5</sup> The ADAS-Cog includes 11 tasks, some of which are observer-based, which measure functioning in memory, language, and visuomotor domains. Although the ADAS-Cog has been established as a valid measure of cognitive performance in AD and is sensitive to cognitive changes attributable to disease progression or the effects of treatment, recent evidence suggests that some of the component tests are not sensitive enough to detect impairment in Alzheimer’s disease.<sup>6</sup> The ADAS-Cog has been shown to detect differences in cognitive functioning between PD-MCI and PDD and might therefore be sensitive to changes in cognition that occur as the disease progresses.<sup>7</sup> Furthermore, patients with PDD undergoing treatment with rivastigmine show improved performance on the ADAS-Cog, indicating that this measure may be useful for indexing treatment benefits.<sup>8</sup> However, it is important to note that patients with PDD exhibit

---

<sup>1</sup> Beishon et al., “Addenbrooke’s Cognitive Examination III (ACE-III) and Mini-ACE for the Detection of Dementia and Mild Cognitive Impairment.”

<sup>2</sup> Beishon et al., “Addenbrooke’s Cognitive Examination III (ACE-III) and Mini-ACE for the Detection of Dementia and Mild Cognitive Impairment.”

<sup>3</sup> Chade et al., “Detecting Cognitive Impairment in Patient’s with Parkinson’s Disease with a Brief Cognitive Screening Tool”; Sousa, Figueiredo, and Dozzi Brucki, “Addenbrooke’s Cognitive Examination III.”

<sup>4</sup> Rosen, Mohs, and Davis, “A New Rating Scale for Alzheimer’s Disease.”

<sup>5</sup> Cano et al., “The ADAS-Cog in Alzheimer’s Disease Clinical Trials.”

<sup>6</sup> Cano et al., “The ADAS-Cog in Alzheimer’s Disease Clinical Trials.”

<sup>7</sup> Harvey et al., “Evaluation of Dementia Rating Scales in Parkinson’s Disease Dementia.”

<sup>8</sup> Weintraub, Somogyi, and Meng, “Rivastigmine in Alzheimer’s Disease and Parkinson’s Disease Dementia.”

superior performance on the majority of ADAS-Cog subscales compared with patients with Alzheimer’s disease, and the profile of impairments differs significantly,<sup>9</sup> suggesting that this measure may not be optimized for detecting cognitive deficits in PD. Finally, there are more-recently developed adaptations of the ADAS-Cog that include additional subtests to increase sensitivity to cognitive impairment in MCI.<sup>10</sup> Notably, ADAS-Cog was the outcome measure used in the clinical trial for the only approved drug for PDD, rivastigmine.<sup>11</sup>

**Alzheimer’s Disease Cooperative Study—Activities of Daily Living.** The Alzheimer’s Disease Cooperative Study—Activities of Daily Living (ADCS-ADL)<sup>12</sup> assesses functional impairment in amnesic MCI and Alzheimer’s disease and is administered either as an interview with a caregiver or as a questionnaire completed by a caregiver. Caregivers rate the patient’s capacity to successfully complete a range of instrumental activities of daily living (IADLs), such as the ability to manage appointments, engage in usual social and occupational roles, and complete house chores. The ADCS-ADL has been widely used to track declines in function as AD progresses.<sup>13</sup> It has been suggested for use in DLB trials.<sup>14</sup>

**Cambridge Cognitive Assessment-Revised.** The Cambridge Cognitive Assessment–Revised (CAMCOG-R)<sup>15</sup> is a cognitive subtest of the Cambridge Examination for Mental Disorders of the Elderly, a standardized assessment for diagnosis and monitoring of dementia. The CAMCOG-R is used as a screening tool and is composed of measures of cognitive domains commonly impaired in PD, PDD, and DLB, such as memory, attention, executive functioning, visuospatial skills, and language. The CAMCOG-R has been shown to be capable of detecting cognitive impairment in PD,<sup>16</sup> and of tracking decline in cognitive functioning as the disease progresses.<sup>17</sup> However, the utility of this measure has not been evaluated in the context of PDD or DLB.

**Cambridge Neuropsychological Test Automated Battery.** The Cambridge Neuropsychological Test Automated Battery (CANTAB)<sup>18</sup> is a computerized neuropsychological

---

<sup>9</sup> Bronnick et al., “Profile of Cognitive Impairment in Dementia Associated with Parkinson’s Disease Compared with Alzheimer’s Disease.”

<sup>10</sup> Kueper, Speechly, and Montero-Odasso, “The Alzheimer’s Disease Assessment Scale-Cognitive Subscale (ADAS-Cog).”

<sup>11</sup> Emre et al., “Rivastigmine for Dementia Associated with Parkinson’s Disease.”

<sup>12</sup> Galasko et al., “An Inventory to Assess Activities of Daily Living for Clinical Trials in Alzheimer’s Disease.”

<sup>13</sup> Potashman et al., “Psychometric Properties of the Alzheimer’s Disease Cooperative Study.”

<sup>14</sup> Rodriguez-Porcel et al., “Clinical Outcome Measures in Dementia with Lewy Bodies.”

<sup>15</sup> Roth et al., “CAMDEX.”

<sup>16</sup> Athey, Porter, and Walker, “Cognitive Assessment of a Representative Community Population with Parkinson’s Disease (PD) Using the Cambridge Cognitive Assessment–Revised (CAMCOG-R).”

<sup>17</sup> Athey and Walker, “Demonstration of Cognitive Decline in Parkinson’s Disease Using the Cambridge Cognitive Assessment (Revised) (CAMCOG-R).”

<sup>18</sup> Fray, Robbins, and Sahakian, “Neuropsychiatric Applications of CANTAB.”

assessment battery that can be customized according to the population being studied and the research questions being addressed. Modules available for inclusion in the battery evaluate psychomotor speed, memory, working memory, attention, executive functioning, and visuospatial skills. Components of the CANTAB have been used in studies of PD and have been shown to be effective at classifying PD-MCI.<sup>19</sup> However, this measure is not validated for use in PDD or DLB.

**Clinical Dementia Rating Scale Sum of Boxes.** The Clinical Dementia Rating Scale Sum of Boxes,<sup>20</sup> which was developed for Alzheimer’s disease, is a general index of impairment that has been validated for use in staging dementia severity.<sup>21</sup> The Clinical Dementia Rating Scale Sum of Boxes is administered as a semistructured interview of patients and informants, during which the interviewer assesses the following cognitive and functional domains: memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care. Domains are rated on a 4- or 5-point scale and then entered into an algorithm to obtain the Clinical Dementia Rating Scale global score, while the sum of boxes score is calculated by summing scores in each domain.<sup>22</sup> The Clinical Dementia Rating Scale Sum of Boxes has been proposed for adaptation in PD and has been used in DLB trials.<sup>23</sup>

**Cognitive Drug Research Computerized Cognitive Assessment System.** The Cognitive Drug Research Computerized Cognitive Assessment System<sup>24</sup> is a computerized assessment battery that was specifically designed to evaluate the impact of novel drug compounds on cognitive efficiency or mental processing speed in randomized controlled trials. It is composed of measures of memory, executive function, visuospatial skills, and attention; it has been shown to be sensitive to impairments in PD, PDD, and DLB; and it has been used to assess outcomes in clinical trials of rivastigmine in these populations.<sup>25</sup>

**Clinical Global Impression.** The Clinical Global Impression (CGI)<sup>26</sup> is an interview-based assessment often used in clinical practice to assess symptom severity for a variety of conditions,

---

<sup>19</sup> Lawson et al., “Which Neuropsychological Tests?”

<sup>20</sup> Cedarbaum et al., “Rationale for Use of the Clinical Dementia Rating Sum of Boxes as a Primary Outcome Measure for Alzheimer’s Disease Clinical Trials.”

<sup>21</sup> O’Bryant et al., “Staging Dementia Using Clinical Dementia Rating Scale Sum of Boxes Scores.”

<sup>22</sup> Morris, “The Clinical Dementia Rating (CDR).”

<sup>23</sup> Wyman-Chick and Scott, “Development of Clinical Dementia Rating Scale Cutoff Scores for Patients with Parkinson’s Disease”; Walker et al., “Olanzapine in Dementia with Lewy Bodies”; Elder et al., “Consecutive Sessions of Transcranial Direct Current Stimulation Do Not Remediate Visual Hallucinations in Lewy Body Dementia.”

<sup>24</sup> Wesnes, “The Value of Assessing Cognitive Function in Drug Development”; Parrott and Wesnes, “Promethazine, Scopolamine and Cinnarizine.”

<sup>25</sup> Wesnes et al., “Benefits of Rivastigmine on Attention in Dementia Associated with Parkinson Disease”; Allcock et al., “Impaired Attention Predicts Falling in Parkinson’s Disease”; Wesnes et al., “Effects of Rivastigmine on Cognitive Function in Dementia with Lewy Bodies.”

<sup>26</sup> Busner and Targum, “The Clinical Global Impressions Scale.”

including PD. Clinicians rate the clinical severity of patient symptoms on a 1- to 7-point scale based on the clinicians' impressions derived during the assessment, and these impressions tend to incorporate a variety of factors that are relevant to the condition being evaluated. In the context of PD, the CGI incorporates impressions of the core features of PD, including motor, cognitive, and functional abilities.<sup>27</sup> The CGI has been used to establish baseline symptom severity as well as to evaluate treatment responsiveness.<sup>28</sup>

**Cognitive Functional Composite.** The Cognitive Functional Composite (CFC)<sup>29</sup> was developed to evaluate (1) the cognitive domains that are most vulnerable to decline in AD and (2) the functional consequences of AD. It is composed of existing cognitive assessments of episodic memory, working memory, and executive functioning, as well as a questionnaire that measures impairments in the ability to carry out IADLs. The CFC has also been suggested for use in DLB trials.<sup>30</sup>

**Cogstate Battery.** The Cogstate Battery (CB)<sup>31</sup> is a computerized assessment battery that was developed to screen and monitor cognitive changes that occur in normative aging and in the context of disease processes. It is composed of four tests that measure psychomotor function, attention, working memory, and visual memory. Prior research has suggested that the CBB may be used to differentiate cognitively healthy individuals from those with amnesic MCI and AD, although the refinement of cut-off scores may be needed.<sup>32</sup> The CB has been used in a randomized controlled trial of transcranial direct-current stimulation in patients with PD to index cognitive processing speed.<sup>33</sup> However, this measure has yet to be validated for use as a screening, diagnostic, or monitoring tool in PD, PDD, or DLB.

**Direct Assessment of Functional Status.** Similar to the Everyday Cognition Battery (ECB) and the University of California San Diego Performance-Based Skills Assessment (USPA), the Direct Assessment of Functional Status (DAFS)<sup>34</sup> is a performance-based assessment for evaluating successfully completed complex tasks that are dependent on a number of cognitive domains that are impaired in dementia and likely to be encountered in a person's daily life. The DAFS includes 85 items on which performance is rated for completion of tasks in seven

---

<sup>27</sup> Busner and Targum, "The Clinical Global Impressions Scale."

<sup>28</sup> Arnold et al., "High Doses of Pergolide Improve Clinical Global Impression in Advanced Parkinson's Disease"; Weintraub et al., "Rasagiline for Mild Cognitive Impairment in Parkinson's Disease"; Riedel, Klotsche, and Wittchen, "Motor Impairment, Depression, Dementia."

<sup>29</sup> Jutten et al., "The Cognitive-Functional Composite Is Sensitive to Clinical Progression in Early Dementia."

<sup>30</sup> Rodriguez-Porcel et al., "Clinical Outcome Measures in Dementia with Lewy Bodies Trials."

<sup>31</sup> Maruff et al., "Validity of the Cogstate Brief Battery."

<sup>32</sup> Alden et al., "Diagnostic Accuracy of the Cogstate Brief Battery for Prevalent MCI and Prodromal AD (MCI A+T+) in a Population-Based Sample."

<sup>33</sup> Dobbs et al., "Generalizing Remotely Supervised Transcranial Direct Current Stimulation (tDCS)."

<sup>34</sup> Loewenstein et al., "A New Scale for the Assessment of Functional Status in Alzheimer's Disease and Related Disorders."



functional status domains: orientation, communication, financial reasoning, shopping skills, transport, dressing and grooming, and feeding. Individuals with AD dementia exhibit impaired performance on the DAFS relative to similarly-aged cognitively healthy individuals.<sup>35</sup> The DAFS has not been widely used in research focused on PD-related cognitive and functional impairments, although the studies that have included it have demonstrated that patients with PD who also have cognitive impairment exhibit poor performance on this measure,<sup>36</sup> particularly among patients with PDD.<sup>37</sup>

**Everyday Cognition Battery.** The ECB<sup>38</sup> is another assessment designed to measure the functional consequences of cognitive impairment. *Everyday cognition* is defined as the ability to successfully perform cognitively demanding tasks that an individual would be likely to encounter in daily life, such as reading and interpreting information on a food label or evaluating financial information. The battery is composed of four tasks to assess inductive reasoning, domain-specific knowledge, declarative memory, and working memory within the context of evaluating information related to nutrition and meal preparation, medication management, and personal financial management. Individuals with PD who do not have a diagnosis of dementia have been shown to exhibit impairments on the ECB relative to cognitively healthy individuals without PD.<sup>39</sup> Furthermore, treatment with rivastigmine, a cholinesterase inhibitor that is used to manage dementia in AD and PD, is associated with improvement in ECB scores among patients with PD-MCI, suggesting that the ECB is sensitive to treatment effects.<sup>40</sup>

**Lumos Labs NeuroCognitive Performance Test.** The NeuroCognitive Performance Test (NCPT)<sup>41</sup> is a cognitive assessment platform developed by Lumos Lab, the research division of Lumosity, a for-profit company that designs commercially available cognitive training programs. The NCPT is modular and can be used to develop customized assessment batteries composed of tests that are based on validated neuropsychological assessments. The NCPT has not been validated for use in PD, PDD, or DLB.

**Mattis Dementia Rating Scale.** The Mattis Dementia Rating Scale (MDRS)<sup>42</sup> is a screening tool for assessing general cognitive functioning and evaluating the degree of cognitive impairment in patients with dementia. The scale is composed of five subtests that evaluate the following domains: attention, verbal and motor initiation and perseveration, visuospatial

---

<sup>35</sup> McDougall et al., “The Revised Direct Assessment of Functional Status for Independent Older Adults.”

<sup>36</sup> Deck et al., “Cognitive Functional Abilities in Parkinson’s Disease.”

<sup>37</sup> Brennan et al., “The Penn Parkinson’s Daily Activities Questionnaire-15.”

<sup>38</sup> Allaire and Marsiske, “Everyday Cognition.”

<sup>39</sup> Young et al., “Everyday Reasoning Abilities in Persons with Parkinson’s Disease.”

<sup>40</sup> Mamikonyan et al., “Rivastigmine for Mild Cognitive Impairment in Parkinson Disease.”

<sup>41</sup> Human Cognition Project, “Tools for Research Collaborators”; Morrison et al., “Reliability and Validity of the NeuroCognitive Performance Test, A Web-Based Neuropsychological Assessment.”

<sup>42</sup> Mattis, Jurica, and Leitten, *Dementia Rating Scale*.

construction, conceptualization, and memory. Evidence suggests that the MDRS is useful for detecting MCI among patients with PD and for discriminating individuals with PDD from cognitively healthy individuals with PD.<sup>43</sup> The MDRS has been shown to yield distinct performance profiles for individuals with PDD and DLB compared with AD.<sup>44</sup> Similar to the Montreal Cognitive Assessment (MoCA), the MDRS is listed as a recommended screening assessment of global cognitive performance in PD by the International Parkinson and Movement Disorder Society.<sup>45</sup>

**Mini-Mental State Examination.** The Mini-Mental State Examination (MMSE)<sup>46</sup> is a well-validated screening instrument that was designed to detect MCI that emerges in the context of neurodegenerative disease. It was developed to be easily administered by any health care professional in a wide variety of clinical settings. Cognitive domains that are covered by the MMSE include overall orientation, memory, attention, language, and visual construction. The MMSE has been shown to differentiate individuals with dementia from those who are cognitively healthy and to be useful for tracking changes in global cognition over time, including in PDD and DLB.<sup>47</sup> However, ceiling effects have been observed with the MMSE, whereby individuals with documented MCI frequently score above the established cutoff score of 26 used for detecting impairment. Furthermore, there is some evidence that individuals with autopsy-confirmed DLB do not exhibit impairments on the MMSE, suggesting that it may not be a useful screening tool for the cognitive deficits that are typical in DLB.<sup>48</sup> Therefore, as with other screening instruments, it is not recommended for use as a diagnostic tool or for identifying cognitive impairment among individuals without dementia.<sup>49</sup>

**Montreal Cognitive Assessment.** The MoCA<sup>50</sup> is another widely used screening tool for identifying mild cognitive impairment in a range of patient populations, including PD and DLB. The MoCA assesses the same domains covered by the MMSE, as well as additional domains,

---

<sup>43</sup> Pirogovsky et al., “The Utility of the Mattis Dementia Rating Scale in Parkinson’s Disease Mild Cognitive Impairment”; Llebaria et al., “Cut-Off Score of the Mattis Dementia Rating Scale for Screening Dementia in Parkinson’s Disease.”

<sup>44</sup> Aarsland et al., “Performance on the Dementia Rating Scale in Parkinson’s Disease with Dementia and Dementia with Lewy Bodies”; Connor et al., “Cognitive Profiles of Autopsy-Confirmed Lewy Body Variant vs Pure Alzheimer Disease.”

<sup>45</sup> Skorvanek et al., “Global Scales for Cognitive Screening in Parkinson’s Disease.”

<sup>46</sup> Arevalo-Rodriguez et al., “Mini-Mental State Examination (MMSE) for the Detection of Alzheimer’s Disease and Other Dementias in People with Mild Cognitive Impairment (MCI).”

<sup>47</sup> Biundo et al., “MMSE and MoCA in Parkinson’s Disease and Dementia with Lewy Bodies.”

<sup>48</sup> Nelson et al., “Relative Preservation of MMSE Scores in Autopsy-Proven Dementia with Lewy Bodies.”

<sup>49</sup> Arevalo-Rodriguez et al., “Mini-Mental State Examination (MMSE) for the Detection of Alzheimer’s Disease and Other Dementias in People with Mild Cognitive Impairment (MCI)”; Creavin et al., “Mini-Mental State Examination (MMSE) for the Detection of Dementia in Clinically Unevaluated People Aged 65 and Over in Community and Primary Care Populations.”

<sup>50</sup> Nasreddine et al., “The Montreal Cognitive Assessment, MoCA.”

such as executive functioning, conceptual reasoning, and visuospatial skills. Compared with other cognitive screening tools, such as the MMSE, the MoCA is more sensitive to subtle cognitive deficits in neurodegenerative disease.<sup>51</sup> The MoCA has been shown to more reliably detect cognitive impairment and dementia in PD compared with the MMSE.<sup>52</sup> Furthermore, it is listed as a recommended screening assessment of global cognitive performance by the International Parkinson and Movement Disorder Society.<sup>53</sup>

**Movement Disorders Society-Sponsored Revision of the Unified Parkinson’s Disease Rating Scale.** The Unified Parkinson’s Disease Rating Scale (MDS-UPDRS)<sup>54</sup> is a widely used clinical scale for evaluating symptom severity in PD and consists of four components: non-motor experiences of daily living, motor experiences of daily living, motor examination, and motor complications. The MDS sponsored a revision of the UPDRS because the original scale did not systemically evaluate non-motor features of PD. The revised scale includes items to assess psychological symptoms (e.g., depressed mood, anxiety, apathy), autonomic dysregulation (e.g., urinary incontinence), sleep difficulties, and cognitive impairment. However, it is important to note that cognition is assessed via a single item (“Over the past week have you had problems remembering things, following conversations, paying attention, thinking clearly, or finding your way around the house or in town?”). Thus, the MDS-UPDRS is not a robust indicator of cognitive deficits in PD and should not be used as a standalone measure of cognition.<sup>55</sup>

**Parkinson’s Disease Cognitive Functional Rating Scale.** The Parkinson’s Disease Cognitive Functional Rating Scale (PD-CFRS)<sup>56</sup> was developed to evaluate functional impairments in executing activities of daily living that are attributable to worsening cognitive functioning in PD (as opposed to motor impairment characteristic of the disease) during the prodromal period prior to the onset of dementia. It was developed to improve estimation of the relationship between cognitive changes and functional impairments in PD and identify individuals with PD who may be at heightened risk for later development of PDD. The PD-CFRS is a 12-item self-report measure that asks respondents to rate the extent to which they have difficulty performing such activities as managing their finances, arranging their schedules and daily activities, and solving problems in novel or difficult situations. The scale has been shown to reliably differentiate individuals with PD who have normal cognitive functioning from those

---

<sup>51</sup> Siqueira et al., “Can MoCA and MMSE Be Interchangeable Cognitive Screening Tools?”

<sup>52</sup> Hoops et al., “Validity of the MoCA and MMSE in the Detection of MCI and Dementia in Parkinson Disease.”

<sup>53</sup> Skorvanek et al., “Global Scales for Cognitive Screening in Parkinson’s Disease.”

<sup>54</sup> Goetz et al., “Movement Disorder Society-Sponsored Revision of the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS).”

<sup>55</sup> Goetz et al., “Movement Disorder Society-Sponsored Revision of the Unified Parkinson’s Disease Rating Scale (MDS-UPDRS).”

<sup>56</sup> Kulisevsky et al., “Measuring Functional Impact of Cognitive Impairment.”

who have PD-MCI on the basis of their degree of functional impairment, and it was designed to be sensitive to changes in cognition and daily functioning over time.

**Parkinson's Disease Cognitive Rating Scale.** The Parkinson's Disease Cognitive Rating Scale (PD-CRS)<sup>57</sup> is a task-based neuropsychological assessment designed to evaluate the full spectrum of cognitive deficits experienced by patients with PD. Unlike the PD-CFRS, the Penn Parkinson's Daily Activities Questionnaire-15 (PDAQ-15), and ECB (described previously), the PD-CRS does not specifically capture functional impairments associated with cognitive decline in PD. It is composed of nine tasks that measure the following cognitive domains: sustained attention, working memory, verbal fluency and comprehension, visuospatial skills, executive functioning, and verbal memory. The battery has been validated for identifying dementia in PD but may not be sensitive to variation in cognitive functioning across the clinical spectrum of PD.<sup>58</sup> The International Parkinson and Movement Disorder Society has listed the PD-CRS as a recommended scale for global cognitive assessment and screening in PD.<sup>59</sup>

**Penn Parkinson's Daily Activities Questionnaire-15.** Similar to the PD-CFRS, the PDAQ-15<sup>60</sup> was designed to assess the degree of functional impairment in PD that is attributable to cognitive deficits as opposed to motor deficits. This was done to evaluate the extent to which therapeutics developed to target cognitive outcomes in PD also deliver benefits to patients in terms of their daily functioning, as is required for therapeutics developed to treat AD. The PDAQ-15 is an abbreviated version of the PDAQ, which was composed of 50 questions and time-consuming to complete, making it burdensome to administer in research and clinical care settings. The PDAQ-15 was shown to differentiate individuals with PD who have normal cognitive functioning from those who have PD-MCI or PDD on the basis of their degree of cognitive-functional impairment.

**Preclinical Alzheimer Cognitive Composite.** The AD Cooperative Study designed the Preclinical Alzheimer Cognitive Composite (PACC)<sup>61</sup> to assess subtle cognitive changes that occur years before the onset of diagnosable cognitive impairment among individuals who later develop AD dementia. This was motivated by evidence that secondary prevention efforts may be effective for delaying the emergence of MCI and dementia, necessitating the development of a measure that reliably detects individuals at high risk and can therefore be used to evaluate the effectiveness of secondary prevention approaches. The PACC is a composite of four well-validated assessments: the Total Recall score from the Free and Cued Selective Reminding Test,

---

<sup>57</sup> Pagonabarraga et al., "Parkinson's Disease-Cognitive Rating Scale."

<sup>58</sup> Serrano-Dueñas et al., "Validation of the Parkinson's Disease-Cognitive Rating Scale Applying the Movement Disorder Society Task Force Criteria for Dementia Associated with Parkinson's Disease"; Rosca and Simu, "Parkinson's Disease-Cognitive Rating Scale for Evaluating Cognitive Impairment in Parkinson's Disease."

<sup>59</sup> Skorvanek et al., "Global Scales for Cognitive Screening in Parkinson's Disease."

<sup>60</sup> Brennan et al., "The Penn Parkinson's Daily Activities Questionnaire-15."

<sup>61</sup> Donohue et al., "The Preclinical Alzheimer Cognitive Composite."

the Delayed Recall score on the Logical Memory IIa subtest of the Weschler Memory Scale, the Symbol Digit Substitution Task from the Weschler Adult Intelligence Scale–Revised, and the total score on the MMSE. These assessments measure domains of cognition shown to be sensitive to change among individuals with evidence of amyloid accumulation and neurodegeneration who are otherwise considered cognitively healthy, including episodic memory, executive functioning, and orientation. The PACC has yet to be validated for use in pre-clinical PD, PDD, or DLB.

**Repeatable Battery for the Assessment of Neuropsychological Status.** The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)<sup>62</sup> is a neuropsychological battery that was developed to identify and characterize the severity and nature of cognitive impairments in dementia. It was designed to be relatively brief in its administration and sensitive to cognitive deficits across the clinical spectrum of cognitively healthy through severe dementia, and it has been standardized on a population of adults aged 20–89. It is composed of 11 tasks that map onto five indexes of cognitive functioning: immediate memory, visuospatial and constructional, language, attention, and delayed memory. The RBANS has been shown to have utility for identifying patients with dementia,<sup>63</sup> including PDD and DLB,<sup>64</sup> as well as for identifying individuals with MCI,<sup>65</sup> and it is commonly used to track changes in cognition over time. Evidence also suggests that it may be sensitive to the effects of treatment for PD.<sup>66</sup>

**Scales for Outcomes in Parkinson’s Disease–Cognition.** The Scales for Outcomes in Parkinson’s Disease–Cognition (SCOPA-Cog)<sup>67</sup> was developed to specifically assess domains of cognition known to be more predominantly affected in PD relative to other neurocognitive disorders. It is composed of ten items that evaluate executive functioning, attention, visuospatial skills, and memory. Research has demonstrated that the SCOPA-Cog is sensitive to differences in cognitive functioning across the clinical spectrum of PD, reliably differentiating individuals who are cognitively healthy from those who have PD-MCI and PDD, and it can distinguish between PD-MCI and PDD.<sup>68</sup> The SCOPA-Cog has also been shown to capture declines in cognitive functioning over time as the disease progresses.<sup>69</sup>

---

<sup>62</sup> Randolph et al., “The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).”

<sup>63</sup> Beatty et al., “Analyzing the Subcortical Dementia Syndrome of Parkinson’s Disease Using the RBANS.”

<sup>64</sup> Hanna-Pladdy et al., “Predictors of Mild Cognitive Impairment in Early-Stage Parkinson’s Disease”; Rodriguez-Porcel et al., “Clinical Outcome Measures in Dementia with Lewy Bodies Trials.”

<sup>65</sup> Karantzoulis et al., “The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)”; Duff et al., “Diagnostic Accuracy of the RBANS in Mild Cognitive Impairment.”

<sup>66</sup> Rinehardt et al., “Cognitive Change on the Repeatable Battery of Neuropsychological Status (RBANS) in Parkinson’s Disease With and Without Bilateral Subthalamic Nucleus Deep Brain Stimulation Surgery.”

<sup>67</sup> Marinus et al., “Assessment of Cognition in Parkinson’s Disease.”

<sup>68</sup> Isella et al., “Diagnosis of Possible Mild Cognitive Impairment in Parkinson’s Disease.”

<sup>69</sup> Zhu, van Hilten, and Marinus, “Predictors of Dementia in Parkinson’s Disease.”

**University of California San Diego Performance-Based Skills Assessment.** The USPA<sup>70</sup> is a measure of everyday functioning that was initially developed to assess performance-based functional capacity among adults with severe mental illness. It includes cognitively complex tasks that are analogous to tasks that individuals would carry out in their daily lives, such as planning an activity or writing a check. The USPA has since been validated for detection of functional impairment related to MCI among individuals at risk for AD.<sup>71</sup> Among patients with PD, performance on the USPA can be used to discriminate between cognitively normal individuals and those with diagnosable cognitive impairment (i.e., individuals with PD-MCI and PDD).<sup>72</sup>

**Virtual Reality Functional Capacity Assessment Tool.** The Virtual Reality Functional Capacity Assessment Tool (VRFCAT)<sup>73</sup> is a computerized virtual reality assessment of functional capacity that simulates activities encountered in everyday life that are cognitively complex, capturing many of the functional domains that are measured by other non-computerized performance-based tools. Performance on the VRFCAT has been shown to correlate with global cognitive functioning,<sup>74</sup> and the VRFCAT discriminates individuals with cognitive decline from those who are cognitively healthy, including among patients with PD.<sup>75</sup> A letter of intent has been accepted in the Food and Drug Administration's FDA clinical outcome assessment qualification program to use VRFCAT to measure functional capacity in patients with schizophrenia.

---

<sup>70</sup> Patterson et al., "UCSD Performance-Based Skills Assessment."

<sup>71</sup> Goldberg et al., "Performance-Based Measures of Everyday Function in Mild Cognitive Impairment."

<sup>72</sup> Holden et al., "Validation of a Performance-Based Assessment of Cognitive Functional Ability in Parkinson's Disease."

<sup>73</sup> Atkins et al., "Assessment of Age-Related Differences in Functional Capacity Using the Virtual Reality Functional Capacity Assessment Tool (VRFCAT)"; Ruse et al., "Virtual Reality Functional Capacity Assessment in Schizophrenia."

<sup>74</sup> Atkins et al., "Assessment of Instrumental Activities of Daily Living in Older Adults with Subjective Cognitive Decline Using the Virtual Reality Functional Capacity Assessment Tool (VRFCAT)."

<sup>75</sup> Turner, Atkins, and Keefe, "Virtual Reality Functional Capacity Assessment Tool (VRFCAT-SL) in Parkinson's Disease"; Atkins et al., "Assessment of Instrumental Activities of Daily Living in Older Adults with Subjective Cognitive Decline Using the Virtual Reality Functional Capacity Assessment Tool (VRFCAT)."

## Appendix B. Roundtable Attendees

---

### *Meeting Chair*

Tanya Simuni, MD, Northwestern University

### *Funders, Conveners, and Community Partners*

Zachary Chaney, The Michael J. Fox Foundation

Cheryl Coon, Ph.D., Critical Path Institute

David Dexter, Ph.D., Parkinson's UK

Billy Dunn, M.D., Senior Advisor to The Michael J. Fox Foundation

Sonya Eremenco, M.A., Critical Path Institute

Keith Fargo, Ph.D., Lewy Body Dementia Association

Rebecca Fuller, Ph.D., CHDI Management

Fred Goldstein, M.S., Community Advocate

Rick Grant, Community Advocate

Catherine Kopil, Ph.D., The Michael J. Fox Foundation

Helen Mathews, Cure Parkinson's

Nadezda Radoja, Ph.D., National Institute on Aging

Diane Stephenson, Ph.D., Critical Path Institute

Angela Taylor, Lewy Body Dementia Association

Yuge Xiao, The Michael J. Fox Foundation

### *Regulatory Agencies*

Teresa Buracchio, M.D., U.S. Food and Drug Administration

Michelle Campbell, Ph.D., U.S. Food and Drug Administration

Emily Freilich, M.D., U.S. Food and Drug Administration

Laura Jawidzik, MD, U.S. Food and Drug Administration

Ranjit Mani, M.D., U.S. Food and Drug Administration

### *Academia*

Bradley Boeve, M.D., Mayo Clinic

Kathrin Brockmann, M.D., University of Tuebingen

Richard Camicioli, M.D., University of Alberta

David Cella, Ph.D., Northwestern University

Michael Donohue, Ph.D., University of Southern California

James Galvin, M.D., M.P.H., University of Miami

Jennifer Goldman, M.D., M.S., Barrow Neurological Institute and JPG Enterprises, LLC  
Jessica Langbaum, Ph.D., Banner Health  
Rachael Lawson, Ph.D., MSc, Newcastle University  
James Leverenz, M.D., Cleveland Clinic  
Jennifer Mammen, Ph.D., APRN-CNP, UMass Dartmouth (in absentia)  
Kenneth Marek, M.D., Institute for Neurodegenerative Disorders  
Tiago Mestre, M.D., MSc, University of Ottawa  
Kathleen Poston, M.D., MS, Stanford University Medical Center  
Madeline Sharp, M.D., McGill University  
Caroline Tanner, M.D., Ph.D., University of California San Francisco  
John-Paul Taylor, M.B.B.S., Ph.D., Newcastle University  
Daniel Weintraub, M.D., University of Pennsylvania  
Michele York, Ph.D., ABPP-CN, Baylor College of Medicine

### *Industry*

Kevin Biglan, M.D., M.P.H., Eli Lilly  
Chris Edgar, Ph.D., Cogstate  
Christopher Randolph, Ph.D., ABPP-CN, WCG  
Tien Dam, M.D., Neumora Therapeutics  
Gennaro Pagano, M.D., M.S., Ph.D., eM.B.A., F. Hoffman-La Roche  
Arthur Simen, M.D., Ph.D., Takeda Pharmaceuticals

### *RAND Team*

Shannon Donofry, Ph.D., RAND  
Claire O'Hanlon, Ph.D., M.P.P., RAND



## Abbreviations

---

AD	Alzheimer's disease
ADAS-Cog	Alzheimer's Disease Assessment Scale-Cognitive
CAMCOG-R	Cambridge Cognitive Assessment-Revised
CANTAB	Cambridge Neuropsychological Test Automated Battery
CB	Cogstate Battery
CFC	Cognitive Functional Composite
CGI	Clinical Global Impression
DAFS	Direct Assessment of Functional Status
DLB	dementia with Lewy bodies
DLB-MCI	dementia with Lewy bodies mild cognitive impairment
ECB	Everyday Cognition Battery
IADL	instrumental activities of daily life
MCI	mild cognitive impairment
MDRS	Mattis Dementia Rating Scale
MDS-UPDRS	Movement Disorders Society-sponsored revision of the Unified Parkinson's Disease Rating Scale
MJFF	Michael J. Fox Foundation
MMSE	mini-mental status examination
MoCA	Montreal Cognitive Assessment
NCPT	NeuroCognitive Performance Test
PACC	preclinical Alzheimer's cognitive composite
PD	Parkinson's disease
PDD	Parkinson's disease dementia
PD-CFRS	Parkinson's Disease Cognitive Functional Rating Scale
PD-CRS	Parkinson's Disease Cognitive Rating Scale
PD-MCI	Parkinson's disease-mild cognitive impairment
RBANS	Repeatable Battery for the Assessment of Neuropsychological Status
UPSA	University of California San Diego Performance-Based Skills Assessment
VRFCAT	Virtual Reality Functional Capacity Assessment Tool

## References

---

- Aarsland, D., I. Litvan, D. Salmon, D. Galasko, T. Wentzel-Larsen, and J. P. Larsen, "Performance on the Dementia Rating Scale in Parkinson's Disease with Dementia and Dementia with Lewy Bodies: Comparison with Progressive Supranuclear Palsy and Alzheimer's Disease," *Journal of Neurology, Neurosurgery and Psychiatry*, Vol. 74, No. 9, September 2003.
- Alden, Eva C., Shehroo B. Pudumjee, Emily S. Lundt, Sabrina M. Albertson, Mary M. Machulda, Walter K. Kremers, Clifford R. Jack, Jr., David S. Knopman, Ronald C. Petersen, Michelle M. Mielke, and Nikki H. Stricker, "Diagnostic Accuracy of the Cogstate Brief Battery for Prevalent MCI and Prodromal AD (MCI A<sup>+</sup> T<sup>+</sup>) in a Population-Based Sample," *Alzheimer's and Dementia*, Vol. 17, No. 4, April 2021.
- Allaire, Jason C., and Michael Marsiske, "Everyday Cognition: Age and Intellectual Ability Correlates," *Psychology and Aging*, Vol. 14, No. 4, December 1999.
- Allcock, L. M., E. N. Rowan, I. N. Steen, K. Wesnes, R. A. Kenny, D. J. Burn, "Impaired Attention Predicts Falling in Parkinson's Disease," *Parkinsonism and Related Disorders*, Vol. 15, No. 2, February 2009.
- Arevalo-Rodriguez, Ingrid, Nadja Smailagic, Marta Roqué i Figuls, Agustín Ciapponi, Erick Sanchez-Perez, Antri Giannakou, Olga L Pedraza, Xavier Bonfill Cosp, and Sarah Cullum, "Mini-Mental State Examination (MMSE) for the Detection of Alzheimer's Disease and Other Dementias in People with Mild Cognitive Impairment (MCI)," *Cochrane Database of Systematic Reviews*, No. 3, March 5, 2015.
- Arnold, Guy, Thomas Gasser, Alexander Storch, Axel Lipp, Andreas Kupsch, Hans-Peter Hundemer, and Johannes Schwarz, "High Doses of Pergolide Improve Clinical Global Impression in Advanced Parkinson's Disease: A Preliminary Open Label Study," *Archives of Gerontology and Geriatrics*, Vol. 41, No. 3 November–December 2005.
- Athey, Richard J., Robert W. Porter, and Richard W. Walker, "Cognitive Assessment of a Representative Community Population with Parkinson's Disease (PD) Using the Cambridge Cognitive Assessment–Revised (CAMCOG-R)," *Age and Ageing*, Vol. 34, No. 3, May 2005.
- Athey, Richard J., and Richard W. Walker, "Demonstration of Cognitive Decline in Parkinson's Disease Using the Cambridge Cognitive Assessment (Revised) (CAMCOG-R)," *International Journal of Geriatric Psychiatry*, Vol. 21, No. 10, October 2006.

- Atkins, Alexandra S., A. Khan, D. Ulshen, A. Vaughan, D. Balentin, H. Dickerson, L. E. Liharska, B. Plassman, K. Welsh-Bohmer, and R. S. E. Keefe, "Assessment of Instrumental Activities of Daily Living in Older Adults with Subjective Cognitive Decline Using the Virtual Reality Functional Capacity Assessment Tool (VRFCAT)," *Journal of Prevention of Alzheimer's Disease*, Vol. 5, No. 4, 2018.
- Atkins, A. S., I. Stroescu, N. B. Spagnola, V.G. Davis, T.D. Patterson, M. Narasimhan, P.D. Harvey, and R.S.E. Keefe, "Assessment of Age-Related Differences in Functional Capacity Using the Virtual Reality Functional Capacity Assessment Tool (VRFCAT)," *Journal of Prevention of Alzheimer's Disease*, Vol. 2, No. 2, June 2015.
- Beatty, William W., Katherine A. Ryder, Samuel T. Gontkovsky, James G. Scott, Kelli L. McSwan, and Kersi J. Bharucha, "Analyzing the Subcortical Dementia Syndrome of Parkinson's Disease Using the RBANS," *Archives of Clinical Neuropsychology*, Vol. 18, No. 5, July 2003.
- Beishon, Lucy C., Angus P. Batterham, Terry J. Quinn, Christopher P. Nelson, Ronney B. Panerai, Thompson Robinson, and Victoria J. Haunton, "Addenbrooke's Cognitive Examination III (ACE-III) and Mini-ACE for the Detection of Dementia and Mild Cognitive Impairment," *Cochrane Database of Systematic Reviews*, Vol. 12, No. 12, December 17, 2019.
- Biundo, Roberta, L. Weis, S. Bostantjopoulou, E. Stefanova, C. Falup-Pecurariu, M. G. Kramberger, G. J. Geurtsen, A. Antonini, D. Weintraub, and D. Aarsland, "MMSE and MoCA in Parkinson's Disease and Dementia with Lewy Bodies: A Multicenter 1-Year Follow-Up Study," *Journal of Neural Transmission*, Vol. 123, No. 4, April 2016.
- Brennan, Laura, Andrew Siderowf, Jonathan D. Rubright, Jacqueline Rick, Nabila Dahodwala, John E. Duda, Howard Hurtig, Matthew Stern, Sharon X. Xie, Lior Rennert, Jason Karlawish, Judy A. Shea, John Q. Trojanowski, and Daniel Weintraub, "The Penn Parkinson's Daily Activities Questionnaire-15: Psychometric Properties of a Brief Assessment of Cognitive Instrumental Activities of Daily Living in Parkinson's Disease," *Parkinsonism and Related Disorders*, Vol. 25, April 2016.
- Bronnick, Kolbjorn, Murat Emre, Roger Lane, Sibel Tekin, and Dag Aarsland, "Profile of Cognitive Impairment in Dementia Associated with Parkinson's Disease Compared with Alzheimer's Disease," *Journal of Neurology, Neurosurgery and Psychiatry*, Vol. 78, No. 10, October 2007.
- Busner, Joan, and Steven D. Targum, "The Clinical Global Impressions Scale: Applying a Research Tool in Clinical Practice," *Psychiatry (Edgmont)*, Vol. 4, No. 7, July 2007.

- Cano, Stefan J., Holly B. Posner, Margaret L. Moline, Stephen W. Hurt, Jina Swartz, Tim Hsu, and Jeremy C. Hobart, "The ADAS-Cog in Alzheimer's Disease Clinical Trials: Psychometric Evaluation of the Sum and Its Parts," *Journal of Neurology, Neurosurgery and Psychiatry*, Vol. 81, No. 12, December 2010.
- Cedarbaum, Jesse M., Mark Jaros, Chito Hernandez, Nicola Coley, Sandrine Andrieu, Michael Grundman, and Bruno Vellas, "Rationale for Use of the Clinical Dementia Rating Sum of Boxes as a Primary Outcome Measure for Alzheimer's Disease Clinical Trials," *Alzheimer's and Dementia*, Vol. 9, Supp. 1, February 2013.
- Chade, Anabel, María Roca, Teresa Torralva, Ezequiel Gleichgerrcht, Nicolás Fabbro, Gonzalo Gómez Arévalo, Oscar Gershanik, and Facundo Manes, "Detecting Cognitive Impairment in Patients with Parkinson's Disease with a Brief Cognitive Screening Tool: The Addenbrooke's Cognitive Examination (ACE)," *Dementia and Neuropsychologia*, Vol. 2, No. 3, July–September 2008.
- Connor, Donald J., David P. Salmon, Teresa J. Sandy, Douglas Galasko, Lawrence A. Hansen, and Leon J. Thal, "Cognitive Profiles of Autopsy-Confirmed Lewy Body Variant vs Pure Alzheimer Disease," *Archives of Neurology*, Vol. 55, No. 7, 1998.
- Creavin, Sam T., Susanna Wisniewski, Anna H. Noel-Storr, Clare M. Trevelyan, Thomas Hampton, Dane Rayment, Victoria M. Thom, Kirsty J. E. Nash, Hosam Elhamoui, Rowena Milligan, Anish S. Patel, Demetra V. Tsivos, Tracey Wing, Emma Phillips, Sophie M. Kellman, Hannah L. Shackleton, Georgina F. Singleton, Dethany E. Neale, Martha E. Watton, and Sarah Cullum, "Mini-Mental State Examination (MMSE) for the Detection of Dementia in Clinically Unevaluated People Aged 65 and Over in Community and Primary Care Populations," *Cochrane Database of Systematic Reviews*, Vol. 2016, No. 1, January 13, 2016.
- Deck, Benjamin L., Sharon X. Xie, Gyujae Choi, Jacqueline Rick, Andrew Siderowf, Samuel Rudovsky, Alice Chen-Plotkin, John E. Duda, James F. Morley, Nabila Dahodwala, John Q. Trojanowski, and Daniel Weintraub, "Cognitive Functional Abilities in Parkinson's Disease: Agreement Between Patients and Informants," *Movement Disorders Clinical Practice*, Vol. 6, No. 6, July 2019.
- Dobbs, Bryan, Natalie Pawlak, Milton Biagioni, Shashank Agarwal, Michael Shaw, Giuseppina Pilloni, Marom Bikson, Abhishek Datta, and Leigh Charvet, "Generalizing Remotely Supervised Transcranial Direct Current Stimulation (tDCS): Feasibility and Benefit in Parkinson's Disease," *Journal of NeuroEngineering and Rehabilitation*, Vol. 15, No. 1, December 7, 2018.

- Donohue, Michael C., Reisa A. Sperling, David P. Salmon, Dorene M. Rentz, Rema Raman, Ronald G. Thomas, Michael Weiner, and Paul S. Aisen, "The Preclinical Alzheimer Cognitive Composite: Measuring Amyloid-Related Decline," *JAMA Neurology*, Vol. 71, No. 8, August 2014.
- Duff, Kevin, Valerie L. Hobson, Leigh J. Beglinger, and Sid E. O'Bryant, "Diagnostic Accuracy of the RBANS in Mild Cognitive Impairment: Limitations on Assessing Milder Impairments," *Archives of Clinical Neuropsychology*, Vol. 25, No. 5, August 2010.
- Elder, Greg J., Sean J. Colloby, Michael J. Firbank, Ian G. McKeith, and John-Paul Taylor, "Consecutive Sessions of Transcranial Direct Current Stimulation Do Not Remediate Visual Hallucinations in Lewy Body Dementia: A Randomised Controlled Trial. *Alzheimer's Research and Therapy*, Vol. 11, No. 1, January 18, 2019.
- Emre, Murat, Dag Aarsland, Alberto Albanese, E. Jane Byrne, Gunther Deuschl, Peter P. De Deyn, Franck Durif, Jamie Kulisevsky, Teus van Laar, Andrew Lees, Werner Poewe, Alain Robillard, Mario M. Rosa, Erik Wolters, Peter Quarg, Sibel Tekin, and Roger Lane, "Rivastigmine for Dementia Associated with Parkinson's Disease," *New England Journal of Medicine*, Vol. 351, No. 24, December 9, 2004.
- Fray, Paul J., Trevor W. Robbins, and Barbara J. Sahakian, "Neuropsychiatric Applications of CANTAB," *International Journal of Geriatric Psychiatry*, Vol. 11, No. 4, 1996.
- Galasko, D., D. Bennett, M. Sano, C. Ernesto, R. Thomas, M. Grundman, and S. Ferris, "An Inventory to Assess Activities of Daily Living for Clinical Trials in Alzheimer's Disease. The Alzheimer's Disease Cooperative Study," *Alzheimer Disease and Associated Disorders*, Vol. 11, Supp. 2, 1997.
- Goetz, Christopher G., Barbara C. Tilley, Stephanie R. Shaftman, Glenn T. Stebbins, Stanley Fahn, Pablo Martinez-Martin, Werner Poewe, Cristina Sampaio, Matthew B. Stern, Richard Dodel, Bruno Dubois, Robert Holloway, Joseph Jankovic, Jaime Kulisevsky, Anthony E. Lang, Andrew Lees, Sue Leurgans, Peter A. LeWitt, David Nyenhuis, C. Warren Olanow, Olivier Rascol, Anette Schrag, Jeanne A. Teresi, Jacobus J. van Hilten, and Nancy LaPelle, "Movement Disorder Society-Sponsored Revision of the Unified Parkinson's Disease Rating Scale (MDS-UPDRS): Scale Presentation and Clinimetric Testing Results," *Movement Disorders*, Vol. 23, No. 15, November 15, 2008.
- Goldberg, Terry E., Jeremy Koppel, Lynda Keehlisen, Erica Christen, Ute Dreses-Werringloer, Concepcion Conejero-Goldberg, Marc L. Gordon, and Peter Davies, "Performance-Based Measures of Everyday Function in Mild Cognitive Impairment," *American Journal of Psychiatry*, Vol. 167, No. 7, July 2010.

- Hanna-Pladdy, Brenda, Katherine Jones, Romeo Cabanban, Rajesh Pahwa, Kelly E. Lyons, “Predictors of Mild Cognitive Impairment in Early-Stage Parkinson's Disease,” *Dementia and Geriatric Cognitive Disorders Extra*, Vol. 3, No. 1, January–December 2013.
- Harvey, Philip D., Steven H. Ferris, Jeffrey L. Cummings, Keith A. Wesnes, Chuanchieh Hsu, Roger M. Lane, and Sibel Tekin, “Evaluation of Dementia Rating Scales in Parkinson's Disease Dementia,” *American Journal of Alzheimer's Disease and Other Dementias*, Vol. 25, No. 2, March 2010.
- Holden, Samantha K., Luis D. Medina, Brian Hoyt, Stefan H. Sillau, Brian D. Berman, Jennifer G. Goldman, Daniel Weintraub, and Benzi M. Kluger, “Validation of a Performance-Based Assessment of Cognitive Functional Ability in Parkinson's Disease,” *Movement Disorders*, Vol. 33, No. 11, November 2018.
- Hoops, S., S. Nazem, A. D. Siderowf, J. E. Duda, S. X. Xie, M. B. Stern, and D. Weintraub, “Validity of the MoCA and MMSE in the Detection of MCI and Dementia in Parkinson Disease,” *Neurology*, Vol. 73, No. 21, November 24, 2009.
- Human Cognition Project, “Tools for Research Collaborators,” webpage, undated. As of December 20, 2023:  
<https://www.lumosity.com/hcp/research/tools>
- Isella, V., C. Mapelli, N. Morielli, C. Siri, D. De Gaspari, G. Pezzoli, A. Antonini, M. Poletti, U. Bonuccelli, L. Picchi, A. Napolitano, M. Vista, and I. M. Apollonio, “Diagnosis of Possible Mild Cognitive Impairment in Parkinson's Disease: Validity of the SCOPA-Cog,” *Parkinsonism and Related Disorders*, Vol. 19, No. 12, December 2013.
- Jutten, Roos J., John E. Harrison, A. J. Brunner, R. Vreeswijk, R. A. J. van Deelen, Frank Jan de Jong, Esther M. Opmeer, Craig W. Ritchie, André Aleman, Philip Scheltens, and Sietske A. M. Sikkes, “The Cognitive-Functional Composite Is Sensitive to Clinical Progression in Early Dementia: Longitudinal Findings from the Catch-Cog Study Cohort,” *Alzheimer's and Dementia*, Vol. 6, No. 1, April 17, 2020.
- Karantzoulis, Stella, Julia Novitski, Michael Gold, and Christopher Randolph, “The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): Utility in Detection and Characterization of Mild Cognitive Impairment Due to Alzheimer's Disease,” *Archives of Clinical Neuropsychology*, Vol. 28, No. 8, December 2013.
- Kueper, Jacqueline K., Mark Speechley, and Manuel Montero-Odasso, “The Alzheimer's Disease Assessment Scale-Cognitive Subscale (ADAS-Cog): Modifications and Responsiveness in Pre-Dementia Populations. A Narrative Review,” *Journal of Alzheimer's Disease*, Vol. 63, No. 2, 2018.

- Kulisevsky, Jaime, Ramón Fernández de Bobadilla, Javier Pagonabarraga, Saül Martínez-Horta, Antonia Campolongo, Carmen García-Sánchez, Berta Pascual-Sedano, Roser Ribosa-Nogué, and Carolina Villa-Bonomo, "Measuring Functional Impact of Cognitive Impairment: Validation of the Parkinson's Disease Cognitive Functional Rating Scale," *Parkinsonism and Related Disorders*, Vol. 19, No. 9, September 2013.
- Lawson, Rachael A., Caroline H. Williams-Gray, Marta Camacho M, Gordon W. Duncan, Tien K. Khoo, David P. Breen, Roger A. Baker, Lynn Rochester, David J. Burn, and Alison J. Yarnall, "Which Neuropsychological Tests? Predicting Cognitive Decline and Dementia in Parkinson's Disease in the ICICLE-PD Cohort," *Journal of Parkinson's Disease*, Vol. 11, No. 3, 2021.
- Llebaria, Gisela, Javier Pagonabarraga J, Jamie Kulisevsky, Carmen García-Sánchez, Berta Pascual-Sedano, Alexandre Gironell, and Mercè Martínez-Corral, "Cut-Off Score of the Mattis Dementia Rating Scale for Screening Dementia in Parkinson's Disease," *Movement Disorders*, Vol. 23, No. 11, August 15, 2008.
- Loewenstein, D. A., E. Amigo, R. Duara, A. Guterman, D. Hurwitz, N. Berkowitz, F. Wilkie, G. Weinberg, B. Black, B. Gittelman, et al., "A New Scale for the Assessment of Functional Status in Alzheimer's Disease and Related Disorders," *Journal of Gerontology*, Vol. 44, No. 4, July 1989.
- Mamikonyan, Eugenia, Sharon X. Xie, Emilie Melvin, and Daniel Weintraub, "Rivastigmine for Mild Cognitive Impairment in Parkinson Disease: A Placebo-Controlled Study," *Movement Disorders*, Vol. 30, No. 7, June 2015.
- Marinus, J., M. Visser, N. A. Verwey, F. R. J. Verhey, H. A. M. Middelkoop, A. M. Stiggelbout, and J. J. van Hilten, "Assessment of Cognition in Parkinson's Disease," *Neurology*, Vol. 61, No. 9, November 11, 2003.
- Maruff, Paul, Elizabeth Thomas, Lucette Cysique, Bruce Brew, Alex Collie, Peter Snyder, and Robert H. Pietrzak, "Validity of the Cogstate Brief Battery: Relationship to Standardized Tests and Sensitivity to Cognitive Impairment in Mild Traumatic Brain Injury, Schizophrenia, and AIDS Dementia Complex," *Archives of Clinical Neuropsychology*, Vol. 24, No. 2, March 2009.
- Mattis, Steven, Paul J. Jurica, and Christopher L. Leitten, *Dementia Rating Scale: Professional Manual*, Psychological Assessment Resources, 1988.
- McDougall, Graham J., Heather Becker, Phillip W. Vaughan, Taylor W. Acee, and Carol L. Delville, "The Revised Direct Assessment of Functional Status for Independent Older Adults," *The Gerontologist*, Vol. 50, No. 3, June 2010.
- Morris, J. C., "The Clinical Dementia Rating (CDR): Current Version and Scoring Rules," *Neurology*, Vol. 43, No. 11, November 1993.

- Morrison, Glenn E., Christa M. Simone, Nicole F. Ng, and Joseph L. Hardy, "Reliability and Validity of the NeuroCognitive Performance Test, a Web-Based Neuropsychological Assessment," *Frontiers in Psychology*, Vol. 6, 2015.
- Nasreddine, Ziad S., Natalie A. Phillips, Valérie Bédirian, Simon Charbonneau, Victor Whitehead, Isabelle Collin, Jeffrey L. Cummings, and Howard Chertkow, "The Montreal Cognitive Assessment, MoCA: A Brief Screening Tool for Mild Cognitive Impairment," *Journal of the American Geriatrics Society*, Vol. 53, No. 4, April 2005.
- Nelson, P. T., R. J. Kryscio, G. A. Jicha, E. L. Abner, F. A. Schmitt, L. O. Xu, G. Cooper, C. D. Smith, and W. R. Markesbery, "Relative Preservation of MMSE Scores in Autopsy-Proven Dementia with Lewy Bodies," *Neurology*, Vol. 73, No. 14, October 6, 2009.
- O'Bryant, Sid E., Stephen C. Waring, C. Munro Cullum, James Hall, Laura Lacritz, Paul J. Massman, Philip J. Lupo, Joan S. Reisch, and Rachelle Doody, "Staging Dementia Using Clinical Dementia Rating Scale Sum of Boxes Scores: A Texas Alzheimer's Research Consortium Study," *Archives of Neurology*, Vol. 65, No. 8, 2008.
- Pagonabarraga, Javier, Jaime Kulisevsky, Gisela Llebaria, Carmen García-Sánchez, Berta Pascual-Sedano, and Alexandre Gironell, "Parkinson's Disease-Cognitive Rating Scale: A New Cognitive Scale Specific for Parkinson's Disease," *Movement Disorders*, Vol. 23, No. 7, May 15, 2008.
- Parrott, A. C., and K. Wesnes, "Promethazine, Scopolamine and Cinnarizine: Comparative Time Course of Psychological Performance Effects," *Psychopharmacology*, Vol. 92, No. 4, 1987.
- Patterson, Thomas L., Sherry Goldman, Christine L. McKibbin, Troy Hughs, and Dilip V. Jeste, "UCSD Performance-Based Skills Assessment: Development of a New Measure of Everyday Functioning for Severely Mentally Ill Adults," *Schizophrenia Bulletin*, Vol. 27, No. 2, 2001.
- Pirogovsky, Eva, Dawn M. Schiehser, Irene Litvan, Kristalyn M. Obtera, Mathes M. Burke, Stephanie L. Lessig, David D. Song, Lin Liu, and J. Vincent Filoteo, "The Utility of the Mattis Dementia Rating Scale in Parkinson's Disease Mild Cognitive Impairment," *Parkinsonism and Related Disorders*, Vol. 20, No. 6, June 2014.
- Potashman, Michele, Menglan Pang, Muna Tahir, Saeid Shahraz, Sascha Dichter, Robert Pernecky, and Sandra Nolte, "Psychometric Properties of the Alzheimer's Disease Cooperative Study—Activities of Daily Living for Mild Cognitive Impairment (ADCS-MCI-ADL) Scale: A Post Hoc Analysis of the ADCS ADC-008 Trial," *BMC Geriatrics*, Vol. 23, No. 1, March 6, 2023.
- Randolph, C., M. C. Tierney, E. Mohr, and T. N. Chase, "The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS): Preliminary Clinical Validity," *Journal of Clinical and Experimental Neuropsychology*, Vol. 20, No. 3, June 1998.



- Riedel, Oliver, Jens Klotsche, and Hans-Ulrich Wittchen, "Motor Impairment, Depression, Dementia: Which Forms the Impression of Disease Severity in Parkinson's Disease?" *Parkinsonism and Related Disorders*, Vol. 20, No. 12, December 2014.
- Rinehardt, Eric, Kevin Duff, Michael Schoenberg, Michelle Mattingly, Kersi Bharucha, and James Scott, "Cognitive Change on the Repeatable Battery of Neuropsychological Status (RBANS) in Parkinson's Disease With and Without Bilateral Subthalamic Nucleus Deep Brain Stimulation Surgery," *Clinical Neuropsychologist*, Vol. 24, No. 8, November 2010.
- Rodriguez-Porcel, Federico, Kathryn A. Wyman-Chick, Carla Abdelnour Ruiz, Jon B. Toledo, Daniel Ferreira, Prabitha Urwyler, Rimona S. Weil, Joseph Kane, Andrea Pilotto, Arvid Rongve, et al., "Clinical Outcome Measures in Dementia with Lewy Bodies Trials: Critique and Recommendations," *Translational Neurodegeneration*, Vol. 11, No. 1, May 2, 2022.
- Rosca, Elena Cecilia, and Mihaela Simu, "Parkinson's Disease-Cognitive Rating Scale for Evaluating Cognitive Impairment in Parkinson's Disease: A Systematic Review," *Brain Sciences*, Vol. 10, No. 9, August 25, 2020.
- Rosen, W. G., R. C. Mohs, and K. L. Davis, "A New Rating Scale for Alzheimer's Disease," *American Journal of Psychiatry*, Vol. 141, No. 11, November 1984.
- Roth, M., E. Tym, C. Q. Mountjoy, F. A. Huppert, H. Hendrie, S. Verma, and R. Goddard, "CAMDEX: A Standardised Instrument for the Diagnosis of Mental Disorder in the Elderly with Special Reference to the Early Detection of Dementia," *British Journal of Psychiatry*, Vol. 149, No. 6, December 1986.
- Ruse, Stacy A., Philip D. Harvey, Vicki G. Davis, Alexandra S. Atkins, Kolleen H. Fox, and Richard S. E. Keefe, "Virtual Reality Functional Capacity Assessment in Schizophrenia: Preliminary Data Regarding Feasibility and Correlations with Cognitive and Functional Capacity Performance," *Schizophrenia Research: Cognition*, Vol. 1, No. 1, March 2014.
- Serrano-Dueñas, Marcos, Maite Serrano, Diana Villena, and David Granda, "Validation of the Parkinson's Disease-Cognitive Rating Scale Applying the Movement Disorder Society Task Force Criteria for Dementia Associated with Parkinson's Disease," *Movement Disorders Clinical Practice*, Vol. 4, No. 1, March 1, 2016.
- Siqueira, Glória S. A., Paula de M. S. Hagemann, Daniela de S. Coelho, Flávia Heloísa Dos Santos, and Paulo H. F. Bertolucci, "Can MoCA and MMSE Be Interchangeable Cognitive Screening Tools? A Systematic Review," *The Gerontologist*, Vol. 59, No. 6, November 16, 2019.
- Skorvanek, Matej, Jennifer G. Goldman, Marjan Jahanshahi, Connie Marras, Irena Rektorova, Ben Schmand, Erik van Dujin, Christopher G. Goetz, Daniel Weintraub, Glenn T. Stebbins, and Pablo Martinez-Martin, "Global Scales for Cognitive Screening in Parkinson's Disease: Critique and Recommendations," *Movement Disorders*, Vol. 33, No. 2, February 2018.

- Sousa, Nariana Mattos Figueiredo, and Sonia Maria Dozzi Brucki, "Addenbrooke's Cognitive Examination III: Diagnostic Utility for Detecting Mild Cognitive Impairment and Dementia in Parkinson's Disease," *Arquivos de Neuro-Psiquiatria*, Vol. 81, No. 2, February 2023.
- Turner, Travis H., Alexandra Atkins, and Richard S. E. Keefe, "Virtual Reality Functional Capacity Assessment Tool (VRFCAT-SL) in Parkinson's Disease," *Journal of Parkinson's Disease*, Vol. 11, No. 4, 2021.
- Walker, Z., J. Grace, R. Overshot, S. Satarasinghe, A. Swan, C. L. Katona, and I. G. McKeith, "Olanzapine in Dementia with Lewy Bodies: A Clinical Study," *International Journal of Geriatric Psychiatry*, Vol. 14, No. 6, June 1999.
- Weintraub, Daniel, Robert A. Hauser, Jordan J. Elm, Fernando Pagan, Matthew D. Davis, and Azha Choudhry, "Rasagiline for Mild Cognitive Impairment in Parkinson's Disease: A Placebo-Controlled Trial," *Movement Disorders*, Vol. 31, No. 5, May 2016.
- Weintraub, Daniel, Monique Somogyi, and Xiangyi Meng, "Rivastigmine in Alzheimer's Disease and Parkinson's Disease Dementia: An ADAS-Cog Factor Analysis," *American Journal of Alzheimer's Disease & Other Dementias*, Vol. 26, No. 6, September 2011.
- Wesnes, Keith A., "The Value of Assessing Cognitive Function in Drug Development," *Dialogues in Clinical Neuroscience*, Vol. 2, No. 3, September 2000.
- Wesnes, K. A., I. McKeith, C. Edgar, M. Emre, and R. Lane, "Benefits of Rivastigmine on Attention in Dementia Associated with Parkinson Disease," *Neurology*, Vol. 65, No. 10, November 22, 2005.
- Wesnes, K. A., I. G. McKeith, R. Ferrara, M. Emre, T. Del Ser, P. F. Spano, A. Cicin-Sain, R. Anand, and R. Spiegel, "Effects of Rivastigmine on Cognitive Function in Dementia with Lewy Bodies: A Randomised Placebo-Controlled International Study Using the Cognitive Drug Research Computerised Assessment System," *Dementia and Geriatric Cognitive Disorders*, Vol. 13, No. 3, 2002.
- Wyman-Chick, Kathryn A., and B. J. Scott, "Development of Clinical Dementia Rating Scale Cutoff Scores for Patients with Parkinson's Disease," *Movement Disorders Clinical Practice*, Vol. 2, No. 3, September 2015.
- Young, Tiffany L., Antoneta Granic, Tuo Yu Chen, Christine B. Haley, and Jerri D. Edwards, "Everyday Reasoning Abilities in Persons with Parkinson's Disease," *Movement Disorders*, Vol. 25, No. 16, December 2010.
- Zhu, Kangdi, Jacobus J. van Hilten, and Johan Marinus, "Predictors of Dementia in Parkinson's Disease; Findings from a 5-Year Prospective Study Using the SCOPA-COG," *Parkinsonism and Related Disorders*, Vol. 20, No. 9, September 2014.