

Parkinson's Disease Version 2.0 NINDS CDE Project Cognitive Subgroup Summary

The goal of the NINDS Parkinson's Disease (PD) v2.0 CDE Cognitive Subgroup is to recommend global cognitive scales or batteries that can be readily used in data collection for clinical research that have broad applicability to all stages of cognitive abilities in PD (normal cognition, mild cognitive impairment and dementia) and that have been utilized and undergone some validity testing in PD. The subgroup followed a modified version of the [APA definition](#) that states that cognitive abilities are skills involved in performing the tasks associated with perception, visuospatial abilities, attention, learning, memory, working memory, understanding, awareness, reasoning, abstraction, judgment, planning, intuition, and language. The subgroup focused on addressing global cognitive scales or batteries used in PD rather than detailed cognitive tests at the domain-specific level.

The subgroup reassessed instruments from the NINDS CDE PD v1.0 Project and divided the work among members based on expertise. The subgroup also reviewed the global cognitive scales for screening in PD recommended in Skorvanek et al., 2018. They expanded their review to include computerized batteries and questionnaires of daily cognitive function (i.e., instrumental activities of daily living). Each scale had a primary and secondary reviewer. Table 1 below shows the recommended Cognitive CDEs.

The subgroup created a Summary Table of recommended neuropsychological scales and batteries and rated each scale on usage. Table 2 shows the rating of properties for the usage of Paper-and-Pencil instruments. Each recommended instrument within the Cognitive Subdomain was scored on suitability for mild cognitive impairment and/or dementia: (1) Screening Instrument for initial identification of possible disorder, (2) Severity, (3) if Longitudinal, i.e., sensitivity to change over time, (4) Diagnostic Criteria and Instrument to help categorize patients into those with and without a disorder, and (5) Administration Time measured in minutes.

The subgroup's choice of cognitive assessment battery depended on the stage/severity of PD, and the study design. Different batteries may be necessary when cognition is a primary endpoint, when cognition is an exploratory/secondary issue and where cognitive impairment may be an exclusion factor to study participation.

Table 1. Recommended Cognitive CDEs

Subdomain	Scale Name	Classification	Purpose, Other Information, Scale Use
Cognitive	Addenbrooke's Cognitive Examination-III (ACE-III)	Supplemental	Paper-pencil test of global cognitive abilities.
	Alzheimer's Disease Assessment Scale-Cognition (ADAS-cog)	Supplemental	Paper-pencil test of global cognitive abilities.
	Cambridge Cognitive Assessment-Revised (CAMCOG-R)	Supplemental	Paper-pencil test of global cognitive abilities.
	Cambridge Neuropsychological Test Automated Battery (CANTAB)	Supplemental	Computerized battery with multiple cognitive tests.

Subdomain	Scale Name	Classification	Purpose, Other Information, Scale Use
	CANTAB Connect	Exploratory	Computerized battery with multiple cognitive tests using a web-based testing platform for self-administration.
	CDR System	Supplemental	Computerized battery with multiple cognitive tests.
	Cogstate Brief Battery	Exploratory	Computerized battery with multiple cognitive tests using a web-based testing platform for self-administration.
	Lumos Labs NeuroCognitive Performance Tests (NCPT)	Exploratory	Computerized battery with multiple cognitive tests using a web-based testing platform for self-administration.
	Mattis Dementia Rating Scale (MDRS)	Supplemental	Paper-pencil test of global cognitive abilities.
	Mini-Mental State Examination (MMSE)	Supplemental	Paper-pencil test of global cognitive abilities.
	Montreal Cognitive Assessment (MoCA)	Core	Paper-pencil test of global cognitive abilities.
	NeuroTrax BrainCare™	Exploratory	Computerized battery with multiple cognitive tests using a cloud-based application.
	Parkinson's Disease-Cognitive Rating Scale (PD-CRS)	Supplemental	Paper-pencil test of global cognitive abilities.
Daily Cognitive Function	Scales for Outcomes in Parkinson's Disease-Cognitive (SCOPA-COG)	Supplemental	Paper-pencil test of global cognitive abilities.
	Parkinson's Disease - Cognitive Function Rating Scale (PD-CFRS)	Supplemental	Questionnaire to assess daily cognitive function.
	Penn Parkinson's Daily Activities Questionnaire-15 (PDAQ-15)	Exploratory	Questionnaire to assess daily cognitive function.

Note: Although the MoCA and Mattis DRS-2 scored equally high on rating scale usage, only the MoCA is classified as "Core" given its more extensive use in PD and its significantly shorter administration time. All raters should be trained on the administration of cognitive instruments to increase the validity and reliability of the results.

Table 2: NINDS CDE Subgroup – Cognitive
Recommended CDEs Ratings

Instrument Type/Name	Rating Scale Usage				Administration Time
	Screening Instrument ^a	Severity ^b	Longitudinal ^c	Diagnostic Instrument ^d	
Paper-and-Pencil					
ADAS-cog [◊]	2	2	N/A	2	25-45 min
Addenbrooke’s Cognitive Examination-III (ACE-III)	1.5	2	3	2	15-20 min
CAMCOG-R [†]	2	2	2	2	25-30 min
Mattis DRS-2 [□]	1	1	1	1	20-50 min
MMSE [□]	2.5	2	2	2.5	10-12 min
Montreal Cognitive Assessment (MoCA) [▲]	1	1	1	1	10-15 min
PD-CRS [◊]	1.5	1.5	1.5	1.5	14-23 min
SCOPA-COG [◊]	2	1.5	3	3	10-15 min

^a Screening Instrument - For initial identification of possible disorder

^b Rating Scale - For measurement of disorder severity

^c Longitudinal - Sensitivity to change over time

^d Diagnostic Criteria and Instrument – Categorization of patients into those with and without a disorder

[†] Instrument available from author– refer to Instrument Summary for information on availability

[◊] Instrument available in public domain – refer to Instrument Summary for information on availability

[▲] Free to investigators– refer to Instrument Summary for information on availability

[□] Copyrighted Instrument – refer to Instrument Summary for information on availability

Please note: The disorder refers to cognitive impairment in Parkinson's disease including mild cognitive impairment and dementia. Each of the above scales are being given a score of 1, 2, 3 for suitability (1= highest or best, 3= lowest or worst). A scale may be suitable for mild cognitive impairment and/or dementia.

Other scales were reviewed by the subgroup but were not recommended for PD v2.0 (Table 3). They were not classified as Exploratory since they do not currently fill gaps in PD research in the context of cognition.

Table 3. Excluded Scales

Cognitive Batteries	Cognitive Functional Measures
Automated Neuropsychological Assessment Metrics-4 Battery for Parkinson's Disease (ANAM4-PD)	Everyday Cognition Battery (ECB)
Mini-Mental Parkinson (MMP)	Everyday Cognition Scale

Cognitive Batteries	Cognitive Functional Measures
NIH Toolbox Cognitive Battery	UCSD Performance-Based Skills Assessment (UPSA)
Parkinson's Neuropsychometric Dementia Assessment (PANDA)	Direct Assessment of Functional Status (DAFS)
Repeatable Battery for the Assessment of Neuropsychological Status (RBANS)	

The subgroup reviewed the global scales for cognitive screening as outlined by the Movement Disorder Society and discussed the alignment to the CDE recommendations.

When choosing a cognitive test or battery in PD, consideration must be given to potential impact of parkinsonism (i.e., motor symptoms) on any tests or subtests that are timed or involve motor skills. In addition, whether it should be noted if the patient exhibits features common when the disease is advanced that could affect/prevent the evaluation (e.g., being sleepy, having psychosis).

Global cognitive tests provide an efficient way to quantify overall severity of cognitive impairment but cannot by themselves be used to diagnose MCI or dementia. Instead, these instruments provide a means for the clinician to engage a patient in a thorough diagnostic process. In research, these tests provide a useful means of matching patient groups to be studied in terms of overall severity of cognitive impairment. Much more work is needed in cross-sectional studies to specify test sensitivity and specificity in identifying MCI and dementia. Much more work is also needed in longitudinal studies to address which tests have most utility in detecting treatment effects and progression of impairment for each of MCI and dementia separately. Global tests may have more utility in predicting which persons with MCI develop dementia than which persons develop MCI given that the earliest and most subtle cognitive changes are likely to go undetected by global cognitive tests.

Reference

Skorvanek M, Goldman JG, Jahanshahi M, Marras C, Rektorova I, Schmand B, van Duijn E, Goetz CG, Weintraub D, Stebbins GT, Martinez-Martin P; members of the MDS Rating Scales Review Committee. Global scales for cognitive screening in Parkinson's disease: Critique and recommendations. *Mov Disord*. 2018 Feb;33(2):208-218.