French consensus procedure for assessing cognitive function in Parkinson's disease

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Abstract

Introduction – One of the objectives of the French expert centers for Parkinson's disease (NS-Park) network was to determine a consensus procedure for assessing cognitive function in patients with Parkinson's. This article presents this procedure and briefly describes the selected tests.

Methods – A gathering of 13 experts used the Delphi method for consensus building to define the overall structure and components of the assessment procedure. For inclusion in the battery, tests had to be validated in the French language, require little motor participation, have normative data and be recognized by the international community. Experimental tasks and tests requiring specific devices were excluded.

Results – Two possibilities were identified, depending on whether an abbreviated or comprehensive assessment of cognitive function was necessary. For an abbreviated assessment, the experts recommended the Montreal Cognitive Assessment (MoCA) as a screening test for cognitive impairment or dementia. For a comprehensive neuropsychological assessment, the experts recommended assessing the brain's global efficiency plus the five main cognitive domains (attention and working memory, executive function, episodic memory, visuospatial function and language) that may be impaired in Parkinson's disease, using two tests for each domain.

Discussion and conclusion – A common procedure for assessing cognitive function is now available across the French network dedicated to Parkinson's disease, and is recommended for both research and clinical practice. The NS-Park will also help to promote standardization of the neuropsychological assessment of Parkinson's disease.

Key words: Cognition – Assessment – Dementia – Mild cognitive impairment

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1. Introduction

The French investigative network of expert centers for Parkinson's disease (NS-Park) has the objective to perform and promote clinical research on Parkinson's disease (PD) and other movement disorders (www.reseau-cic-parkinson.inserm.fr). It is integrated into the French Clinical Research Infrastructure Network (F-CRIN), which supports the performance of national and international clinical trials. The NS-Park network includes 24 centers located throughout the French territory (see Appendix 1). It is organized into four task forces and five working groups (more details of the network's organization are available at its website: www.reseau-cic-parkinson.inserm.fr). One of these working groups is dedicated to advanced-

stage PD, and its objectives include the determination of a consensus procedure for assessing cognitive function in PD patients. Defining such a procedure has two main advantages: first, it would promote standardization of neuropsychological assessment in clinical practice and for research; and second, it would help in the exchange of data for research purposes, and in the development of large databases for clinical trials and epidemiological studies.

Besides its hallmark motor symptoms, cognitive impairment is commonly seen in PD even at the early stages [1,2]. Although it is a heterogeneous condition, the prototypical pattern is dominated by a dysexecutive syndrome, slowed processing speed and attention disorder [3,4]. Visuospatial, memory and language deficits may also be observed, and when such deficits arise early in the course of the disease, they are considered risk factors for a more rapid progression to dementia [5]. Thus, in clinical practice, assessing cognitive function and detecting cognitive deficits are major challenges, as even mild cognitive impairment in PD (PD-MCI) has been shown to be a risk factor for developing PD dementia [6–8], a condition with dramatic personal, familial and social consequences.

Moreover, the cognitive status of the patient has an influence on the usual care—in particular, the therapeutic orientation (such as avoiding anticholinergic drugs or reducing dopamine agonists) in patients with altered cognition. In PD patients, cognitive assessment should therefore be done on a regular basis, even in secondary care, throughout the course of the disease. Although guidelines for the assessment of cognitive function in parkinsonian syndromes are available [9–11], up to now there has been no consensus in France on the use of a specific and standardized battery of tests.

Thus, the objectives of this report are to present the assessment procedure that was recently achieved by expert consensus and to briefly describe the selected tests.

2. Methods

2.1. Survey

The Delphi consensus method [12] was used to define the overall structure and components of the procedure for assessing cognitive function. This qualitative method comes from the human sciences, and aims to obtain a reliable consensus of opinion among a group of experts regarding a specific question. It uses a series of questionnaires interspersed with feedback as the structure for a group-communication process. Initially, there is no direct confrontation among the experts; this allows different opinions to emerge on a topic and avoids domination by a few experts. Several variants of the process have been devised [13], as it has been adapted to reach a consensus while gathering together a large number of individuals from

diverse locations.

In the present case, a panel of experts (neurologists and neuropsychologists, each specialized in the assessment and management of cognitive disorders in parkinsonian syndromes) was formed, including participants from several centers affiliated with the NS-Park network. The first contact was by an email in which the analyst (K.D.) outlined the objectives and presented a proposal for the first battery of tests, on which the participants were to offer their advice and suggest possible alternatives. These responses were then summarized by the analyst and anonymously transmitted to the same group with a new proposal for the battery of tests, and so on until the fourth round of consultation, when the experts met in a face-to-face meeting to finalize the proposed tests. Following that meeting, the test materials, as well as their administration and scoring instructions, were collated into a single electronic document and made available to the network members.

2.2. Criteria for test selection

For inclusion in the battery, the tests had to be validated in the French language, limited to a minimum of motor participation, have available normative data and be recognized by the international community. The tests excluded were experimental tasks and those requiring specific devices (such as tactile screens and specific software).

3. Results

3.1. Expert panel characteristics

The expert panel comprised four neurologists and nine neuropsychologists. All of them were affiliated with a movement-disorders department, and had long-term experience of cognitive assessment in patients with PD and other movement disorders.

3.2. Definition of the test battery

As per the expert consultation, it was decided that there were two distinct possibilities for a test battery, depending on whether cognition was to be assessed in an abbreviated form (for outpatients care, or as a secondary outcome in a research context) or a comprehensive form (in tertiary care, or as a primary outcome in a research context). In either case, the expert panel strongly recommended that cognitive tests be performed in the ‘on-drug’ state and not ‘off-drug’. Wearing-off periods were also to be avoided.

3.2.1. Abbreviated assessment

In these cases, the experts considered that a brief overall assessment was sufficient. In line with the guidelines available in the international literature [14,15], the Montreal Cognitive Assessment (MoCA) test was selected [16]. This is a brief 30-item screening instrument that has demonstrated sensitivity for detecting cognitive impairment in PD patients [17]. In clinical practice, Hoops et al. [18] suggested a score of ≤ 26 as the screening cutoff point for PD-MCI, but recommended caution with this cutoff, as their patients were recruited in specialty centers and the majority were highly educated. Dalrymple-Alford et al. [15] recommended a score of ≤ 25 as the screening cutoff for PD-MCI, and a score of ≤ 21 for PD dementia. Karlawish et al. [19] showed that a cutoff score of ≤ 22 is optimal for patients who are still able to give their consent for participation in drug trials or surgery. In a research context, as there is no validated cutoff value for screening cognitive impairment or dementia in French-speaking PD patients, the experts considered that such a value had to be determined by the study investigators, based on the study objectives and inclusion/exclusion criteria of the participants.

3.2.2. Comprehensive assessment

When a thorough understanding of the patient's cognitive status is required, the experts considered that such cognitive assessment should include a rating scale of global cognitive status and tests to assess the main cognitive domains that may be affected by PD (attention and working memory, executive function, episodic memory, visuospatial function and language), as recommended by the International Parkinson and Movement Disorder Society (MDS) Task Force for PD-MCI [20]. Based on the results of a recent study [11], it was also decided that two tests for each cognitive domain were sufficient.

The experts' proposed procedure is described below and also summarized in Table 1, along with the approximate time needed to administer each of the tests.

3.2.2.1. Overall cognitive efficiency

The MoCA [16] was selected because of its sensitivity for detecting cognitive impairment in PD patients.

3.2.2.2. Attention and working memory

Two tests were selected. The Symbol Digit Modalities Test (SDMT) [21] is a substitution task that requires the subject to associate numbers with symbols, usually by putting numbers in boxes. However, in this case, an oral version of the test was chosen to limit motor demands.

Performance is assessed by the number of correct substitutions made within 90 seconds.

The Digit Span Forward and Backward subtests of the Wechsler Adult Intelligence Scale, Fourth Edition (WAIS-IV), [22] are widely recognized as useful assessment tasks of verbal short-term memory. Performance is assessed by the raw score for each subtest and the memory span.

3.2.2.3. Executive function

Two tests were selected for this. The Letter–Number Sequencing task is an oral version of the Trail Making Test. The detailed procedure for PD patients has been described elsewhere [23]. In brief, the test consists of two stages: a baseline phase, during which the subject is instructed to say the alphabet and count forward from 1 to 26; and an alternating phase, during which the subject is instructed to alternate between both series (A-1, B-2, and so on) until all 26 items have been named. Performance is evaluated in terms of the time taken to complete the test's two phases (baseline and alternating), and the number of errors made in the alternating phase. The Color–Word Interference Test (CWIT) of the Delis–Kaplan Executive Function System (D-KEFS) [24], a variant of the Stroop Color and Word Test, has the advantage of assessing both inhibition of a dominant automatic response and mental flexibility. The test consists of four parts of 50 items each: (i) naming the color of boxes; (ii) reading color words; (iii) naming the color of color names; and (iv) alternating between naming the color and reading color names. Performance is evaluated according to the time taken to complete each part of the test and the number of errors (overall and self-corrected) in each part.

3.2.2.4. Episodic memory

The 16-item Free and Cued Recall Test [25] was selected to assess verbal episodic memory. It is the more commonly used test in French-speaking countries, and details of the procedure have been described elsewhere [26]. After controlling for encoding, there are three free and cued recall trials, followed by yes/no recognition. After a 20-min interval, there is also a delayed free and cued recall trial. Performance is assessed by the number of correct responses (free, cued and total recall) in each trial.

Due to its reduced motor requirement, the 10/36 Spatial Recall Test (SRT), a test largely used in patients with multiple sclerosis [27,28], was selected to assess visuospatial learning and memory [29]. A 10 × 10 grid containing a pattern of 10 checkers is placed for 10 sec in front of the subject with the instruction to remember the location of the checkers. After this, the subject has to reproduce the pattern on a blank grid. There are three successive recall trials as

well as a delayed recall after 7 min. Performance is assessed by the number of correct checker locations in both the immediate and delayed recall trials.

3.2.2.5. Visuospatial function

A 15-item version of the Benton Judgment of Line Orientation Test (BJLOT) [30] was selected to assess visuospatial ability. Performance is assessed by the number of correct responses. Visuoconstruction is assessed by the CLOX clock-drawing test [31], which comprises two steps: the first is to draw a clock that shows the time 1:45; the second is to copy a drawing of a clock showing that time. Scoring each part takes into account the presence of the main elements of a clock face and their spatial organization.

3.2.2.6. Language

A semantic fluency test (naming as many animals as possible in 60 sec) and a 15-item version of the Boston Naming Test [32] were selected for this domain. For each test, performance is assessed by the number of correct responses.

4. Discussion

Our expert panel was able to reach a consensus on a standard procedure to assess cognitive function across the French NS-Park network. The procedure differs according to whether cognition needs to be assessed in an abbreviated or comprehensive form. The MoCA is recommended in all cases, but on its own for an abbreviated assessment, and with further tests to assess the five main cognitive domains (attention and working memory, executive function, episodic memory, visuospatial function and language, with two tests for each domain) for a comprehensive assessment.

The recommendation to use the MoCA to assess overall cognitive efficiency in PD may be surprising to French clinicians, who widely use the Mattis Dementia Rating Scale (MDRS). However, this issue was debated by the experts, who concluded that the MDRS is too time-consuming and brings little additional information compared with the MoCA. Also, the score of the MDRS is often used as a selection criterion for deep brain stimulation. However, after several rounds of discussion, the experts concluded that the cognitive selection criteria for surgery in PD should not rely on a single score related to a global scale, but should instead depend on an analysis of the patient's performance profile from a comprehensive neuropsychological assessment to detect any 'red flags' and dementia. Moreover, van Steenoven et al. [17] developed a method for converting MDRS scores to MoCA scores, and

showed that a cutoff value of ≤ 130 for the former corresponded to a cutoff value of ≤ 21 for the latter. This is in agreement with the data provided by Karlawish et al. [19].

Our comprehensive assessment procedure for cognitive function is similar to that recommended by Goldman et al. [11]. Indeed, according to that group, the best-performing test battery included the Trail Making Test, the SDMT, the clock-drawing test, the Boston Naming Test, the animal-naming fluency test, the figural memory test, the BJLOT and the intersecting pentagon drawing task of the Mini-Mental State Examination (MMSE). The only discrepancies with our present consensus procedure concern: (i) attention/working memory, for which we have recommended the Digit Span Forward and Backward subtests in addition to the SDMT; (ii) executive function, for which we have selected the D-KEFS CWIT in addition to the oral version of the Trail Making Test; (iii) non-verbal memory, for which we have recommended the 10/36 SRT instead of the figural memory test which, as a computer-controlled test, was excluded by our expert panel because it requires specific devices that may not be readily available at every clinical center; and (iv) the intersecting pentagons task of the MMSE, which is easily replaced by the cube drawing task of the MoCA. Thus, both batteries have many similarities.

Our proposed procedure also complies with recommendations of the MDS Task Force for the diagnosis of PD-MCI [20], which proposed two levels of assessment: an abbreviated assessment (level I); and a comprehensive assessment (level II). Moreover, the MDS has indicated that a comprehensive assessment requires formal neuropsychological testing with at least two tests for each of the five cognitive domains and that determination of the subtype (single- or multiple-domain) of PD-MCI is only possible with such comprehensive assessment.

One of the strengths of our consensus procedure is that most of the tests do not require fine motor abilities, which is particularly helpful for patients with PD and related disorders. For example, this was the argument used to select the 10/36 SRT for assessing non-verbal episodic memory.

In clinical practice, a comprehensive battery is appropriate for identifying the main cognitive syndromes observed in PD [33]. It also helps to identify any atypical symptoms related to other neurodegenerative diseases, such as Alzheimer's disease and vascular disease. In a research context, the consensus procedure also supports multicenter studies of cognitive function in PD, and facilitates the exchange of data and development of large databases. In addition, by taking into account other international recommendations for assessing cognitive function in PD [9–11], and as all the selected tests are also available in the English language,

this helps the French NS-Park network to design international multicenter studies.

The experts have also recommended that cognitive assessment, whatever the level (I or II), be completed by assessment of the Instrumental Activities of Daily Living (IADL), which can detect loss of autonomy and possible dementia, as well as assess the behavioral disorders often associated to PD (depression, anxiety, apathy, sleep disorders) that may interfere with cognitive performance. Another working group of the NS-Park network is currently preparing its recommendations for the assessment of such behavioral disorders in PD.

However, several limitations of this consensus procedure should also be mentioned. First, for some tests, normative data for the French-speaking population are only partial, and not necessarily representative of all age groups and all levels of formal education. Thus, demographic corrections are not always possible. Indeed, in future, these normative data need to be completed, a task that could be done with the help the NS-Park network. In particular, as the prevalence of PD increases with age [34], it might be useful to extend normative data to include the older age ranges.

Second, some but not all of the suggested tests in the comprehensive neuropsychological battery have parallel forms for retest. As a consequence, to limit any learning effects, it is recommended to use parallel forms of the tests whenever possible and to not administer the test battery again within time intervals of < 6 months.

Third, no test to assess social cognition, or specifically, theory of mind, was included in our battery, although disorders of this cognitive domain have been reported in PD [35] as in other neurodegenerative disorders. Although social cognitive processes have been shown to correlate with executive function, the two domains do not overlap completely. In any case, so far, no theory of mind test for PD has been validated for everyday clinical practice, although such a test should probably be added in future.

Fourth, the first round of the expert panel agreed that tests requiring specific devices, such as computers and special software, were not appropriate for a consensus procedure that would primarily be applicable only to the French network dedicated to PD. Although this is understandable for many practical reasons (including the need for similar versions of the operating system at all clinical centers, administrative permission to cross firewalls, standardization of material/content), this limits investigations of, for example, the possibility to finely control the involvement of motor slowing in diseases where motor and cognitive functions strongly overlap.

In conclusion, there is now a consensus on a French-language battery of neuropsychological tests to use for assessing cognition in PD and related disorders. Although the main objective

of the NS-Park network is to promote clinical research on PD and other movement disorders, this consensus procedure is not limited to research and is highly recommended for the evaluation of cognitive function in clinical practice, too. By promoting standardization of such neuropsychological assessment, this consensus would also reinforce the links between research and clinical practice.

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Table 1 – French consensus procedure for assessing cognitive function in Parkinson's disease with two levels of assessment: abbreviated and comprehensive.

Abbreviated assessment		
Montreal Cognitive Assessment (MoCA)		
Comprehensive assessment		
Cognitive domain	Selected tests	Approximate duration (min)¹
Global efficiency	MoCA	7
Attention & working memory	Symbol Digit Modalities Test (oral)	3
	Digit Span Forward and Backward subtests	10
Episodic memory	16-item Free/Cued Recall Test	20
	10/36 Spatial Recall Test	10
Executive function	Oral Letter–Number Sequencing task	5
	D-KEFS Color–Word Interference Test	7
Visuospatial function	Benton Judgement of Line Orientation (15-item)	10
	CLOX clock-drawing test	5
Language	Boston Naming Test (15-item short-form)	5
	Animal fluency test (60 sec)	1

¹ Raw estimations, as these vary according to the patient; in general, the total time to administer the whole battery is unlikely to exceed 90 min.