Neuropsychological testing

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Abstract

Neuropsychological testing is a key diagnostic tool for assessing people with dementia and mild cognitive impairment, but can also help in other neurological conditions such as Parkinson's disease, stroke, multiple sclerosis, traumatic brain injury, and epilepsy. While cognitive screening tests offer gross information, detailed neuropsychological evaluation can provide data on different cognitive domains (visuo-spatial function, memory, attention, executive function, language, praxis) as well as neuropsychiatric and behavioural features. We should regard neuropsychological testing as an extension of the neurological examination applied to higher-order cortical function, since each cognitive domain has an anatomical substrate. Ideally, neurologists should discuss the indications and results of neuropsychological assessment with a clinical neuropsychologist. This paper summarises the rationale, indications, main features, most common tests, and pitfalls in neuropsychological evaluation.

Neuropsychological testing explores cognitive functions to obtain information on the structural and functional integrity of the brain, and to score the severity of cognitive damage and its impairment on daily life activities. It is a core diagnostic tool for assessing people with mild cognitive impairment, dementia and Alzheimer's disease,[1] but is also relevant in other neurological diseases such as Parkinson's disease,[2] stroke,[3,4] multiple sclerosis,[5] traumatic brain injury,[6] and epilepsy.[7] Given the relevance and extensive use of neuropsychological testing, it is important that neurologists know when to request a neuropsychological evaluation and how to understand the results. Neurologists and clinical neuropsychologists in tertiary centres often discuss complex cases, but in smaller hospitals and in private practice this may be more difficult. This paper presents information on neuropsychological testing in adult patients, and highlights common pitfalls in its interpretation. A very recent paper published on the February 2018 issue of *Practical Neurology* focused on neuropsychological assessment in epilepsy.[7]

NEUROPSYCHOLOGICAL TESTING AND ITS CLINICAL ROLE

Why is neuropsychological testing important? From early in their training, neurologists are taught to collect information on a patient's symptoms, and to perform a neurological examination to identify clinical signs. They then collate symptoms and signs into a syndrome, to identify a lesion in a specific site of the nervous system, and this guides further investigations. Since cognitive symptoms and signs suggest damage to specific brain areas, comprehensive cognitive assessment should also be part of the neurological examination. Neuropsychological testing may be difficult to perform during office practice or at the bedside but the data obtained nevertheless can clearly complement the neurological examination.

When is neuropsychological testing indicated and useful? Neuropsychological assessment is indicated when detailed information about cognitive function will aid clinical management:

- to assess the presence or absence of deficits and to delineate their pattern and severity
- to help to establish a diagnosis (e.g., Alzheimer's disease or fronto-temporal dementia) or to distinguish a neurodegenerative condition from a mood disorder (e.g., depression or anxiety)

- to clarify the cognitive effects of a known neurological condition (multiple sclerosis, stroke or brain injury).

Neuropsychological testing may address questions about cognition in helping to guide a (differential) diagnosis, obtain prognostic information, monitor cognitive decline, control the regression of cognitive–behavioural impairment in reversible diseases, guide prescription of a medication, measure the treatment response or adverse effects of a treatment, define a baseline value to plan cognitive rehabilitation, or to provide objective data for medico-legal situations (Box 1). When requesting a neuropsychological assessment, neurologists should mention any previous testing, and attach relevant reports, so that the neuropsychologist has all the available relevant information.

Conversely, there are situations when cognitive evaluation should not be routinely recommended, e.g., when patient is too severely affected, the diagnosis is already clear, testing may cause the patient distress and/or anxiety, the patient has only recently undergone neuropsychological assessment, there is only a low likelihood of an abnormality (though the test may still bring reassurance), and when there are neuropsychiatric symptoms (Table 1). Neuropsychological assessment is time-consuming (1–2 hours) and demanding for the patient, and so neurologists much carefully select subjects for referral.

How is neuropsychological testing done? Neuropsychological evaluation requires a neurologist or a psychologist with documented experience in cognitive evaluation (i.e., a neuropsychologist). The clinician starts with a structured interview, then administers tests and questionnaires (Table 2), and then scores and interprets the results.

- **The interview** aims to gather information about the medical and psychological history, the severity and the progression of cognitive symptoms, their impact on daily life, the patient's awareness of their problem, and their attitude, mood, spontaneous speech, and behaviour.
- **Neuropsychological tests** are typically presented as 'pencil and paper' tasks; they are intrinsically performance based, since patients have to prove their cognitive abilities in the presence of the examiner. The tests are standardised, and so the procedures, materials, and scoring are consistent. Therefore, different examiners can use the same methods at

different times and places, and still reach the same outcomes.

- **The scoring and analysis** of the test results allow the clinician to identify any defective functions, and to draw a coherent cognitive picture. The clinician should note any associations and dissociations in the outcomes, and use these to compare with data derived from the interview including observation of the patient, the neuroanatomical evidence, and theoretical models, to identify a precise cognitive syndrome.

What information can neuropsychological testing offer? Neuropsychological assessment provides general and specific information about cognitive performance.

Brief cognitive screening tools, such as the Mini-Mental State Examination (MMSE), the Montreal Cognitive Assessment (MoCA), and the Addenbrookes Cognitive Examination (ACE-R), provide a quick and easy global, although rough, measure of a person's cognitive function,[8,9] when more comprehensive testing is not practical or available. Table 3 gives the most common cognitive screening tests, along with scales for measuring neuropsychiatric and behavioural problems, and their impact on daily life. This type of screening test may suffice in some cases, e.g. when the score is low and patient's history strongly suggests dementia, or for staging and following-up cognitive impairment with repeated testing. However, neurologists should be aware of the limitations of such cognitive screening tools. Their lack of some subdomains may result in poor sensitivity, e.g., MMSE may give false negative findings in 'Parkinson's disease-related mild cognitive impairment' because it does not sufficiently explore the executive functions that are the first cognitive subdomains to be involved in Parkinson's disease. The MMSE is particularly feeble in assessing patients with fronto-temporal dementia, many of whom score within the 'normal' range on the test, yet cannot function in social or work situations. [10] Also, young patients with a high level of education may have normal screening tests because these are too easy and poorly sensitive to mild cognitive alterations. Such patients therefore need a thorough assessment.

A comprehensive neuropsychological evaluation explores several cognitive domains (perception, memory, attention, executive function, language, motor and visuo-motor function). The areas and subdomains addressed in neuropsychological examination and the tests chosen depend upon the referral clinical question, the patient's and caregiver's complaints and symptoms, and the

information collected during the interview. Observations made during test administration may guide further exploration of some domains and subdomains. Failure in a single test does not imply the presence of cognitive impairment, since it may have several reasons (e.g., reduced attention in patients with depression). Also, single tests are designed to explore a specific domain or sub-domain preferentially, but most of them examine multiple cognitive functions (e.g. clock drawing test, Table 4). For these reasons, neuropsychological assessment is performed as a battery, with more than one test for each cognitive domain.

The main cognitive domains with their anatomical bases are reviewed below; Table 4 summarises the most widely used cognitive tests for each domain. The neuropsychologist chooses the most reliable and valid test according to the clinical question, the neurological condition, the age, and other specific factors.

Parallel forms (alternative versions using similar material) may reduce the effect of learning effect from repeated evaluations. They may help to track cognitive disorders over time, to stage disease severity, and to measure the effect of pharmacological or rehabilitative treatment.

MAIN COGNITIVE DOMAINS AND THEIR ANATOMICAL BASES

Most cognitive functions involve networks of brain areas.[11] Our summary below is not intended as an old-fashioned or phrenological view about cognition, but rather to provide rough clues on where the brain lesion or disease may be.

Perception. This process allows recognition and interpretation of sensory stimuli. Perception is based on the integration of processing from peripheral receptors to cortical areas (‘bottom-up’), and a control (‘top-down’) to modulate and gate afferent information based on previous experiences and expectations. According to a traditional model, visual perception involves a ventral temporo-occipital pathway for objects and faces recognition, and a dorsal parieto-occipital pathway for perception and movement in space.[12] Acoustic perception involves temporal areas.

Motor control. The classical neurological examination involves evaluation of strength, coordination, and dexterity. Neuropsychological assessment explores other motor features ranging from speed to planning. Visuo-motor ability requires integration of visual perception and motor

skills and is usually tested by asking the subject to copy figures or perform an action. Apraxia is a higher-order disorder of voluntary motor control, planning and execution characterised by difficulty in performing tasks or movements when asked, and not due to paralysis, dystonia, dyskinesia, or ataxia. The traditional model divides apraxia into *ideomotor* (i.e., the patient can explain how to perform an action, but cannot imagine it or make it when required), and *ideational* (i.e., the patient cannot conceptualise an action, or complete the correct motor sequence).[13] However, in clinical practice, there is limited practical value in distinguishing ideomotor from ideational apraxia – see recent review in this journal.[14,15] Apraxia can be explored during routine neurological examination, but neuropsychological assessment may offer a more detailed assessment.

Motor control of goal-orientated voluntary tasks depends on the interplay of limbic and associative cortices, basal ganglia, cerebellum, and motor cortices.

Memory. Memory and learning are closely related. Learning involves acquiring new information, while memory involves retrieving this information for later use. An item to be remembered must first be encoded, then stored, and finally retrieved. There are several types of memory. *Sensory memory*—the ability briefly to retain impressions of sensory information after the stimulus has ended—is the fastest memory process. It represents an essential step for storing information in *short-term memory*, which lasts for a few minutes without being placed into permanent memory stores. *Working memory* allows information to be temporarily stored and managed when performing complex cognitive tasks such as learning and reasoning. Therefore, short-term memory involves only storage of the information, whilst working memory allows actual manipulation of the stored information. Finally, *long-term memory*, the storage of information over an extended period of time, can be subdivided into implicit memory (unconscious/procedural; e.g., how to drive a car) and explicit memory (intentional recollection; e.g., a pet's name). Within explicit memory, episodic memory refers to past experiences that took place at a specific time and place, and can be accessed by recall or by recognition. Recall implies retrieving previously stored information, even if they are not currently present. Recognition refers to the judgment that a stimulus presented has previously occurred.

The neuroanatomical bases of memory are complex.[16] The initial sensory memory includes the

areas of the brain that receive visual (occipital cortex), auditory (temporal cortex), tactile or kinesthetic (parietal cortex) information. Working memory links to the dorsolateral prefrontal cortex (involved in monitoring information) and the ventrolateral prefrontal cortex (involved in maintaining the information). Long-term memory requires a consolidation of information through a chemical process that allows the formation of neural traces for later retrieval. The hippocampus is responsible for early storage of explicit memory; the information is then transmitted to a larger number of brain areas.

Attention. Attention includes the ability to respond discretely to specific stimuli (*focused attention*), to maintain concentration over time during continuous and repetitive tasks (*sustained attention*), to attend selectively to a specific stimulus filtering out irrelevant information (*selective attention*), to shift the focus among two or more tasks with different cognitive requirements (*alternating attention*), and to perform multiple tasks simultaneously (*divided attention*). Spatial neglect refers to failure to control the spatial orientation of attention, and consequently the inability to respond to stimuli.[17]

The occipital lobe is responsible for visual attention, while visuo-spatial analysis involves both the occipital and parietal lobes. Attention to auditory stimuli requires functioning of the temporal lobes, especially the dominant (usually left) one for speech. Complex features of attention require the anterior cingulate and frontal cortices, the basal ganglia and the thalamus.

Executive functions. Executive functions include complex cognitive skills, such as the ability to inhibit or resist an impulse, to shift from one activity or mental set to another, to solve problems or to regulate emotional responses, to begin a task or activity, to hold information in mind for completing a task, to plan and organise current and future tasks, and to monitor one's own performance.[18] Taken together, these skills are part of a supervisory or meta-cognitive system to control behaviour that allows us to engage in goal-directed behaviour, prioritise tasks, develop appropriate strategies and solutions, and be cognitively flexible. These executive functions require normal functioning of the frontal lobe, anterior cingulate cortex, basal ganglia, and many inward and outward connections to the cortical and subcortical areas.

Language. Language includes several cognitive abilities that are crucial for understanding and

producing spoken and written language, as well as naming. Given its complexity, we usually explore language with batteries of tests that use different tasks to investigate its specific aspects (Table 4). According to the traditional neuroanatomical view, language relies primarily on the dominant brain: specifically comprehension lies on the superior temporal lobe, language production on the frontal regions and fronto-parietal/temporal circuits, and conceptual–semantic processing on a network that includes the middle temporal gyrus, the posterior middle temporal regions and superior temporal and inferior frontal lobes.[19] However, recent data from stroke patients do not support this model, but instead indicate that language impairments result from disrupted connectivity within the left hemisphere, and within the bilaterally distributed supporting processes, which include auditory processing, visual attention, and motor planning.[11]

Intellectual ability. Regardless of the theoretical model, there is agreement that intellectual ability—or intellectual quotient (IQ)—is a multi-dimensional construct. This construct includes intellectual and adaptive functioning, communication, caring for one's own person, family life, social and interpersonal skills, community resource use, self-determination, school, work, leisure, health and safety skills. The Wechsler adult intelligence scale revised (WAIS-R) is the best-known intelligence test used to measure adult IQ. WAIS-R comprises 11 subtests grouped into verbal and performance scales (Table 4). Any mismatch between verbal and performance scores might suggest different pattern of impairments, i.e., memory and language vs. visuo-spatial and executive.

COMPARING TO NORMATIVE VALUES

A person’s performance on a cognitive test is interpreted by comparing it to that of a group of healthy individuals with similar demographic characteristics. Thus, the raw score is generally corrected for age, education and sex, and the corrected score rated as normal or abnormal. However, not all neuropsychologists use the same normative values. Furthermore, there are no clear guidelines or criteria for judging normality of cognitive testing. For example, the diagnostic guidelines for mild cognitive impairment in Parkinson’s disease stipulate a performance on neuropsychological tests that is 1–2 standard deviations (SDs) below appropriate norms, whereas

for IQ, a performance that is significantly below average is defined as ≤ 70, i.e., 2 SD below the average score of 100.[2] Sometimes, the neuropsychological outcome is reported as an equivalent score, indicating a level of performance (Figure 1). Understanding how normality is defined—how many SDs below normal values, and the meaning of an equivalent score—is crucial for understanding neuropsychological results correctly, and for comparing the outcomes of evaluations performed in different clinical settings. Furthermore, estimating the premorbid cognitive level, e.g., using the National Adult Reading Test (Table 3), helps to interpret the patient score. 'Crystallised intelligence' refers to consolidated abilities that are generally preserved until late age, compared with other abilities such as reasoning, which show earlier decline. In people with a low crystallised intelligence—and consequently a low premorbid cognitive level—a low-average neuropsychological assessment score may not represent a significant cognitive decline. Conversely, for people with high premorbid cognitive level, a low-average score might suggest a significant drop in cognitive functioning.

REACHING A DIAGNOSIS THROUGH NEUROPSYCHOLOGICAL TESTING

Although the score on a single test is important, it is only the performance on the whole neuropsychological test battery that allows clinicians to identify a person's patterns of cognitive strengths and weaknesses; together with motor and behavioural abnormalities, these may fit into known diagnostic categories (Tables 5, 6).

The neuropsychologist reports the information collected through neuropsychological evaluation in a written clinical report that usually includes the scores of each test administered. The conclusions of the neuropsychological report are important to guide further diagnostic workup, to predict functionality and/or recovery, to measure treatment response and to verify correlations with neuroimaging and laboratory findings.

As well as these quantified scores, it is critically important to have a patient's self-report of functioning, plus qualitative data including observation of how the patient behaved during the test. Psychiatric confounders require particular attention. Neuropsychologists apply scales for depression (e.g., Beck's depression inventory, geriatric depression scale) or anxiety (e.g., state–

trait anxiety inventory) during testing; these may offer information on how coexisting conditions may influence cognition through changes in mood or motivational state. For example, it may be difficult to distinguish between dementia and depressive pseudo-dementia, because depression and dementia are intimately related.[20] Table 7 shows some of the features that may help. Note that antidepressants may ameliorate cognitive deficits, particularly attention and memory, and that opioids may worsen cognitive symptoms.

Knowing that there are other potential factors that may influence neuropsychological testing (and usually worsening performance) should help clinicians to avoid misinterpreting the results (Table 8). For example, in Parkinson's disease, it is important to pay particular care to motor fluctuations, neuropsychiatric symptoms, pain, and drug side effects that can worsen cognitive performance.[21] Conversely, patients with long-lasting psychiatric disease, such as bipolar disorder or schizophrenia, are often referred for neurological and cognitive assessment when they begin to perform worse in daily activities. Frontal changes are common in bipolar disorders and so finding prefrontal dysfunction in such patients should not lead clinicians to suspect an ongoing neurological disorder. Discussion with the clinical neuropsychologist and the psychiatrist may help to understand potential drug side effects and, eventually, to revise treatment.

Key points

- For many neurological diseases, neuropsychological testing offers relevant clinical information that complements the neurological examination
- Neuropsychological tests can identify patterns of cognitive strengths and weaknesses that are specific to particular diagnostic categories
- Neuropsychological testing involves tests that investigate different cognitive functions in a standardised way, and so the procedures, materials, and scoring are consistent; it also involves an anamnestic interview, scoring and interpreting the results, and comparing these with other clinical data, to build a diagnostic hypothesis
- Neuropsychological evaluation must be interpreted in the light of coexisting conditions, in particular sensory, motor, and psychiatric disturbances as well as drug side effects, to avoid misinterpreting the results

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306 Table 1. Conditions in which neuropsychological testing is usually not recommended

Condition	Reason
Patient too severely affected	Not or only slightly informative assessment
	The cost in terms of burden for the patient (i.e., fatigue, anxiety, feeling of failure) may exceed the benefit of gaining information from the assessment
Clear diagnosis	If the diagnosis is clear and neuropsychological testing is required for diagnostic purposes only, it should not be routinely prescribed
Distress and/or anxiety might be produced	Diagnosis has already been defined and it is clear that the patient will fail in testing
Recent (<6 months) neuropsychological assessment	Significant cognitive decline is unlikely in the short time, unless a neurological event has occurred or the patient is affected by rapidly progressive dementia
	Short-interval repeated evaluation may be biased by learning effect, except when parallel versions of tests are used
The a priori likelihood of an abnormality is low	Neuropsychological testing should not be routinely performed when clinical history and examination exclude a neurological or cognitive condition
	Consider prescribing neuropsychological testing, if it is the only way to provide reassurance when a healthy individual is concerned about cognitive decline
Confusion or psychosis	Neuropsychological assessment is not reliable and could exacerbate confusion and/or abnormal behaviour

307 Table 2. Structure of the neuropsychological evaluation

Stage	Contents
Interview with the patient, relative, or caregiver	Reason for referral (i.e., what the physician and patient want to know)
	Medical history, including family history
	Lifestyle and personal history (e.g., employment, education, hobbies)
	Premorbid personality
	Symptoms onset and evolution
	Previous examinations (e.g., CT scan, MR scan, electroencephalography, positron-emission tomography scan)
	Sensory deficits (loss of vision, or hearing)
Qualitative assessment of cognition, mood and behaviour	Mood and motivation (i.e., depression, mania, anxiety, apathy)
	Self-control, or disinhibition
	Subjective description and awareness of cognitive disorders, and their impact on the activities of daily life
	Expectations and beliefs about the disease
	Verbal (fluency, articulation, semantic content) and non-verbal (eye contact, tone of voice, posture) communication
	Clothing, and personal care
	Interview with the relative/caregiver to confirm patient's information, provide explanations, and acquire information on how the patient behaves in daily life
Test administration	Standardised administration of validated tests
Final report	Personal and clinical data
	Qualitative description of cognitive performance, mood and awareness
	Table with score of the tests and normative references values
	Conclusions

308 Table 3. Some cognitive screening tests and other scales for measuring impact of cognitive changes

Test	Domains	Advantages	Limitations
Mini mental state examination (MMSE)	Orientation, memory, attention, calculation, language, visuo-constructive skills, writing	Widely used in clinical practice and research, brief (no time consuming)	Poorly sensitive to executive functions Too easy (ceiling effect) in younger patients
Montreal Cognitive Assessment (MOCA)	Trail making, visuo-constructive skills, naming, memory, attention, sentence repetition, verbal fluency, abstraction, orientation	Sensitive to executive functions, brief (no time consuming)	Too difficult in older patients (floor effect)
Addenbrooke's Cognitive Examination (ACE-R)	Orientation, attention, memory, verbal fluency, language, visuospatial ability	Less time consuming test with a good accuracy for detecting dementia	Poorly sensitive to mild cognitive deficits
Severe Impairment Battery (SIB)	Social interaction, memory, orientation, language, attention, praxis, visuospatial ability, construction, orientation to name	Cognitive screening in patients with moderate to severe dementia	Poorly sensitive in patients who score >12 on the MMSE
National Adult Reading Test (NART)	Crystalised intelligence, estimation of vocabulary size	Premorbid cognitive ability level estimation by oral reading of phonological irregular words	Only feasible for languages that include many irregular words (e.g., English, French) Does not estimate current IQ
Neuropsychiatric inventory (NPI)	Severity of neuropsychiatric symptoms and impact on the caregiver	Complements cognitive tests by exploring behavioural and psychiatric features	Based on the report of the caregiver
Basic and instrumental activities of daily life (BADL/IADL)	Ability to perform instrumental (e.g., house-keeping, shopping, using the telephone) or basic (e.g., using the toilet, dressing) daily life activities	Important to assess the impact of cognitive changes	Poorly sensitive to change in the early stages of dementia

309 Table 4. Common neuropsychological tests grouped by domains, and their characteristics

Test	Functions and subdomains explored	Task	Scoring	Duration
Perception and visuo-spatial function				
Block design test	Spatial component in perception and in motor execution	Replicate the patterns displayed on a series of test cards using 16 colored cubes	Number of correctly placed blocks	60’
Visual object and space perception (VOSP)	Visuo-spatial abilities	Shape detection, incomplete letters, silhouettes, object decision, dot counting, progressive silhouettes, position discrimination, number allocation and cube analysis	Number of correct answers	40-80’
Benton visual retention test	Visual and memory abilities	Reproduce figures after a brief observation	Number of correct answers, number of errors	10-20’
Rey-Osterrieth complex figure	Visuo-spatial planning	Copy a complex geometric figure	Number of correctly copied elements	5-10’
Motor control				
Test for apraxia (ideomotor, ideational, constructional)	Ability to voluntary perform gestures or copy geometrical models	Ideomotor apraxia: imitate gestures; ideational apraxia: pantomime gestures; constructional apraxia: copy geometrical figures	Number of correctly performed actions, number of correctly copied figures	5-10’
Memory				
Digit span (forward and backward)	Short-term auditory memory, working memory	Remember sequences of progressively increasing numbers (forward and backward)	Length of the correctly recalled sequence	1-5’
Rey auditory verbal learning test (immediate and delayed recall)	Long-term auditory/verbal memory, learning strategy, interference, retention of information, learning and retrieval performance	Remember a list of 15 words	Number of correctly recalled words	5-10’
Verbal paired associates	Learning with built-in cues	Remember pairs of words	Number of correctly recalled words	5-10’
Rivermead behavioural memory test	Recall, recognition, immediate and delayed memory (ecologically assessed); well suited for rehabilitation setting	Remember names, belongings, appointments, story, picture and faces, route, messages, orientation	Number of correct answers	30’
Logical memory	Short and long term verbal memory, executive features of memory processing	Remember a story	Number of correctly recalled items	5’
Corsi block-tapping test	Visuo-spatial working memory	Remember a sequence of up to nine identical spatially separated blocks	Length of the correctly recalled sequence	1-5’
Corsi learning supra-span	Visuo-spatial learning	Remember a sequence of eight spatially separated blocks	Number of blocks touched in the correct sequence	10’
Attention				
Trail making test (parts A, B)	Selective and divided attention, visual search speed, scanning	Part A: connect numbers in ascending order; part B: connect numbers and letters alternately	Time required for completing the test	1-5’
Attentional matrices	Sustained, selective and divided attention	Search for a target	Number of correctly identified targets	1-5’
Multiple features target cancellation	Sustained, selective and divided attention	Search for a target	Number of correctly identified targets, time required for completing the test	1-5’

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311 Table 4. Common neuropsychological tests grouped by domains, and their characteristics (continued)

Test	Functions and subdomains explored	Task	Scoring	Duration
Paced auditory serial addition test (PASAT)	Rate of information processing and sustained and divided attention	Single digits are presented every 3'' and the patient must add each new digit to the one immediately prior to it	Number of correct answers	10-15'
Symbol digit modalities test	Complex scanning, visual tracking, speed of processing	A page headed by a key that pairs the single digits 1–9 with nine symbols is shown; the task consists of writing or orally reporting the correct number in the spaces below the symbols	Number of correctly performed associations	1-5'
Executive function				
Frontal assessment battery	The test explores six subdomains: conceptualization, cognitive flexibility, motor sequencing, sensitivity to interference and environmental stimuli, inhibitory control	Perform one task for each of the six subdomains	Number of correct answers	5-10'
Stroop test	Inhibitory control, selective attention	Read words and color naming in congruent and incongruent conditions	Number of errors, time required for completing the test	1-5'
Verbal fluency	Lexical access, cognitive flexibility, ability to use strategies, self-monitor	List as many words as possible using a specific letter or a category	Number of correct words	5-10'
Wisconsin card sorting test	Reasoning, cognitive flexibility, abstraction	Match cards using different criteria according to the clues provided by the examiner	Number of errors, number of correctly identified criteria	20-30'
Raven progressive matrices	Non-verbal logical reasoning	Identify the missing element that completes a pattern of shapes	Number of correct answers	10'
Clock drawing test	Visuo-spatial and praxis abilities, visuo-spatial planning, retrieval of clock time representation	Draw a clock, inserting the hands indicating a specific time (hours and minutes)	Number of correctly drawn elements	1-5'
Tower of London	Problem-solving, planning	Move beads with different colors on a board with pegs to get fixed configurations	Number of correctly reproduced configurations	20'
Cognitive estimation task	Ability to produce reasonable cognitive estimates	Answer questions using general knowledge of the world	Number of errors	10'
Language				
Token test	Verbal comprehension	Carry out verbal commands referring to circles and squares with different colors and sizes	Number of errors	10-15'
Boston naming test	Verbal naming	Name figures	Number of correctly named figures	15-30'
Aachener aphasie test	A battery for evaluating the type and severity of language impairment	The test includes six tasks: verbal comprehension, repetition, written language, naming, oral and written comprehension of words and sentences	Verbal comprehension: number of errors, other tasks: number of correct answers	90'
Comprehensive aphasia test	A battery to evaluate the type and severity of language impairment	Semantic memory, word fluency, recognition memory, gesture object use, arithmetic, repetition, spoken language production, reading aloud, writing	Number of correct answers	90'
Intellectual quotient				
Wechsler adult intelligence scale revised (WAIS-R)	Intellectual quotient (IQ) including verbal and performance scale	Vocabulary, similarities, information, comprehension, arithmetic, digit span, picture completion, block design, letter-number sequencing, reordering figurative stories, figures reconstruction	Number of correct answers	90'

312 Table 5. Patterns of involvement of cognitive and non-cognitive domains in common neurological conditions

	Cognitive domain						Other domains	
	Perception	Memory	Attention	Executive function	Language	Praxia	Movement	Mood and behaviour[†]
Neurological conditions mainly involving cortical areas								
Alzheimer's disease		X			X	X		
Fronto-temporal dementia			X	X				X
Primary progressive aphasia					X			
Dementia with Lewy bodies	X			X			X	X
Corticobasal degeneration				X	X	X	X	
Neurological conditions mainly involving subcortical areas								
Parkinson's disease			X	X			X	
Vascular dementia			X	X			X	X

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314 Table 6. Main features of cortical vs. subcortical patterns of cognitive involvement

Feature	**Cortical cognitive involvement**	**Subcortical cognitive involvement**
Alertness	Normal	Reduced
Speed of cognitive processing	Normal	Slowed
Attention and executive functions	Preserved in early stages	Impaired from onset
Memory	Impaired (amnesia)	Deficit due to poor encoding and attentional deficits; recognition usually better than free recall
Language	Impaired (aphasia)	Normal except for dysarthria
Praxis	Impaired (apraxia)	Normal except for ideomotor slowing
Perception	Impaired (agnosia)	Usually normal
Motivation, behavior and personality	Intact until late stages of disease, unless frontal type	Impaired (patient often apathetic, inert)
Depression	Not common in early stages	Common

315 Table 7. Differential diagnosis between dementia and depressive pseudo-dementia

Features	**Dementia**	**Depressive pseudo-dementia**
Onset	Insidious	Sudden (the patient may recall the exact time when symptoms began)
Evolution	Slow	Fast
Psychiatric history	Negative	May be positive
Awareness	Reduced or absent	Preserved
Functional deficits	Denied or minimised by the patient	Emphasised by the patient
Mood	Incongruous or fluctuating	Depressed
Neuropsychological tests	Worsening on repeated testing	Improvement or stable on repeated testing
Instrumental tests	MR scan, positron-emission tomography scan or biomarkers positive	Negative
Effect of treatment	No change with antidepressants	May improve on antidepressants

316 Table 8. Potential bias factors in the neuropsychological testing

Factor	**Suggestions to avoid the bias effect**
Conditions that may worsen performance	
Noisy or overstimulating environment	Perform neuropsychological evaluation in the appropriate environment
Fatigue or sleepiness	Avoid neuropsychological assessment in the evening or when patient may be tired
	Provide a break
Agitation, distrust, anxiety or fear	Explain the aims of the assessment and how it works
	Use positive feedback (e.g., well done)
	Provide a break
Depression or apathy	Schedule a follow-up assessment when mood or motivation has improved.
Non-native speaker	Assess the patient with the help of an interpreter
	Use non-verbal tests

Medication side effects (e.g., anticholinergics, benzodiazepines, narcotics, neuroleptics, antiepileptics, antihistamines)	Schedule the neuropsychological assessment when off medication or when the drug side effects are lower Be aware of each drug's side effect
Visual impairment	Use oral tests
Hearing impairment	Speak loud, and check if the patient understood the instructions
Pain or headache	Schedule the assessment when the patient is pain-free
Conditions that may ameliorate performance	
Practice	Avoid repeating neuropsychological assessment too frequently Use parallel forms or similar tests

317 Box 1. What the neurologist should consider to get the best from neuropsychological testing (key and specific questions)

Key question	**Specific questions**
Clinical evaluation	Presence of cognitive impairment (e.g., Parkinson's disease, stroke)
	Differential diagnosis (e.g., Alzheimer's disease vs. fronto-temporal dementia)
	Baseline conditions for planning cognitive rehabilitation programs
	Clinical research questions
Follow-up monitoring	Cognitive decline in neurodegenerative diseases
	Cognitive change in subjective cognitive complaints or mild cognitive impairment
	Regression of cognitive-behavioural impairment in reversible diseases (e.g., deficiency of thiamine, vitamin B12 or folate, hypothyroidism)
Therapeutic effects of drugs or procedures	Comparison of pre to post cerebrospinal fluid drainage in normal pressure hydrocephalus
	Cognitive effects of drugs (e.g., antiepileptic or antidepressant drugs)
	Adverse effects of therapies (e.g., chemotherapy, radiotherapy)
Pre-surgical assessment in neurosurgery	Neurosurgery for drug-resistant epilepsy
	Resection of tumours in areas involved in cognitive functions
	Deep-brain stimulation for Parkinson's disease
Medico-legal issues	Competency assessment (e.g., able to sign, live alone)
	Assessment of driving competence
	Insurance issues (e.g., reimbursement)
	Litigation

Figure Legend

Figure 1. The difference between normal/abnormal scores according to standard deviation (SD), percentile rank, and equivalent score (ES). Here is represented the bell-shaped curve showing the normal distribution of score to a given neuropsychological test. Abnormal scores are those falling outside the lower limit of normal range of values, which can be defined as average –1 SD, average -1.5 SD or average -2 SD. Alternatively, scores can be reported as percentile rank, i.e., the point in a distribution at or below which the scores of a given percentage of individuals fall. E.g., a person with a percentile rank of 90 in a given test has scored as well or better than 90 percent of people in the normal sample. Finally, neuropsychological tests can be scored as equivalent scores, with equivalent score = 4 when equal or greater than the average, equivalent score = 3 when falling broadly within normal limits, equivalent score = 2 when still within the norms, equivalent score = 1 when at lower limits, and equivalent score = 0 when definitely abnormal.

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