Cognitive symptoms in patients with Parkinson disease

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Outlines

- Heterogeneity of cognitive profile in Parkinson's disease (PD): mix of different neuropsychological, neurochemical, clinical and neurosubstrates profiles.

- Screening of cognitive deficits for Parkinson MCI and dementia detection: structural interview, cognitive scales and neuropsychological assessments.

Introduction

PD as a Neuropsychiatric Disorder

- DSM-5 encapsulated
  - Depression, psychosis, cognitive impairment, impulse control disorders, anxiety, apathy, disorders of sleep and wakefulness
- Neural substrate relevant to neuropsychiatry
  - Brain regions (basal ganglia, prefrontal cortex), neurotransmitters (dopamine, norepinephrine, serotonin, acetylcholine and glutamate), neural pathways (cortico-striatal-thalamic circuitry)
- Inter- and intra-individual variability allows study- cognitive fluctuation

Non-Motor Symptoms in PD Increasingly Recognized as Important

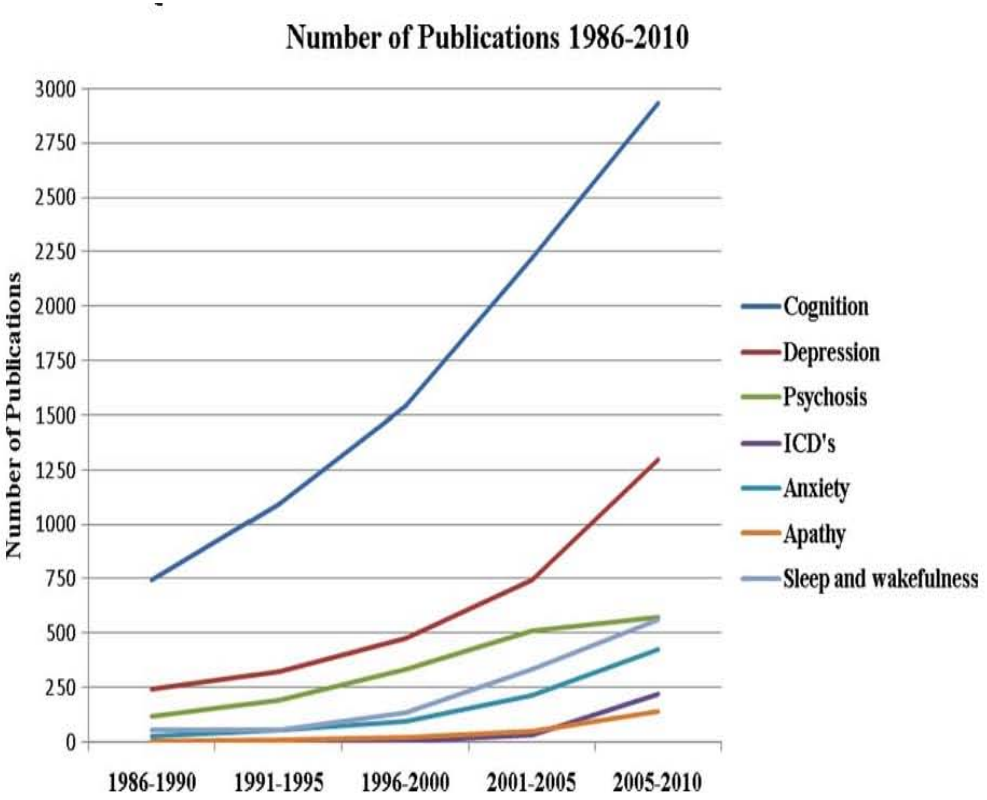


FIG. 1. Number of articles published devoted to Parkinson's disease, 1986–2010. *Cognition* = Parkinson* and (dementia or cognitive impairment); *Depression* = Parkinson* and depression; *Psychosis* = Parkinson* and (psychosis or hallucination); *Anxiety* = Parkinson* and anxiety; ICD's = Parkinson* and (impulse control disorder or dopamine dysregulation syndrome); *Sleep and wakefulness* = Parkinson* and (insomnia or sleepiness or fatigue or REM); *Apathy* = Parkinson* and apathy.

d Burn. *Movement Disorders* 2011;26:1022-1031.

What Concerns Patients, Caregivers and Providers

Table 3 Final prioritised and ranked uncertainties for the management of Parkinson's disease

	Overarching research aspiration: an effective cure for Parkinson's disease
1	What treatments are helpful for reducing balance problems and falls in people with Parkinson's?
2	What approaches are helpful for reducing stress and anxiety in people with Parkinson's?
3	What treatments are helpful for reducing dyskinesias (involuntary movements, which are a side effect of some medications) in people with Parkinson's?
4	Is it possible to identify different types of Parkinson's, eg, tremor dominant? And can we develop treatments to address these different types?
5	What best treats dementia in people with Parkinson's?
6	What best treats mild cognitive problems such as memory loss, lack of concentration, indecision and slowed thinking in people with Parkinson's?
7	What is the best method of monitoring a person with Parkinson's response to treatments?
8	What is helpful for improving the quality of sleep in people with Parkinson's?
9	What helps improve the dexterity (fine motor skills or coordination of small muscle movements) of people with Parkinson's so they can do up buttons, use computers, phones, remote controls etc?
10	What treatments are helpful in reducing urinary problems (urgency, irritable bladder, incontinence) in people with Parkinson's?

MJ 2014;4:e006434.

Limited Therapeutic Options Currently

Therapeutic Prospects for Parkinson Disease

C. Warren Olanow, MD, FRCPC[1] and Anthony H. V. Schapira, MD, FRCP[2]

Dopaminergic therapies such as levodopa have provided benefit for millions of patients with Parkinson's disease (PD) and revolutionized the treatment of this disorder. However patients continue to experience disability despite the best of modern treatment. Dopaminergic and surgical therapies are associated with potentially serious side effects. Non-motor and non-dopaminergic features such as freezing, falling, and dementia are not adequately controlled with available medications and represent the major source of disability for advanced patients. And, the disease continues to relentlessly progress. Major therapeutic unmet needs include a dopaminergic therapy that is not associated with serious side effects, a therapy that addresses the non-motor and non-dopaminergic features of the disease, and a disease-modifying therapy that slows or stops disease progression. This review will consider current attempts to address these issues and the obstacles that must be overcome in order to develop more effective therapies for PD.

ANN NEUROL 2013;74:337–347

Cognitive impairment

Neuropsychological and clinical heterogeneity of cognitive impairment and dementia in patients with Parkinson's disease

Angie A Kehagia, Roger A Barker, Trevor W Robbins

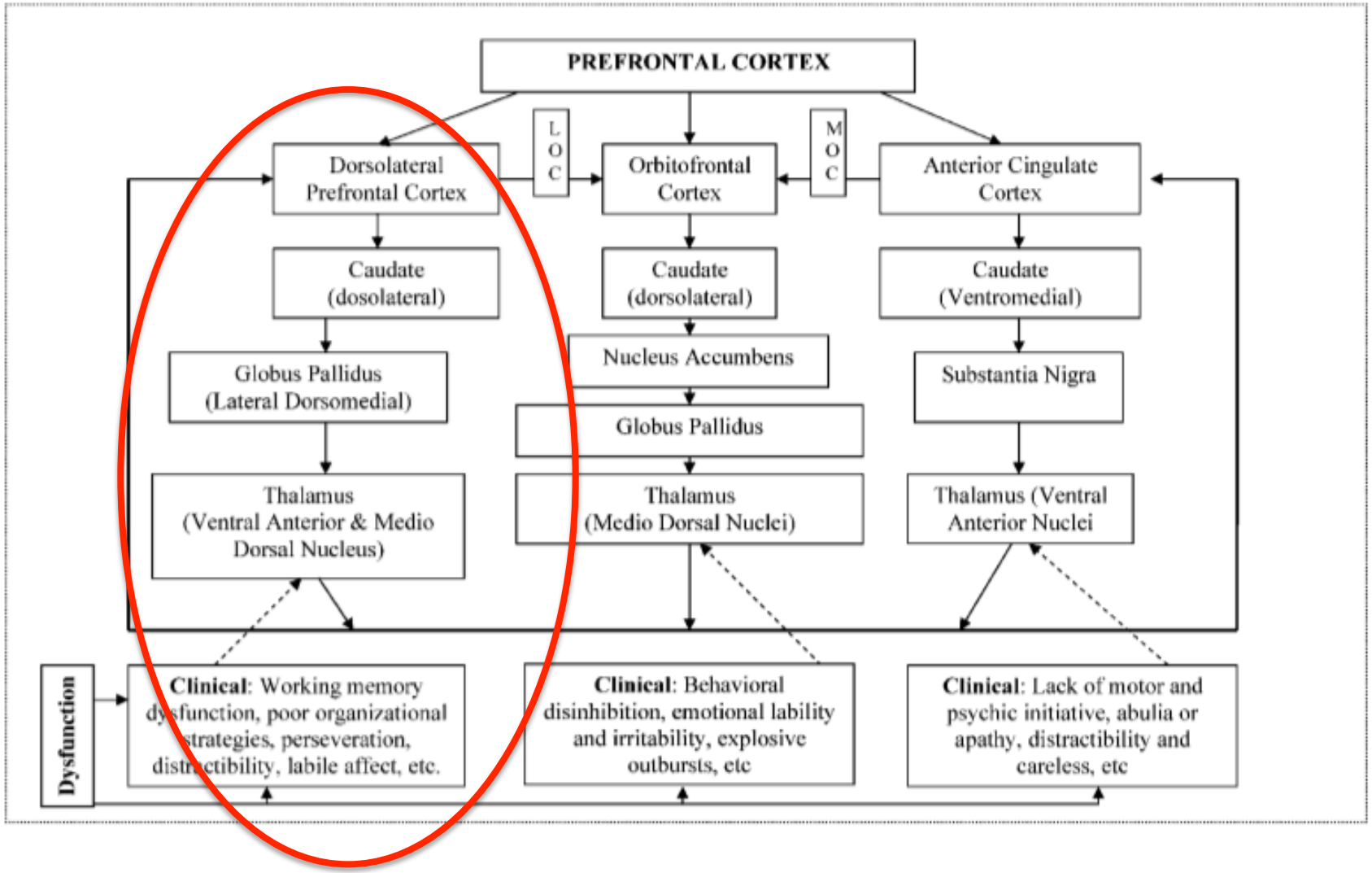
	Type of deficit	Function
Wisconsin card sorting test Tower of London test	Executive	Attention Working memory Planning Concept formation Rule use Cognitive inhibition Use of feedback
Task switching	Executive	Cognitive flexibility Response inhibition Attention Resistance to distractibility or set maintenance
Stroop performance	Executive	Attention Response inhibition
Attentional set-shifting	Executive	Attention Higher-order flexibility (stimulus dimensions) Use of feedback Resistance to distractibility/set maintenance
Reversal learning	Learning	Use of feedback Lower-order flexibility (stimulus exemplars)
Weather prediction	Learning	Use of feedback Attention Working memory Rule formation Abstract reasoning
Gambling or decision making	Impulse control	Use of feedback Response inhibition
Digit span	Memory	Working memory (numbers)
Spatial working memory	Memory	Working memory (spatial representations)
Stop signal task	Motor inhibition	Response inhibition
Delayed responding	Motor inhibition	Attention Resistance to distractibility
Mental rotation	Visuospatial	Motor imagery Visuospatial transformation

Characteristic aspects of mild cognitive impairment usually seen in patients receiving drug treatment.

***Table 1*: Fronto-executive deficits in early Parkinson's disease by neuropsychological task**

Lancet Neurology, 2010

Prefrontal Cortex-striatum networks



Neuropsychological and clinical heterogeneity of cognitive impairment and dementia in patients with Parkinson's disease

Angie A Kehagia, Roger A Barker, Trevor W Robbins

Panel 1: **Effects of dopamine restoration**

Cognitive benefit or amelioration of deficit

- Wisconsin card sorting test
- Tower of London test
- Task switching—concrete rules
- Digit span
- Spatial working memory

Cognitive deterioration from dopaminergic overdose

- Concurrent learning
- Probabilistic reversal learning
- Weather prediction classification
- Gambling and decision making
- Delayed responding with distraction
- Visual hallucinations

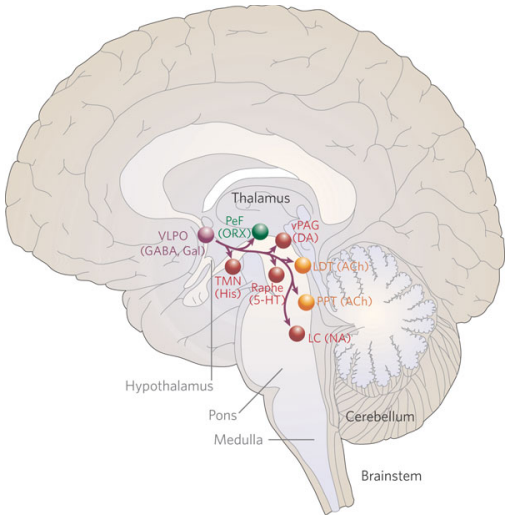
No effect

- Attentional set-shifting (extra-dimensional shifting)
- Task switching—abstract rules
- Pattern and spatial recognition memory
- Associative learning
- Verbal memory

Dopaminergic restoration has ameliorating, deleterious, and in some cases no effects on aspects of mild cognitive impairment that emerge during neuropsychological testing in the early stages of Parkinson's disease.

Lancet Neurology, 2010

Neurotrasmitters projection loss in PD



Noradrenergic dysfunction (locus coeruleus) in PD probably underlies the attentional set shifting deficit, which forms part of the dysexecutive syndrome.

Weintraub et al. *Neurology* 2010;75:448-455.
Kehagia et al. *Brain* 2014;137:1986-1997.

Some frontal cholinergic deficit (cortico-striato-thalamic loop/nigrostriatal system) also compromises early Parkinson's disease cognition.

Bohnen et al. *Archives of Neurolo*gy 2003;60:1745-1748.
Meyer et al. *Arch Gen Psychiatry* 2009;66:866-877.

Review

The cholinergic system and Parkinson disease

Nicolaas I. Bohnen[a,b,c,*], Roger L. Albin[b,c,1]

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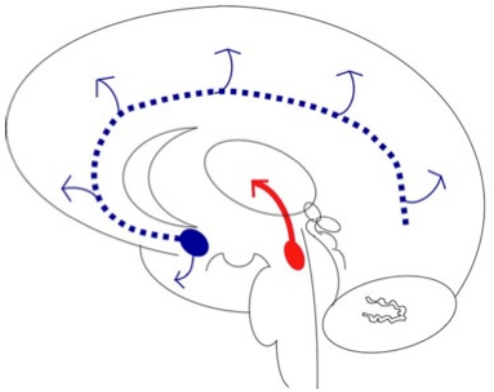
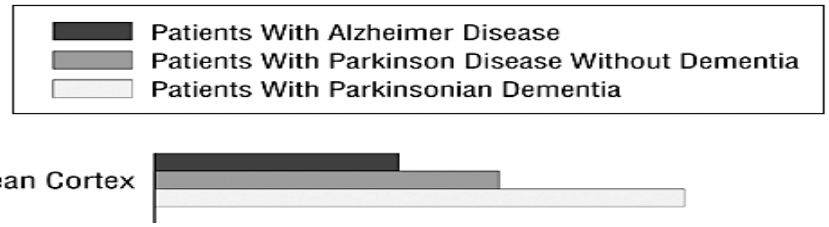
[c] VA Ann Arbor Healthcare System, Ann Arbor, MI, USA

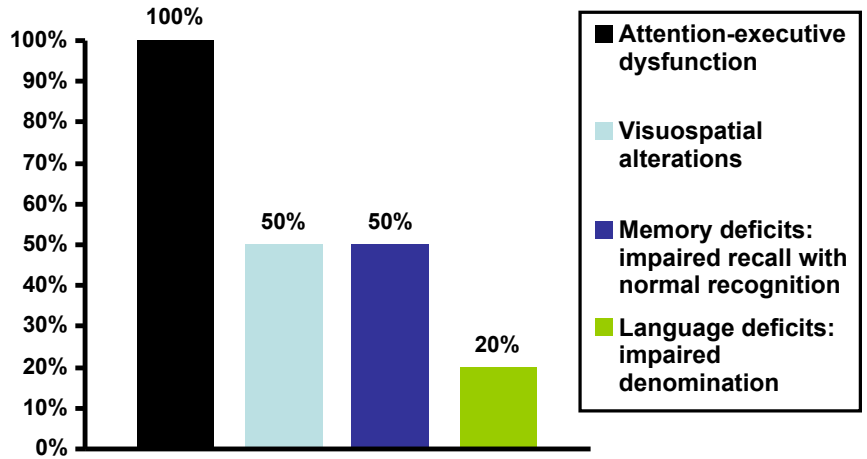


- PET imaging in patients with mild AD, PDD, and PD without dementia show greater and **more extensive reductions in cortical AChE levels in PDD** compared to AD of similar dementia severity [Bohnen NI 2003].

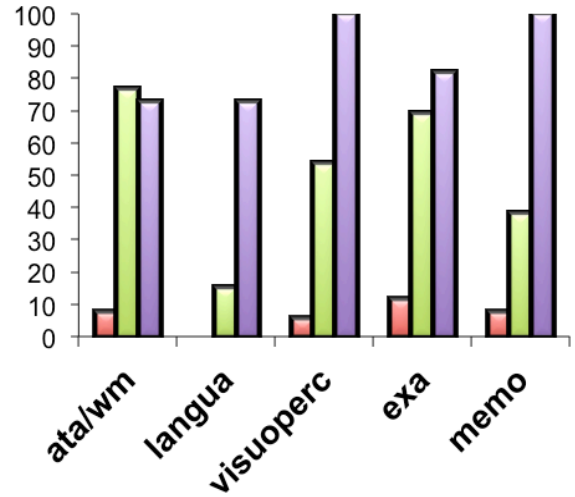


- **Cortical cholinergic denervation affects esecutive processes**[Bedard MA, 1999] and include symptoms such as visual allucination, depression and/or apathy and impaired activities of daily living [BohnenN 2007,2009].
- **Subcortical cholinergic denervation**, may relate to hyposmia, the presence of dopamine non-responsive gait and balance impairments, including falls, in PD [Stein JF et al 2009].

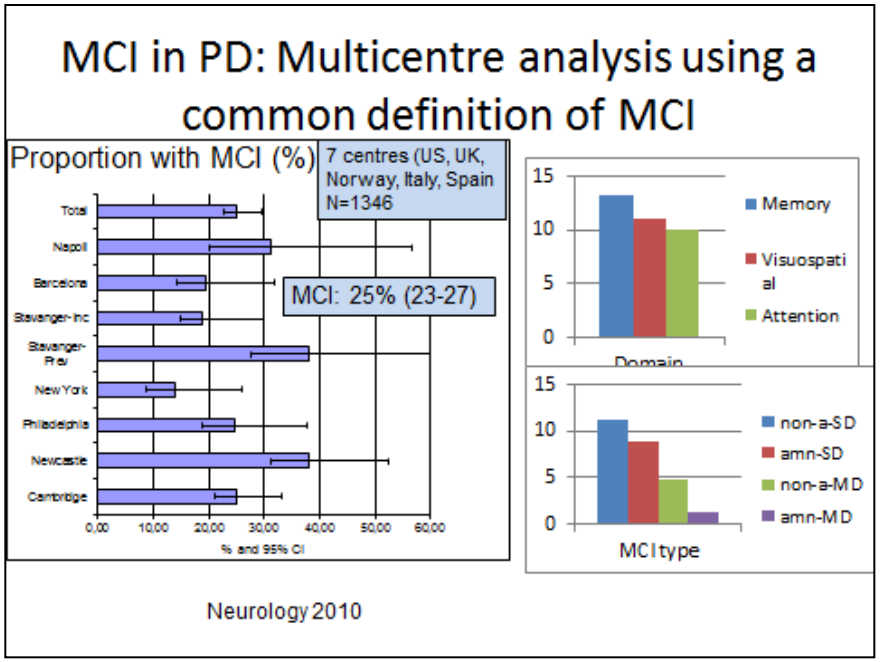
The pattern of Cognitive Impairment in PD is heterogeneous



Muslimovic et al. Neurology 2005; 65: 1239-1245



Biundo et al., J Neural Transm 2013; 120:627-33



Spectrum of cognitive impairment in PD

Normal Cognition

PD-MCI
30% (20-55%)

- Cognitive impairment
- Normal general cognitive functioning
- Normal functioning in activities of daily living

PDD
50% at 15ys

- Severe cognitive impairment
- Impairing daily function

Dementia in Parkinson's Disease (PDD)

- The **point prevalence** is **30%** and the incidence rate is increased 4 to 6 time compared to age-matched controls *(Emre et al., 2007)*.

- The **cumulative prevalence** is reported to be up to 83**%** after 20 years of follow up *(Williams-Gray et al. 2013; Hely et al 2008; Perez et al., 2012)*.

- The **main risk variables** include higher age, lower education, longer disease duration, depression, hallucination, **MCI at baseline**, rigidity, gait disturbance and postural instability.

It affects functioning and quality of life

It increases heathy care burden

……**only 25%** of PD pts with dementia are recognised by clinicians in routine care

Parkinson with mild cognitive impairment (PD-MCI)

Mild cognitive changes even in newly diagnosed, untreated PD, are associated with increasing age, disease duration, and disease severity *(Biundo et al., 2013, Aarsland et al., 2011; Troster et al., 2011; Williams-Gray et al., 2007)*.

PD patients have an increased risk of developing cognitive impairment, and those with MCI may progress to dementia more frequently and more rapidly than those without cognitive impairment (CI) *(Pedersen et al 2013; Barone et al., 2011; Janvin et al., 2006; Williams-Gray et al., 2009).*

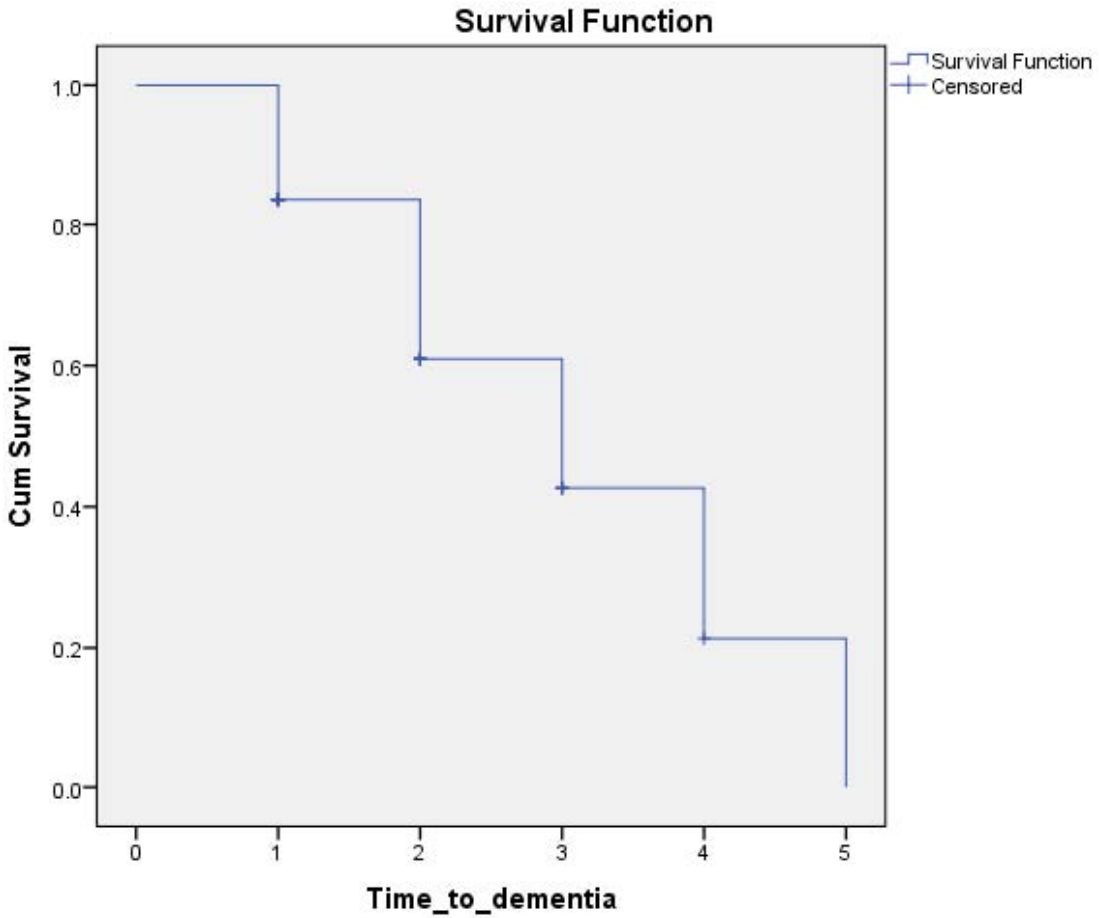
Cognition in Untreated, Early PD: PPMI Study

Cognitive Domain	Variable	Mean (SD) or N (%)
Global	**MOCA score** (N=423)	27.1 (2.3)
	30 - 26	330 (78%)
	21 - 25	89 (21%)
	<21	4 (1%)
Visuospatial	**Benton Judgment of Line Orientation Score** (N=422)	12.8 (2.1)
	Mild Impairment[a]	30 (7%)
	Moderate Impairment[b]	**14 (3%)**
	Severe Impairment[c]	2 (0%)
Memory	**HVLT Immediate Recall** (N=422)	24.4 (5.0)
	Mild Impairment	131 (31%)
	Moderate Impairment	**73 (17%)**
	Severe Impairment	29 (7%)
	HVLT Delayed Recall (N=422)	8.4 (2.5)
	Mild Impairment	139 (33%)
	Moderate Impairment	**70 (17%)**
	Severe Impairment	26 (6%)
	HVLT Retention (N=422)	0.9 (0.2)
	Mild Impairment	89 (21%)
	Moderate Impairment	**47 (11%)**
	Severe Impairment	21 (5%)
	HVLT Discrimination Recognition (N=421)	9.6 (2.6)
	Mild Impairment	102 (24%)
	Moderate Impairment	**38 (9%)**
	Severe Impairment	13 (3%)
Executive abilities-Working memory	**Letter Number Sequencing Raw Score** (N=422)	10.6 (2.7)
	Mild Impairment	28 (7%)
	Moderate Impairment	**19 (4%)**
	Severe Impairment	4 (1%)
	Semantic Fluency Total Score (N=422)	48.7 (11.6)
	Mild Impairment	61 (14%)
	Moderate Impairment	**22 (5%)**
	Severe Impairment	9 (2%)
Processing speed-Attention	**Symbol Digit Modalities Score** (N=422)	41.2 (9.7)
	Mild Impairment	110 (26%)
	Moderate Impairment	**60 (14%)**
	Severe Impairment	27 (6%)

Weintraub et al. *Movement Disorders* 2015;10.1002/mds.26170.

Frequent Progression From MCI to Dementia Over 3-5 Years

Long-term outcomes for <u>incident</u> MCI in <u>established</u> PD



Pigott et al. *Neurology* (in press).

Early MCI detection may ameliorate accuracy of Dementia and enhance the pharmacological and rehabilitation treatment

To implement **rehabilitative interventions** can ultimately have great effect on
patients quality of life,
cognitive symptom relief and
promotion of **functional independence**

FEATURED ARTICLE

CME

Diagnostic Criteria for Mild Cognitive Impairment in Parkinson's Disease: *Movement* Disorder Society Task Force Guidelines

Irene Litvan, MD,[1]* Jennifer G. Goldman, MD, MS,[2] Alexander I. Tröster, PhD,[3] Ben A. Schmand, PhD,[4] Daniel Weintraub, MD,[5] Ronald C. Petersen, MD, PhD,[6] Brit Mollenhauer, MD,[7] Charles H. Adler, MD, PhD,[8] Karen Marder, MD,[9] Caroline H. Williams-Gray, MRCP, PhD,[10] Dag Aarsland, MD, PhD,[11] Jaime Kulisevsky, MD, PhD,[12] Maria C. Rodriguez-Oroz, MD, PhD,[13] David J. Burn, MD, FRCP,[14] Roger A. Barker, BSc, MBBS, MRCP, PhD,[10] and Murat Emre, MD[15]

III. Specific guidelines for PD-MCI level I and level II categories

A. Level I (abbreviated assessment)

- Impairment on a scale of global cognitive abilities validated for use in PD[a] *or*
- Impairment on at least two tests, when a limited battery of neuropsychological tests is performed (i.e., the battery includes less than two tests within each of the five cognitive domains, or less than five cognitive domains are assessed)

B. Level II (comprehensive assessment)

- Neuropsychological testing that includes two tests within each of the five cognitive domains (i.e., attention and working memory, executive, language, memory, and visuospatial)[b]
- Impairment on at least two neuropsychological tests, represented by either two impaired tests in one cognitive domain or one impaired test in two different cognitive domains
- Impairment on neuropsychological tests may be demonstrated by:
  - o Performance approximately 1 to 2 SDs below appropriate norms *or*
  - o Significant decline demonstrated on serial cognitive testing *or*
  - o Significant decline from estimated premorbid levels

Impairment on a scale of globale cognitive ability or in at least two tests

- Two test for each of the 5 cognitive domain: attention, executive, language, memory and visuo-spatial
- Impairment (> 1, 1.5, 2 SD below the normative mean) on at least two NPSI tests

Journal of Parkinson's Disease 4 (2014) 131–137
DOI 10.3233/JPD-130304
IOS Press

Review

Parkinson's Disease Mild Cognitive Impairment: Application and Validation of the Criteria

Fig. 1. Participating countries in the MDS PD-MCI Validation Study Group are marked black.

To validate the MDS PD-MCI criteria by pooling and analyzing cross-sectional and longitudinal neuropsychological databases comprising ≥5,500 PD patients and ≥1,700 controls.

Current issues about PD-MCI

Neuropsychological issues. No specific global cognitive scale (MMSE vs MoCA) or neuropsychological test battery to detect cognitive impairment in PD or cognitive decline over time *(Biundo et al 2013; Marras et al 2010; Lessig et al 2012; Hu et al 2014)*

Statistical issues. A threshold values (-1 or -1.5 or -2 SD) is a rather crude approach assuming each test contributes in an equivalent manner to identify the cognitive state of the individual examined *(Biundo et al.2013)*

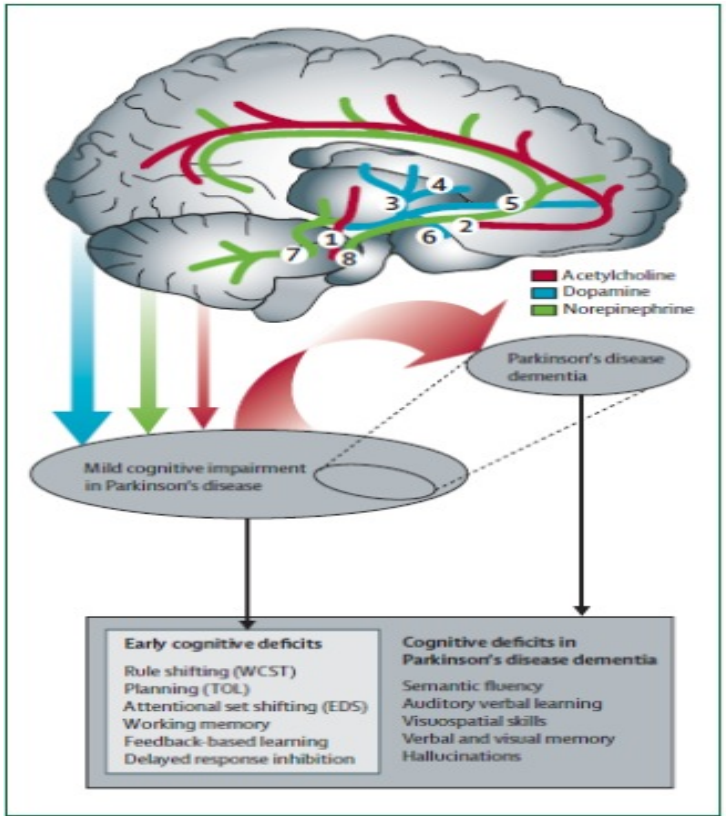
- Neuroimaging issues. Cortical changes associated with cognitive decline in PD are not fully explored and required investigations *(Biundo et al 2014; Rektorova et al 2014; Weintraub 2011, Meltzer 2012)*

- Clinical issues. No consensus about PD-MCI profile that can predict dementia *(Biundo 2014; Williams Gray 2013; Goldamm-Litvan 2011)*

Heterogeneity of cognitive impairment in PD

Different neuropsychological profiles

Diverse underlying neurochemistry



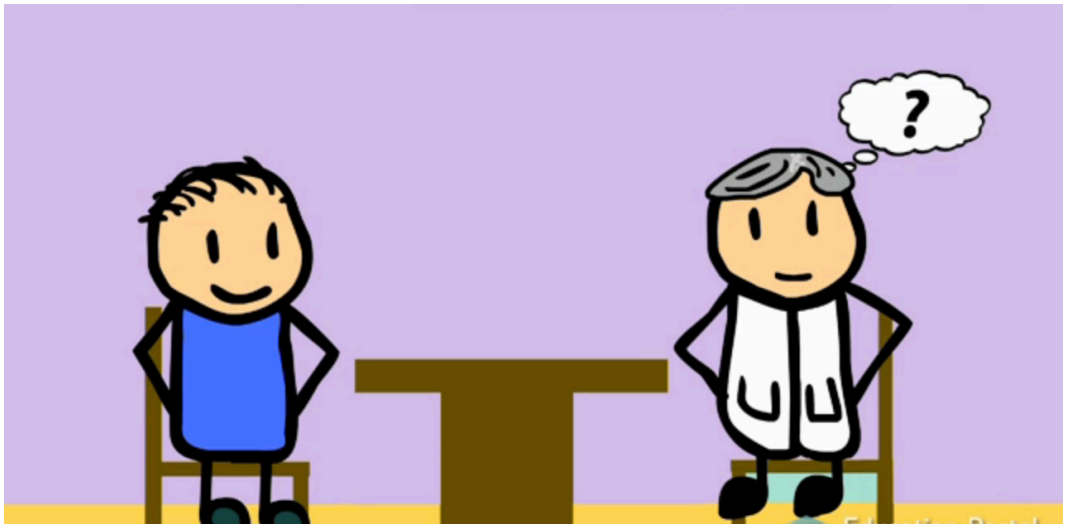
Lancet Neurology, 2010

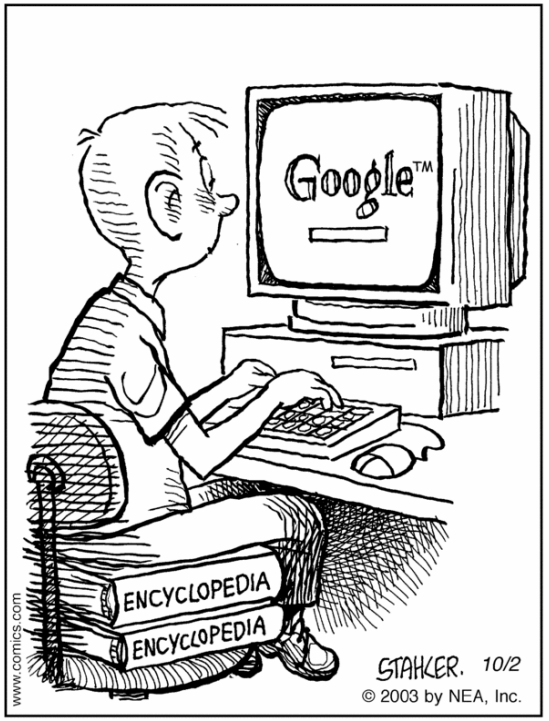
Different clinical mainfestations

Different underlying neurosubstrates

There is neuropsychological overlap because PDD have acetylcholine-based visuo-spatial and memory deficits as well as dopamine-dependent executive deficits, noradrenergic-dependent executive deficits, and some degree of frontal cholinergic deficit might also contribute to cognitive impairment early in the disease course.

..where do we start assessing cognitive status?





PD-MCI detection

FEATURED ARTICLE

CME

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Subject complaints of cognitive deficits

Normal functioning on activity of daily living

Level I
Impairment on a scale of globale cognitive ability

Eliciting cognitive concerns and assessing function related to cognition

- Ask patient AND companion

Global questions: *"do you have concerns about your memory or thinking?" or "does it interfere with your ability to carry out your activities?"*

- Cognitive complaint interview

- Functional rating scales:
  - PD-Cognitive functional rating scale
  - Disability assessment for Dementia
  - Pill Questionnaire
- Neuropsychological assessment

Cognitive complaint interview

	Questions concerning the last 6 months	Response
1	Have you observed a memory change during the last 6 months?	Yes/no
2	During the last 6 months, do you consider that your memory has been worse than the memory of your peers?	Yes/no
3	Do you record less recent events or have you heard your family say 'I have already said so to you'?	Yes/no
4	Do you often forget appointments?	Yes/no
5	Do you often forget where things are left?	Yes/no
6	Do you have more difficulty finding your way in your neighborhood? Have you ever not recognized a route that your family thinks you have already gone?	Yes/no
7	Have you ever forgotten a whole event, even when the family gives you clues, details or pictures of the event?	Yes/no
8	Have you ever encountered difficulty finding particular words (except person names)?	Yes/no
9	Have you reduced your activities (social or leisure's activities, association, papers and invoices) or asked your family to help you because you are afraid you may make a mistake?	Yes/no
10	Have you ever observed mood changes in term of apathy, blunted affect, inertia, loss of volition or interest for activities or persons?	Yes/no

10 items
(6 on memory)

>3 = complaint

Several studies in the elderly have suggested that cognitive complaints (when recorded using standardized items) may help to predict dementia (Thomas Anterion C., 2003; Miranda B et al., 2008)

Thomas Anterion C et al., Psychogeriatrics 2006

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  - PD-Cognitive functional rating scale
  - Pennsylvania Daily Activities Questionnaire
  - Pill Questionnaire
- Neuropsychological assessment

Parkinson's Disease Cognitive Functional Rating Scale (PD-CFRS)

1 Ha difficoltà a maneggiare denaro?Per esempio: controllare il resto, calcolare quanto le serve per fare degli acquisti ecc.	0	1	2	8
2 Riscontra delle difficoltà nella gestione dell'amministrazione di casa?	0	1	2	8
3 Ha delle difficoltà nel pianificare le sue vacanze o degli appuntamenti con amici/ familiari?	0	1	2	8
4 Riscontra delle difficoltà nel gestire la posta in arrivo, o ad organizzare le sue bollette e gli appuntamenti con il medico?	0	1	2	8
5 Ha delle difficoltà nel ricordare quando assumere i farmaci e in quale dose?	0	1	2	8
6 Riscontra delle difficoltà nel pianificare le attività quotidiane nell'arco della sua giornata?	0	1	2	8
7 Trova difficile ultimamente capire come utilizzare gli apparecchi elettrodomestici?	0	1	2	8
8 Riscontra delle difficoltà a pianificare il suo percorso utilizzando mezzi pubblici?	0	1	2	8
9 Trova difficoltà nel gestire delle situazioni o problemi inaspettati?	0	1	2	8
10 Trova difficoltà qualche volta a farsi capire?	0	1	2	8
11 Ha delle difficoltà a comprendere quello che legge (libri, riviste, giornali)?	0	1	2	8
12 Trova difficoltà nel capire come funziona un telefono cellulare?	0	1	2	8

Kulisevsky J. et al. 2013

PD-CFRS cut-off score of > 3 for detecting functional impairment in PD-MCI
PD-CFRS cut-off score of > 6 for detecting functional impairment in PDD

(free of charge for scientific study: jkulisevsky@santpau.cat)

Pennsylvania Daily Activities Questionnaire (PDAQ)

(Weintraub, D; Brennan et al. 2015)

Please check or fill in the following that best describes you.

1. Because of the Parkinson's Disease, how much DIFFICULTY do you currently have reading the newspaper or magazine?

O None (4)	O A Little (3)	O Somewhat (2)	O A Lot (1)	O Cannot Do (0)

2. How much DIFFICULTY do you currently have keeping track of time (e.g. using a clock)?

O None (4)	O A Little (3)	O Somewhat (2)	O A Lot (1)	O Cannot Do (0)

5. How much DIFFICULTY do you currently have handling an unfamiliar problem (e.g. getting the refrigerator fixed)?

O None (4)	O A Little (3)	O Somewhat (2)	O A Lot (1)	O Cannot Do (0)

6. How much DIFFICULTY do you currently have explaining how to do something involving several steps to another person?

O None (4)	O A Little (3)	O Somewhat (2)	O A Lot (1)	O Cannot Do (0)

Eliciting cognitive concerns and assessing function related to cognition

- Ask patient AND companion

Global questions: *"do you have concerns about your memory or thinking?" or "does it interfere with your ability to carry out your activities?"*

- Cognitive complaint interview

- Functional rating scale
  - PD-Cognitive functional rating scale
  - Pennsylvania Daily Activities Questionnaire
  - Pill Questionnaire
- Neuropsychological assessment

Eliciting cognitive concerns and assessing function related to cognition

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Global questions: *"do you have concerns about your memory or thinking?" or "does it interfere with your ability to carry out your activities?"*

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- Functional rating scale
  - PD-Cognitive functional rating scale
  - Pennsylvania Daily Activities Questionnaire
  - Pill Questionnaire
- Neuropsychological assessment

Tools

- Global cognitive rating scale

- Neurospychological testing
  - ➢ Clinical interview
  - ➢ Detailed cognitive testing
  - ➢ Feedback session

½ day

Validated cognitive scales

Non-specific for PD

- Mattis Dementia Rating Scale (MDRS)
  - measures frontal-subcortical deficits
- Mini-Mental State Examination (MMSE)most commonly used for dementia but low sensitivity to detect MCI
- Cambridge Cognitive Assessment (CAMCOG) accurate for diagnosis of PDD
- Frontal Assessment Battery (FAB) Non-compatible with pattern of CI predominant in PD

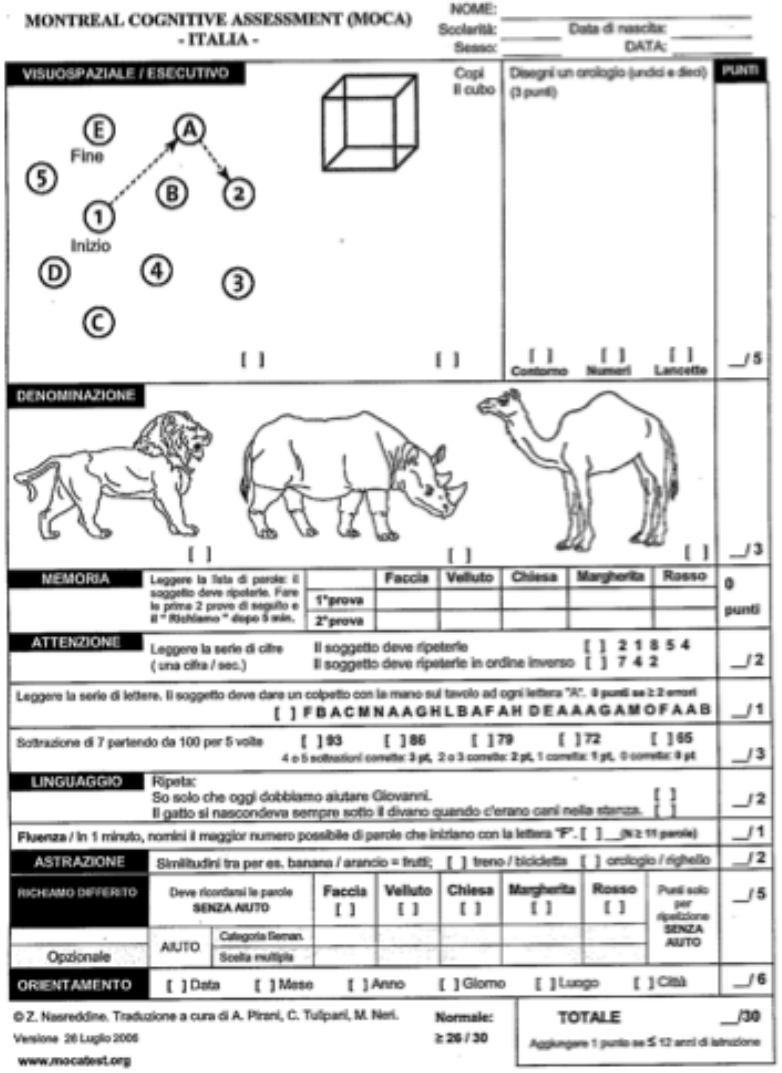
Specific for PD

- The MoCA - brief screening test covering the whole spectrum of CI in PD patients
- Parkinson's Disease – Cognitive Rating Scale (PD-CRS)designed to capture the whole spectrum of CI in PD patients
- Parkinson Neuropsychometric Dementia Assessment (PANDA) designed to screen for CI in PD patients
- Scales for Outcomes of Parkinson's Disease-Cognition (SCOPA-COG) mainly assesses frontal-subcortical function

Reviewed by Kulisevsky and Pagonabarraga. Mov Disord 2009; 24: 1103-1110

Montreal Cognitive Assessment (MoCA)

- MoCA (maximum score 30)
- 7 subscores:
- visuospatial/executive (5 points);
- naming (3 points);
- memory (5 points for delayed recall);
- attention (6 points);
- language (3 points);
- abstraction (2 points);
- orientation (6 points).
- One point is added if the subject has 12 years of education.



MONTREAL COGNITIVE ASSESSMENT (MOCA)
- ITALIA -

NOME:
Scolarità: Data di nascita:
Sesso: DATA:

VISUOSPAZIALE / ESECUTIVO — Copi il cubo — Disegni un orologio (undici e dieci) (3 punti) — PUNTI

Fine — Inizio

[ ] [ ] — [ ] Contorno [ ] Numeri [ ] Lancette — /5

DENOMINAZIONE — [ ] [ ] [ ] — /3

MEMORIA — Leggere la lista di parole: il soggetto deve ripeterle. Fare le prima 2 prove di seguito e il " Richiamo " dopo 5 min.

	Faccia	Velluto	Chiesa	Margherita	Rosso
1°prova					
2°prova					

0 punti

ATTENZIONE — Leggere la serie di cifre (una cifra / sec.) — Il soggetto deve ripeterle [ ] 2 1 8 5 4 — Il soggetto deve ripeterle in ordine inverso [ ] 7 4 2 — /2

Leggere la serie di lettere. Il soggetto deve dare un colpetto con la mano sul tavolo ad ogni lettera "A". 0 punti se ≥ 2 errori
[ ] F B A C M N A A G H L B A F A H D E A A A G A M O F A A B — /1

Sottrazione di 7 partendo da 100 per 5 volte [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65
4 o 5 sottrazioni corrette: 3 pt, 2 o 3 corrette: 2 pt, 1 corretta: 1 pt, 0 corrette: 0 pt — /3

LINGUAGGIO — Ripeta:
So solo che oggi dobbiamo aiutare Giovanni. [ ]
Il gatto si nascondeva sempre sotto il divano quando c'erano cani nella stanza. [ ] — /2

Fluenza / In 1 minuto, nomini il maggior numero possibile di parole che iniziano con la lettera "F". [ ] (N ≥ 11 parole) — /1

ASTRAZIONE — Similitudini tra per es. banana / arancio = frutti; [ ] treno / bicicletta [ ] orologio / righello — /2

RICHIAMO DIFFERITO — Deve ricordarsi le parole SENZA AIUTO

		Faccia [ ]	Velluto [ ]	Chiesa [ ]	Margherita [ ]	Rosso [ ]	Punti solo per ripetizione SENZA AIUTO
Opzionale	AIUTO Categoria Semant.						
	AIUTO Scelta multipla						

/5

ORIENTAMENTO — [ ] Data [ ] Mese [ ] Anno [ ] Giorno [ ] Luogo [ ] Città — /6

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Versione 26 Luglio 2006
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Normale: ≥ 26 / 30

TOTALE /30
Aggiungere 1 punto se ≤ 12 anni di istruzione

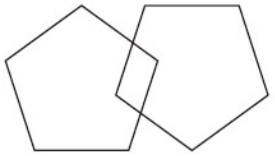
Mini-Mental State Exam (MMSE)

- MMSE (maximum score 30)
- Orientation
- Registration
- Attention and calculation
- 3 words recall
- **Language: denomination, repetition, comprehension, writing.**
- Visuo-spatial skills

The Mini-Mental State Exam

Patient_____ Examiner _____ Date_____

Maximum	Score	
		Orientation
5	( )	What is the (year) (season) (date) (day) (month)?
5	( )	Where are we (state) (country) (town) (hospital) (floor)?
		Registration
3	( )	Name 3 objects: 1 second to say each. Then ask the patient all 3 after you have said them. Give 1 point for each correct answer. Then repeat them until he/she learns all 3. Count trials and record. Trials _____
		Attention and Calculation
5	( )	Serial 7's. 1 point for each correct answer. Stop after 5 answers. Alternatively spell "world" backward.
		Recall
3	( )	Ask for the 3 objects repeated above. Give 1 point for each correct answer.
		Language
2	( )	Name a pencil and watch.
1	( )	Repeat the following "No ifs, ands, or buts"
3	( )	Follow a 3-stage command: "Take a paper in your hand, fold it in half, and put it on the floor."
1	( )	Read and obey the following: CLOSE YOUR EYES
1	( )	Write a sentence.
1	( )	Copy the design shown.



_____ Total Score

ASSESS level of consciousness along a continuum _____

Alert Drowsy Stupor Coma

Attention and Working Memory

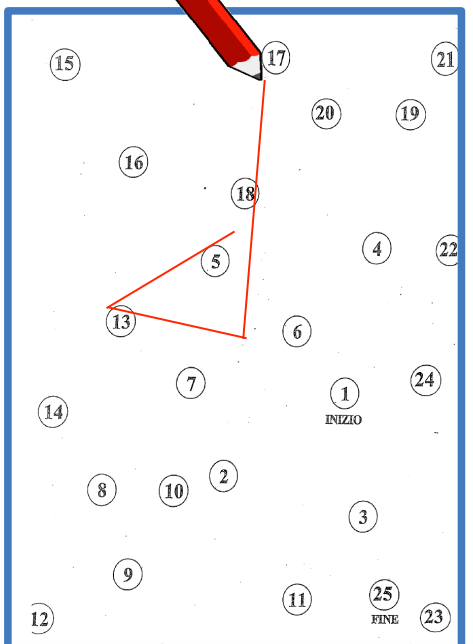
- Spatial span
- Digit Ordering Test
- Trail Making Test

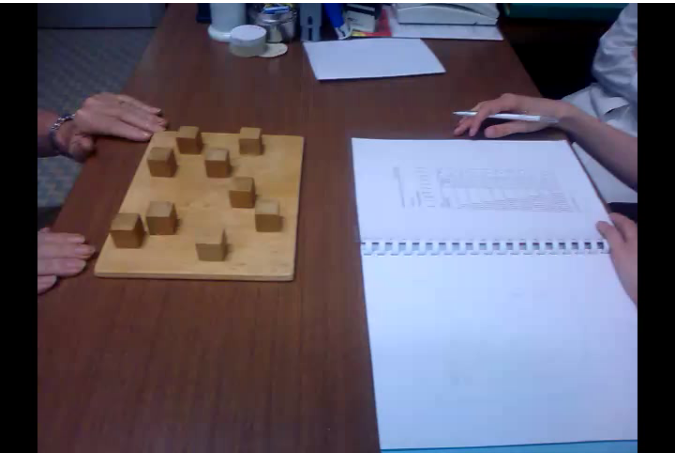
Sustained attention

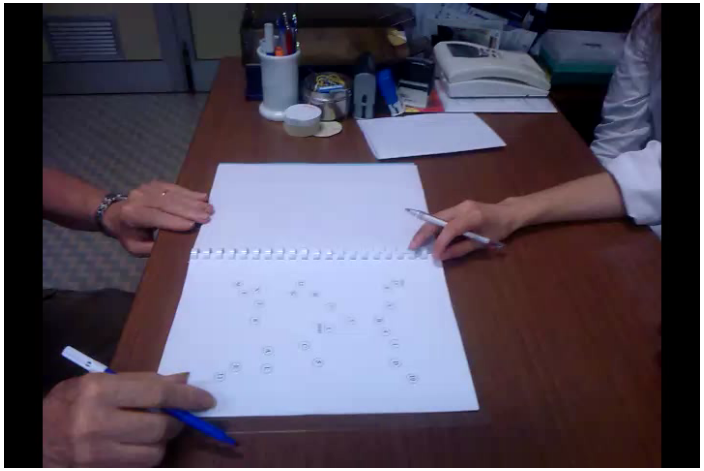
Digit Ordering-B

Item	Span length	Trial 1	1/0	Trial 2	1/0	Score (0–2)
1.	*3*	4 8 3 (3 4 8)		7 2 7 (2 7 7)		
2.	*4*	9 5 8 4 (4 5 8 9)		6 1 6 5 (1 5 6 6)		
3.	*5*	3 7 6 4 2 (2 3 4 6 7)		6 2 9 6 3 (2 3 6 6 9)		
4.	*6*	3 7 2 8 1 6 (1 2 3 6 7 8)		4 1 4 8 3 6 (1 3 4 4 6 8)		
5.	*7*	6 3 2 0 7 1 5 (0 1 2 3 5 6 7)		8 5 4 1 7 5 2 (1 2 4 5 5 7 8)		
6.	*8*	4 8 7 2 9 3 6 1 (1 2 3 4 6 7 8 9)		1 5 2 1 0 7 6 4 (0 1 1 2 4 5 6 7)		
Notes:				Test score (max. 12): Percentile of test score: Maximal span:		

Cognitive flexibility

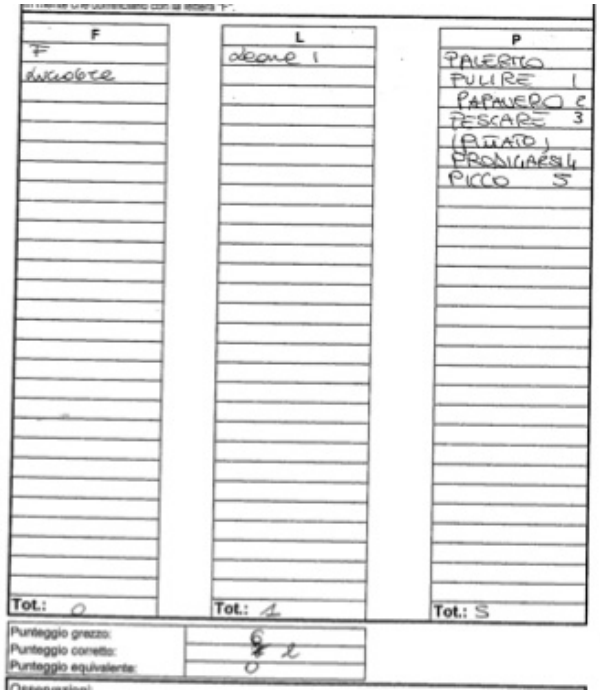






Executive Functions

- Phonemic Fluency (words beginning with a given letter)
- Stroop Test (response inhibition: say the color of the ink)



Green

blu

red

blu

green

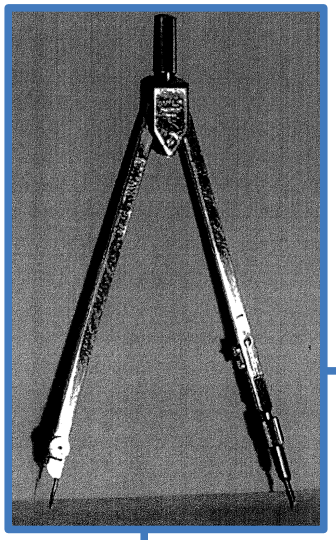
green

red

red

Language

- Denomination Test
- Category Fluency Task (words pertaining to a semantic category)

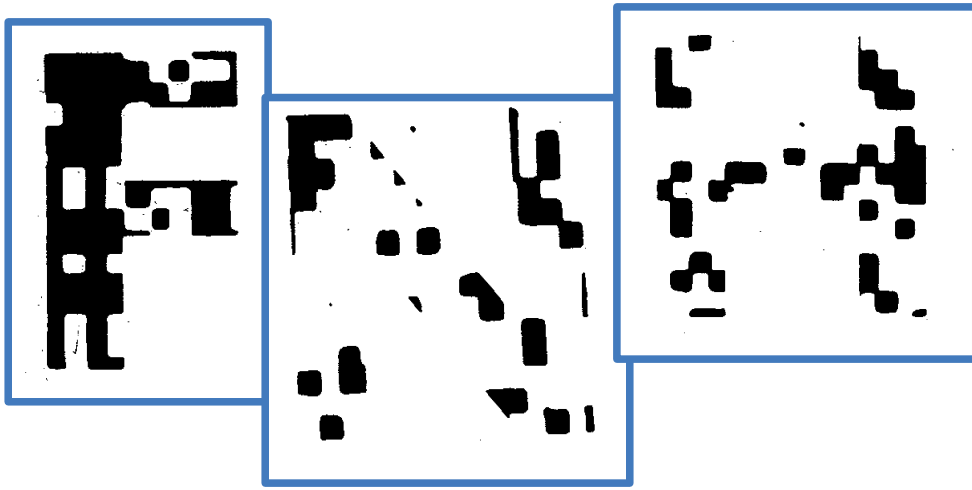


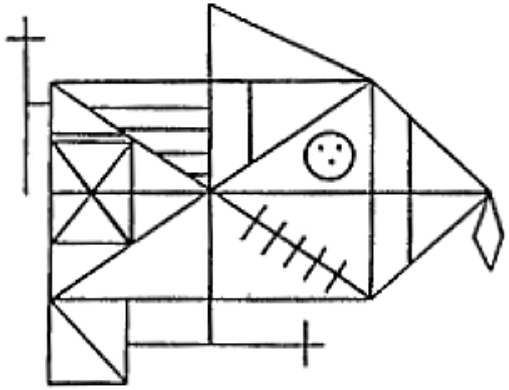
MARCHE D'AUTO		FRUTTI		ANIMALI	
FIAT	1	PERA	1	CANE	1
LANCIA	2	PERDURARE		GHEP	2
MASERATI	3	PULIRE		LEOP	3
FERRARI	4	PICCHIETTARE		ELEFANTE	4
		PANNEGGIARE		PLUTO	0
				PANFILO	0
Tot.:	4	Tot.:	1	Tot.:	4

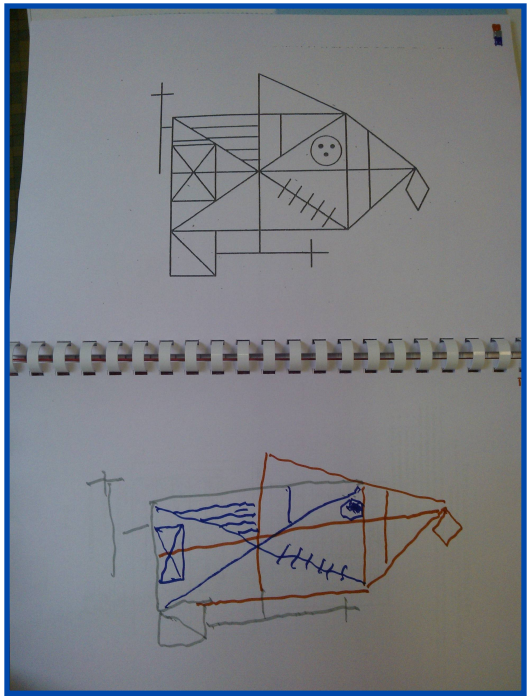
Punteggio grezzo:	9
Punteggio corretto:	6
Punteggio equivalente:	0

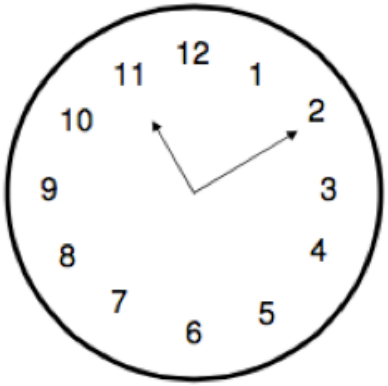
Visuo-spatial Functions

- Letters Recognition (VOSP)
- Rey-Osterrieth Complex Figure Test (copy)
- Clock Drawing test copy



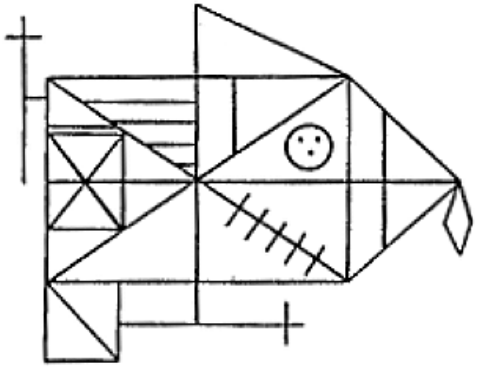


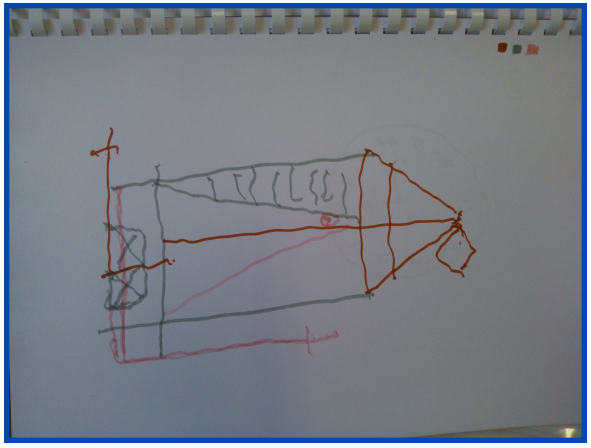




Memory

- Cued Recall Test (frontal or posterior deficits?)
- Prose Memory Test
- Rey-Osterrieth Complex Figure test (recall)





APPRENDIMENTO DI COPPIE DI PAROLE

PRESENTAZIONE 1	CUE	RISPOSTE	PUNTEGGIO
FRUTTA – UVA	BACIO		
SCUSA - FEDE	SCUSA		
MESE – ANNO	NORD		
PONTE – VINO	ARCO		
ALTO – BASSO	ALTO		
BACIO – MURO	PONTE		
NORD – SUD	FRUTTA		
PESCE – MARE	LOTTA		
ARCO – NOME	PESCE		
LOTTA - DITO	MESE		
			TOT 1
PRESENTAZIONE 2			
FRUTTA – UVA	SCUSA		
BACIO – MURO	LOTTA		
SCUSA – FEDE	ALTO		
NORD – SUD	FRUTTA		
ARCO – NOME	PESCE		
PESCE – MARE	ARCO		
ALTO - BASSO	BACIO		
LOTTA – DITO	PONTE		
MESE – ANNO	MESE		
PONTE -VINO	NORD		
			TOT 2
PRESENTAZIONE 3			
ARCO – NOME	PESCE		
MESE – ANNO	FRUTTA		
NORD – SUD	NORD		
SCUSA – FEDE	SCUSA		
LOTTA – DITO	PONTE		
ALTO – BASSO	LOTTA		
PESCE – MARE	MESE		
BACIO – MURO	BACIO		
FRUTTA – UVA	ARCO		
PONTE - VINO	ALTO		
			TOT 3
TOTALE PRESENTAZIONE 1+2+ 3 =			

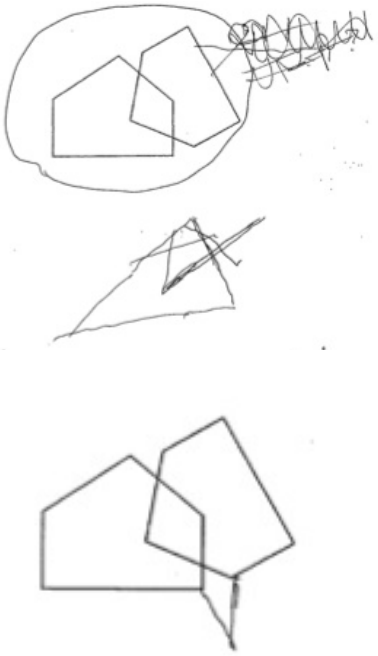
PDD detection

Diagnostic Procedures for Parkinson's Disease Dementia: Recommendations from the Movement Disorder Society Task Force

Movement Disorders
Vol. 22, No. 16, 2007, pp. 2314–2324

TABLE 2. *Diagnostic rating sheet for probable PD-D, recommended by the Movement Disorder Task Force*

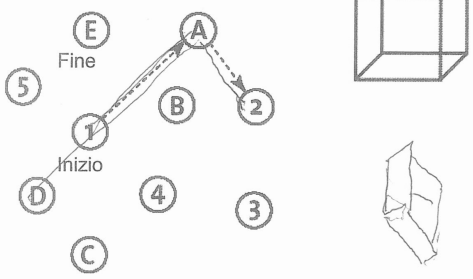
	YES	NO
1. Parkinson's disease	☐	☐
2. Parkinson's disease developed before dementia	☐	☐
3. MMSE <26	☐	☐
4. Dementia has Impact on ADLs	☐	☐
5. Impaired cognition (For Yes, at least of 2 of 4 tests below are abnormal)	☐	☐
Mark which Tests are abnormal		
☐ Months reversed or Sevens backwards		
☐ Lexical fluency or clock drawing		
☐ MMSE pentagons		
☐ 3-word recall		
6. Absence of Major Depression	☐	☐
7. Absence of delirium	☐	☐
8. Absence of other abnormalities that obscure diagnosis	☐	☐
Probable PD-D (items 1–8 must all be YES)	☐	☐



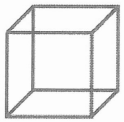
MONTREAL COGNITIVE ASSESSMENT (MOCA)
- ITALIA -

NOME: _____
Scolarità: _____ Data di nascita: _____
Sesso: _____ DATA: _____

VISUOSPAZIALE / ESECUTIVO — **PUNTI**



Copi Il cubo



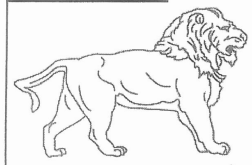
[ ] [ ]

Disegni un orologio (undici e dieci) (3 punti)

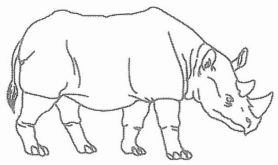
[+] Contorno [4]– Numeri [–] Lancette

4 / 5

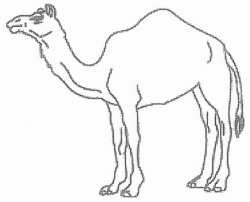
DENOMINAZIONE



[+]



[+]



[+]

3 / 3

MEMORIA — Leggere la lista di parole: il soggetto deve ripeterle. Fare le prime 2 prove di seguito e il " Richiamo " dopo 5 min.

	Faccia	Velluto	Chiesa	Margherita	Rosso
1°prova	–	–	–	–	
2°prova	+	+	+		+

0 punti

ATTENZIONE

Leggere la serie di cifre (una cifra / sec.)

Il soggetto deve ripeterle [–] 2 1 8 5 4
Il soggetto deve ripeterle in ordine inverso [+] 7 4 2

1 / 2

Leggere la serie di lettere. Il soggetto deve dare un colpetto con la mano sul tavolo ad ogni lettera "A". **0 punti se ≥ 2 errori**

[ ] F B A C M N A A G H L B A F A H D E A A A G A M O F A A B

0 / 1

Sottrazione di 7 partendo da 100 per 5 volte [ ] 93 [ ] 86 [ ] 79 [ ] 72 [ ] 65

4 o 5 sottrazioni corrette: **3 pt**, 2 o 3 corrette: **2 pt**, 1 corretta: **1 pt**, 0 corretta: **0 pt**

1 / 3

LINGUAGGIO — Ripeta:

So solo che oggi dobbiamo aiutare Giovanni. [–]
Il gatto si nascondeva sempre sotto il divano quando c'erano cani nella stanza. [–]

0 / 2

Fluenza / In 1 minuto, nomini il maggior numero possibile di parole che iniziano con la lettera "F". [ ] __ **(N ≥ 11 parole)**

0 / 1

ASTRAZIONE — Similitudini tra per es. banana / arancio = frutti; [–] treno / bicicletta [–] orologio / righello

0 / 2

RICHIAMO DIFFERITO — Deve ricordarsi le parole **SENZA AIUTO**

		Faccia [ ]	Velluto [ ]	Chiesa [ ]	Margherita [ ]	Rosso [ ]
	AIUTO Categoria Seman.				–	–
Opzionale	AIUTO Scelta multipla	+	+	+	–	–

Punti solo per ripetizione **SENZA AIUTO**

__ / 5

ORIENTAMENTO [–] Data [+] Mese [–] Anno [+] Giorno [+] Luogo [+] Città

4 / 6

Versione 26 Luglio 2006

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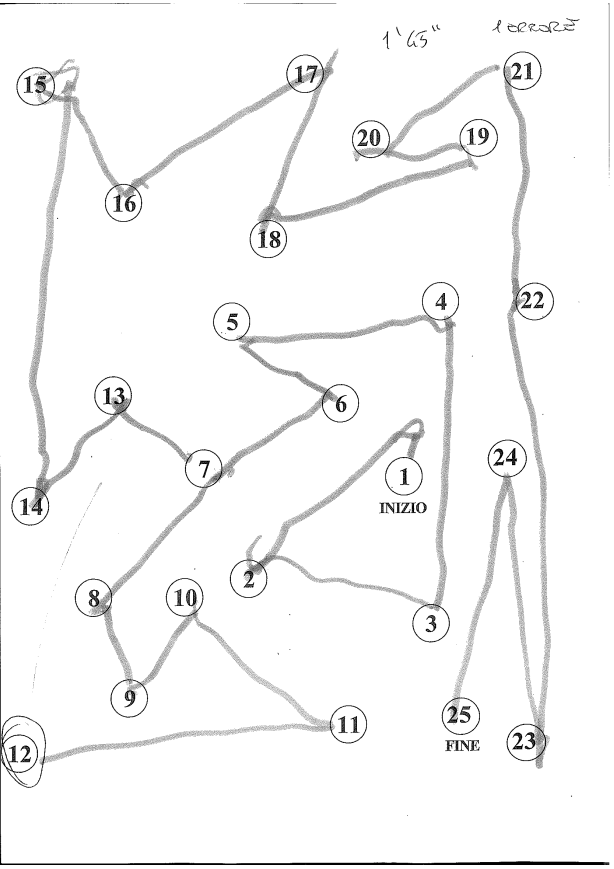
Normale: ≥ 26 / 30

TOTALE 11 /30

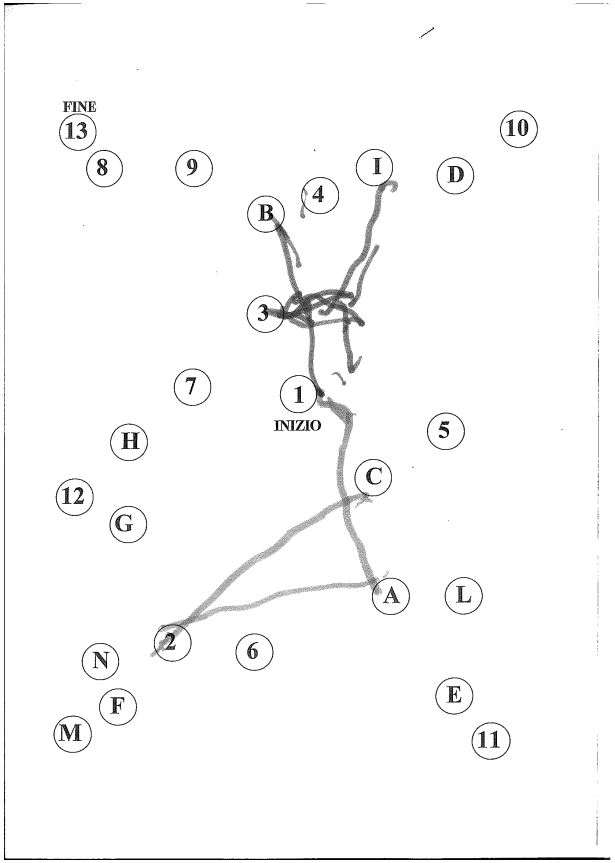
Aggiungere 1 punto se ≤ 12 anni di istruzione

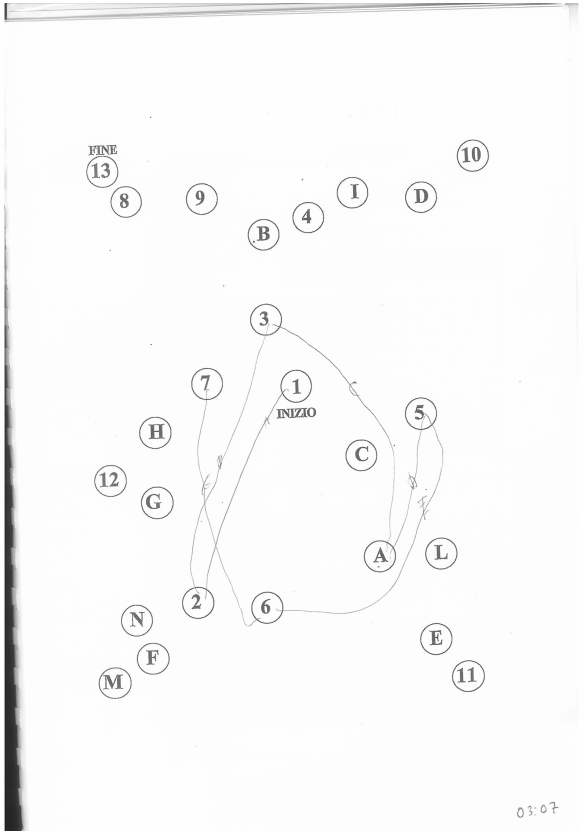
Trail Making test

TMTA

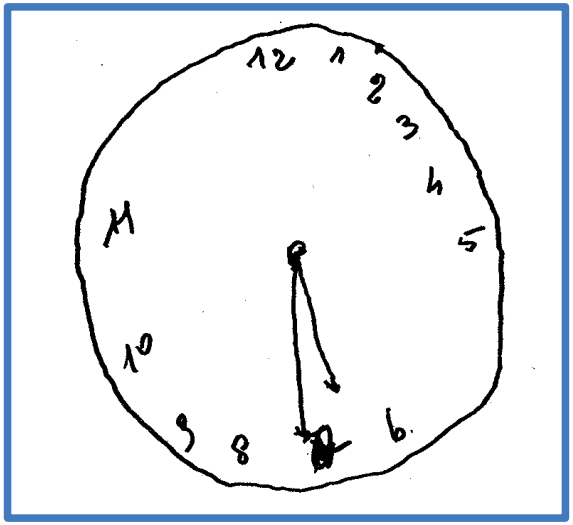


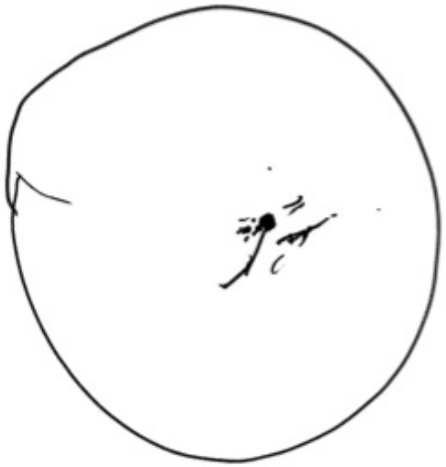
TMTB

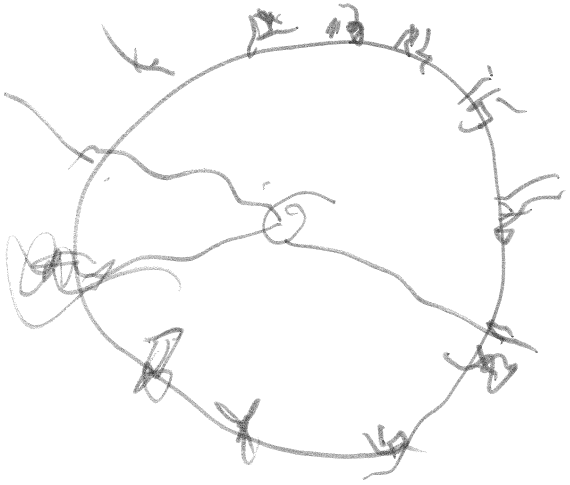




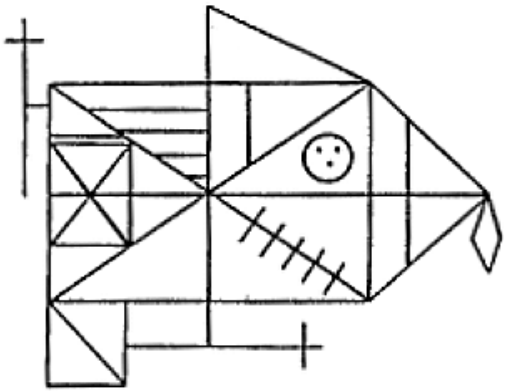
Clock drawing test





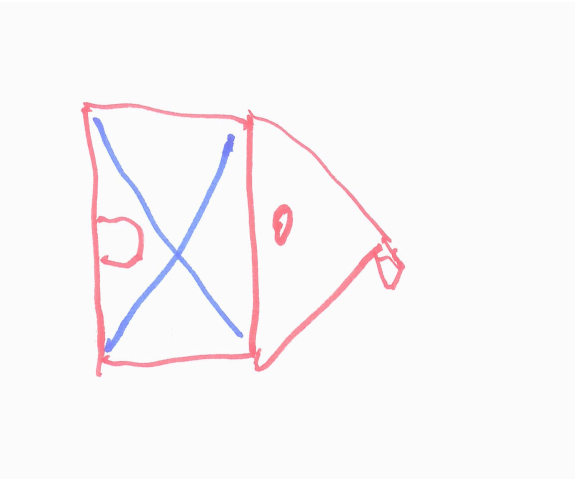


Rey Figure immediate and delayed copy



Direct copy

Delayed copy



Case C.D.

- Men
- Age: 49 years
- Edu: 13 years
- Left/righ handed
- Family history: negative for neurological disease
- Personal history: unremarkeble
- Concomitant pathologies: none
- Disease onset: 2004 (Sx)

Neuropsychological assessments

2009

- Executive deficits
- Attention deficits
- Working memory deficits
- Visuo-perceptive deficits
- Language normal
- Temporo-spatial oriented

2010

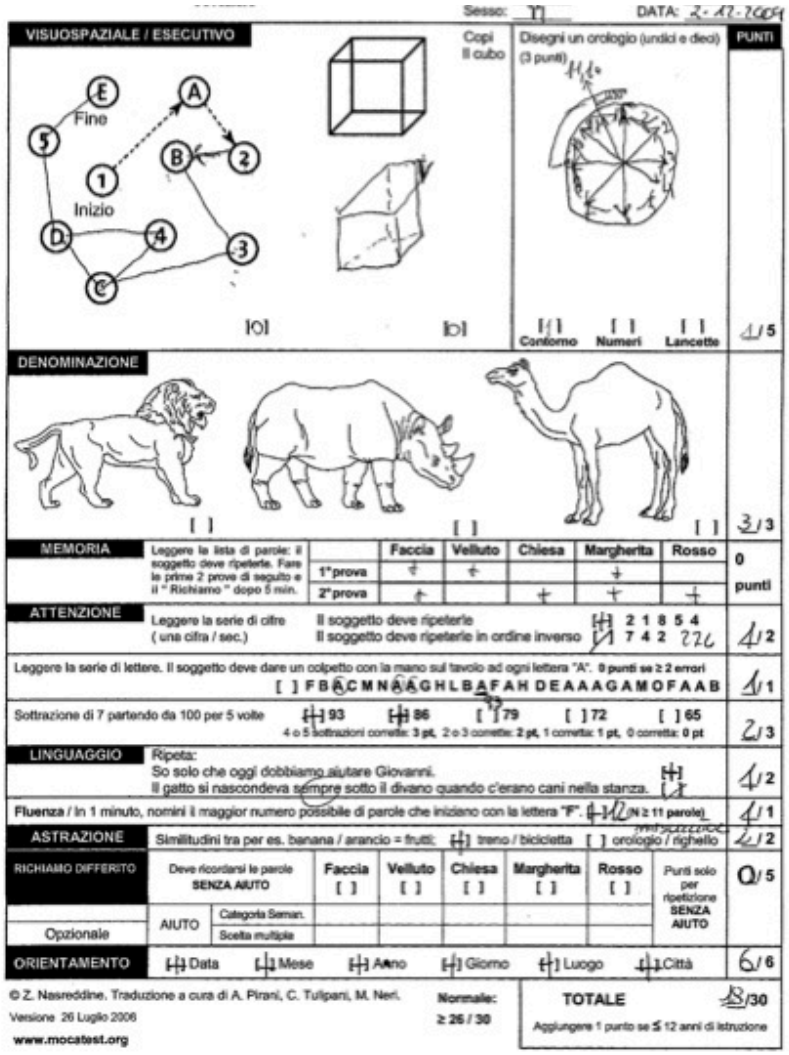
- Temporal disoriented
- Physical and Verbal disinhibition
- Executive deficits + perseveration
- Marked Attention deficits
- Working memory deficits
- Visuo-perceptive deficits
- Amnesic deficits
- ICD (Hypersexuality)
- Depressed (BDI 18)

2011

- Previuos cognition abilities marketly worsened
- Language deficits (anomia)
- Apraxia with closing-in

Neuropsychological assessments

2009 MOCA 18


Sesso: M DATA: 2-12-2009

VISUOSPAZIALE / ESECUTIVO — Copi il cubo — Disegni un orologio (undici e dieci) (3 punti) — PUNTI

Fine / Inizio

Contorno Numeri Lancette — 4/5

DENOMINAZIONE — 3/3

MEMORIA — Leggere la lista di parole: il soggetto deve ripeterle. Fare le prime 2 prove di seguito e il " Richiamo " dopo 5 min.

	Faccia	Velluto	Chiesa	Margherita	Rosso
1°prova					
2°prova					

0 punti

ATTENZIONE — Leggere la serie di cifre (una cifra / sec.) — Il soggetto deve ripeterle: 2 1 8 5 4 — Il soggetto deve ripeterle in ordine inverso: 7 4 2 — 4/2

Leggere la serie di lettere. Il soggetto deve dare un colpetto con la mano sul tavolo ad ogni lettera "A". 0 punti se ≥ 2 errori
[ ] F B A C M N A A G H L B A F A H D E A A A G A M O F A A B — 1/1

Sottrazione di 7 partendo da 100 per 5 volte: 93 — 86 — [ ] 79 — [ ] 72 — [ ] 65
4 o 5 sottrazioni corrette: 3 pt, 2 o 3 corrette: 2 pt, 1 corretta: 1 pt, 0 corretta: 0 pt — 2/3

LINGUAGGIO — Ripeta:
So solo che oggi dobbiamo aiutare Giovanni.
Il gatto si nascondeva sempre sotto il divano quando c'erano cani nella stanza. — 1/2

Fluenza / In 1 minuto, nomini il maggior numero possibile di parole che iniziano con la lettera "F". (N ≥ 11 parole) — 1/1

ASTRAZIONE — Similitudini tra per es. banana / arancio = frutti: treno / bicicletta — [ ] orologio / righello — 2/2

RICHIAMO DIFFERITO — Deve ricordarsi le parole SENZA AIUTO

	Faccia [ ]	Velluto [ ]	Chiesa [ ]	Margherita [ ]	Rosso [ ]	Punti solo per ripetizione SENZA AIUTO
Opzionale — AIUTO: Categoria Seman.						
Opzionale — AIUTO: Scelta multipla						

0/5

ORIENTAMENTO — Data — Mese — Anno — Giorno — Luogo — Città — 6/6

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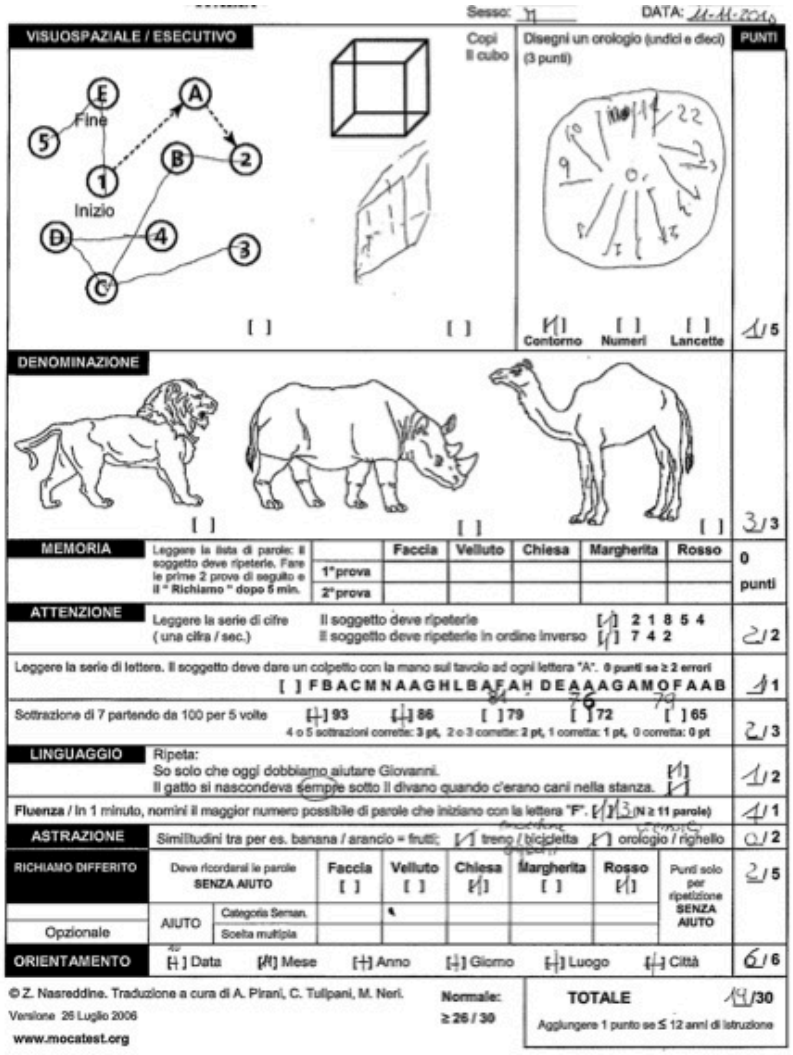
Versione 26 Luglio 2006
www.mocatest.org

Normale: ≥ 26 / 30

TOTALE 18/30
Aggiungere 1 punto se ≤ 12 anni di istruzione

2010 MOCA 19


Sesso: M DATA: 11-11-2010

VISUOSPAZIALE / ESECUTIVO — Copi il cubo — Disegni un orologio (undici e dieci) (3 punti) — PUNTI

Fine / Inizio

Contorno Numeri Lancette — 4/5

DENOMINAZIONE — 3/3

MEMORIA — Leggere la lista di parole: il soggetto deve ripeterle. Fare le prime 2 prove di seguito e il " Richiamo " dopo 5 min.

	Faccia	Velluto	Chiesa	Margherita	Rosso
1°prova					
2°prova					

0 punti

ATTENZIONE — Leggere la serie di cifre (una cifra / sec.) — Il soggetto deve ripeterle: 2 1 8 5 4 — Il soggetto deve ripeterle in ordine inverso: 7 4 2 — 2/2

Leggere la serie di lettere. Il soggetto deve dare un colpetto con la mano sul tavolo ad ogni lettera "A". 0 punti se ≥ 2 errori
[ ] F B A C M N A A G H L B A F A H D E A A A G A M O F A A B — 1/1

Sottrazione di 7 partendo da 100 per 5 volte: 93 — 86 — [ ] 79 — [ ] 72 — [ ] 65
4 o 5 sottrazioni corrette: 3 pt, 2 o 3 corrette: 2 pt, 1 corretta: 1 pt, 0 corretta: 0 pt — 2/3

LINGUAGGIO — Ripeta:
So solo che oggi dobbiamo aiutare Giovanni.
Il gatto si nascondeva sempre sotto il divano quando c'erano cani nella stanza. — 1/2

Fluenza / In 1 minuto, nomini il maggior numero possibile di parole che iniziano con la lettera "F". (N ≥ 11 parole) — 1/1

ASTRAZIONE — Similitudini tra per es. banana / arancio = frutti: treno / bicicletta — orologio / righello — 2/2

RICHIAMO DIFFERITO — Deve ricordarsi le parole SENZA AIUTO

	Faccia [ ]	Velluto [ ]	Chiesa [ ]	Margherita [ ]	Rosso [ ]	Punti solo per ripetizione SENZA AIUTO
Opzionale — AIUTO: Categoria Seman.						
Opzionale — AIUTO: Scelta multipla						

2/5

ORIENTAMENTO — Data — Mese — Anno — Giorno — Luogo — Città — 6/6

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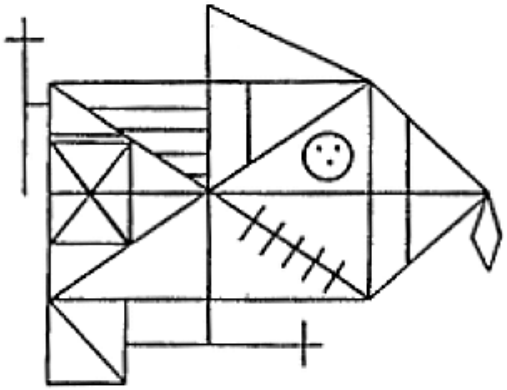
Versione 26 Luglio 2006
www.mocatest.org

Normale: ≥ 26 / 30

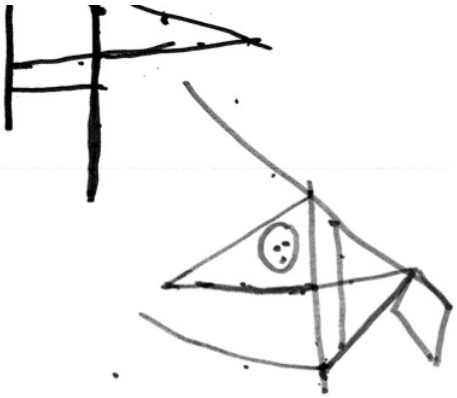
TOTALE 19/30
Aggiungere 1 punto se ≤ 12 anni di istruzione

Visuo-spatial skills impaired

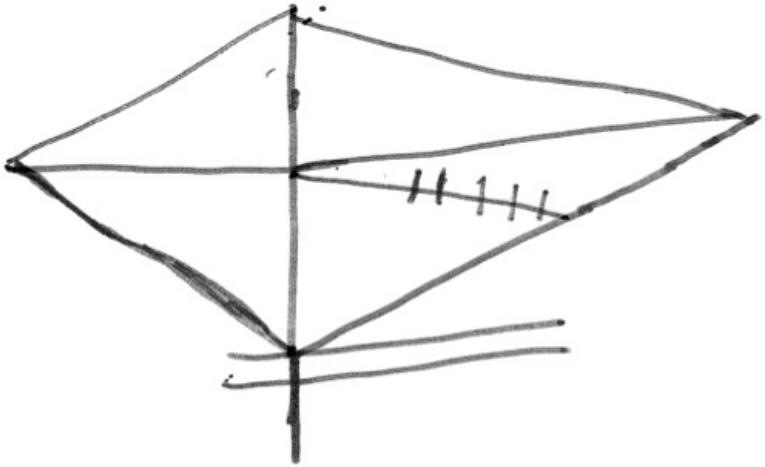
REY' S FIGURE



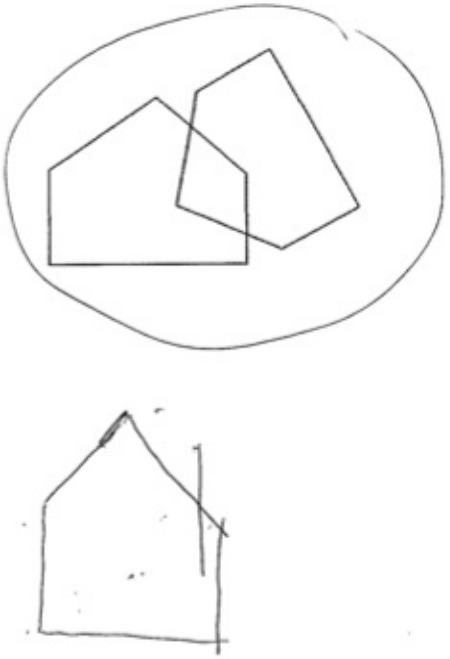
IMMEDIATE COPY



DELAYED RECALL



2010

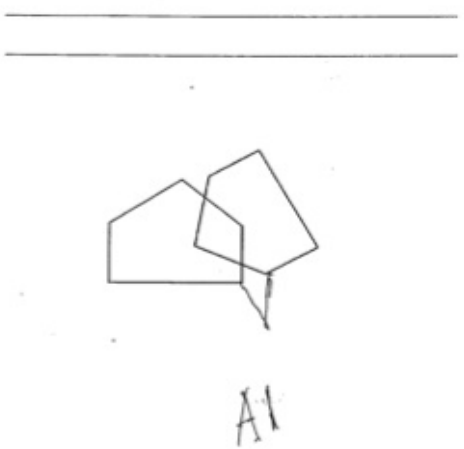


MMSE 20.2

2011

MMSE 8.2

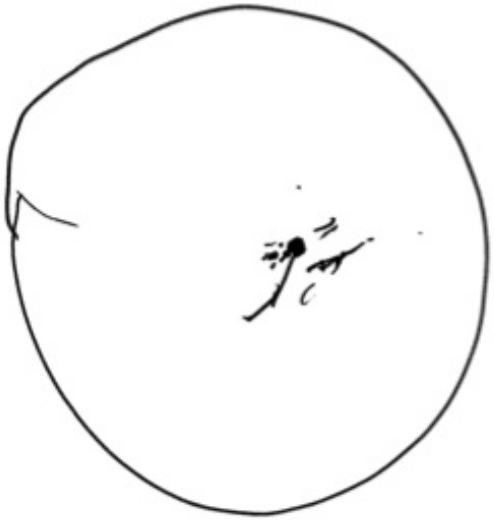
2012



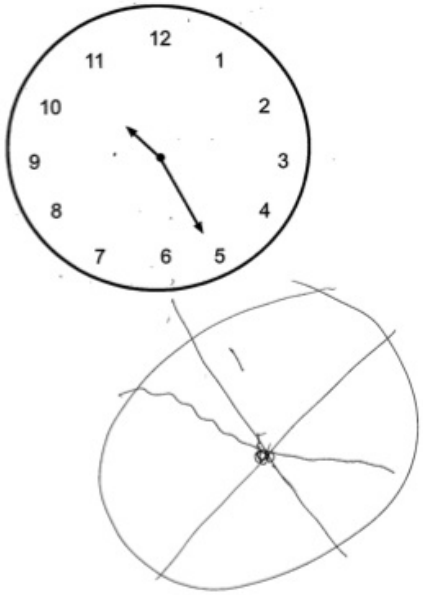
MMSE 6.2

2010

2011



2012



FLUENZE SEMANTICHE

2010

Istruzioni: "Ora le chiederò di dirmi tutti i nomi di (...marche d'auto) che le vengono in mente.
Ha un minuto di tempo.

MARCHE D'AUTO	FRUTTI	ANIMALI
FIAT 1	AVOCADO 1	LEONE 1
LANCIA 2	UVA 2	TIGRE 2
MASERATI 3	MANGO 3	ELEFANTE 3
FERRARI 4	PESCHE 4	DELFINO 4
PEUGEOT 5	MELE 5	GHEPARDO 5
CRYSLER 6	NOCI 6	ORATA 6
DODGE 7	MANDARINO 7	SOGLIOLA 7
PORSCHE 8	ARANCIO 8	SEPPIA 8
OPEL 9		CANE 9
		GATTO 10
Tot.: 9	Tot.: 8	Tot.: 10

Punteggio grezzo:	27
Punteggio corretto:	24
Punteggio equivalente:	0

2011

... che cominciano con la lettera "F".

F	L	P
F	leone 1	PALERMO
[illegible]		PULIRE 1
		PAPAVERO 2
		PESCARE 3
		(PUMO?)
		PRODIGARSI 4
		PICCO 5
Tot.: 0	Tot.: 1	Tot.: 5

Punteggio grezzo:	6
Punteggio corretto:	2
Punteggio equivalente:	0

Osservazioni:

2012

FLUENZA SU CATEGORIA SEMANTICA

Data: Cognome: Nome:

Istruzioni: "Ora le chiederò di dirmi tutti i nomi di (...marche d'auto) che le vengono in mente.
Ha un minuto di tempo.

MARCHE D'AUTO	FRUTTI	ANIMALI
[illegible]	[illegible]	leone
[illegible]	uva	[illegible]
[illegible]	[illegible]	
Tot.:	Tot.:	Tot.:

Punteggio grezzo:	
Punteggio corretto:	
Punteggio equivalente:	

Osservazioni:

Take home messagges

- **Testing Conditions**

✓ ON therapy (verify at the beginning and at the end of testing)

✓ Well rested

- **Assess mood and anxiety**
- **Rule out other medical conditions that may affect cognition:**

✓ Active infection, thyroid, hepatic or renal disorders

Take home messagges

- Ask about cognitive concerns and functions related to cognition (patient + collateral historian)
- Use a global test to screen for cognitive impairment
- If diagnosis is uncertain, refer for neuropsychological testing
- Repeat cognitive assessment every 12-18 months for PD-MCI.

Conclusion

- Cognitive impairment is an important part of PD, can be present early in the course of the disease and frequently leads to dementia.
- Fronto-striatal alterations are characteristic of PD physiopathology
- PD-MCI is an heterogeneous condition with attentive/ executive tasks most frequently altered.
- Identifications of PD-MCI is important to develop therapeutic strategies that may slow down cognitive decline.