Parkinson & Parkinsonismi

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2003. MR, maschio 1931, destrimane

Scolarità: 8 anni

Professione: pasticcere poi assistente edile

Caregiver: vive con la moglie

Sintomo d'esordio: ansia da 3 anni

Familiarità per demenza: negativa

Fumo: no

Alcool: adeguato

Terapia: Norvasc ½ cp; Teraprost ½ cp; Elopram 10 gtt;Lexotan 10 gtt.

Motivo della visita ambulatoriale

Deposto deficit cognitivo caratterizzato da anomie e disturbo di memoria fluttuante, presente da circa un anno, senza impatto sulla funzione quotidiana.

Sintomatologia ansioso depressiva.

Tre episodi di caduta a terra (in bicicletta e mentre stava camminando).

Anamnesi patologica remota

Intervento chirurgico di riduzione ernia inguinale.

Pseudoafachia chirurgica OS.

Calcolosi della colecisti.

Ipertrofia prostatica benigna in trattamento.

Ipertensione arteriosa sistemica in trattamento farmacologico (recentemente sospeso per riscontro di bassi valori pressori).

Sintomatologia ansioso depressiva.

Valutazione Multidimensionale

MMSE	27/30
Test orologio	9/10
ADAS Cog	12,6/70
CDR	0,5/5
IADL	1/6 funzioni perse
BADL	0/6 funzioni perse
Barthel index	100/100
Tinetti scale	e.13/16; a.8/12
UPDRS III	12/56
Hachinski	3/19

Valutazione Psicocomportamentale

GDS	10/15
Hamilton ansia	16/48
NPI	35/144
Deliri	3
Allucinazioni	0
Agitazione	2
Depressione	6
Ansia	6
Euforia	0
Apatia	6
Disinibizione	0
Irritabilità	6
Affaccendamento	4
Insonnia	2

Ricovero in Day Hospital

E.O.N.

Stato Mentale	Vigile, psiche lucida, sensorio indenne, collaborante, orientato nel tempo e nello spazio; lievemente rallentata la comprensione verbale; l'espressione verbale è rallentata e poco fluente per alterato reperimento di vocaboli e difficoltà di mantenere l'attenzione. Facies sofferente.
Nervi Cranici	Nella norma; MOE nella norma; pupille isocoriche, normoreagenti allo stimolo luminoso ed all'accomodazione consensuale; riduzione dello sguardo verso l'alto, ipoacusia; non diplopia, non nistagmo. Lingua normoprotrusa. Ipoacusia bilaterale
Motilità e Tono Muscolare	Non deficit stenico in Mingazzini ed alle prove segmentarie AS e AI bilateralmente; motilità fine conservata; sequenze motorie e movimenti alternati indenni; tono muscolare nella norma, trofismo nella norma. Tremore fine attitudinale alle mani bilateralmente
Sensibilità	Nella norma la sensibilità superficiale AI bilateralmente.
Andatura e Postura	Deambulazione possibile senza appoggio;atteggiamento camptocormico e riduzione dei movimenti pendolari, possibile su punte e talloni, saltello limitato; Romerg negativo. Buono il controllo dei riflessi posturali.
Funzione Cerebellare	Prova indice-naso: nella norma ad occhi aperti e chiusi. Prova degli indici indenne. Adiadococinesia assente.
Riflessi Osteo-Tendinei	Riflessi normoevocabili agli arti superiori e vivaci agli arti inferiori; non Hoffmann, non Babinski.
Riflessi Primitivi	Glabellare esauribile, palmo-mentoniero presente a destra, muso presente; prensione assente.

Sintesi: sindrome extrapiramidale con segni di liberazione frontale

RM encefalo

In sede sovraterntoriale vi è una sfumata iperintensità nelle sequenze T2 e FLAIR nella sostanza bianca adiacente ai corni frontali riferibile ad ipoafflusso vascolare cronico. Minuta lesione ischemica cronica iperintensa in T2 e FLAIR nella sostanza bianca sottocorticale fronto-opercolare sinistra.

Diffusa atrofia cortico sottocorticale più evidente a livello dei lobi temporali e frontali bilateralmente e consensuale dilatazione del sistema ventricolare.

Altri accertamenti diagnostici

SPET cerebrale di flusso: nella norma

EEG: modesto globale rallentamento della attività elettrica cerebrale, con alterazioni elettriche di tipo lento bilaterali.

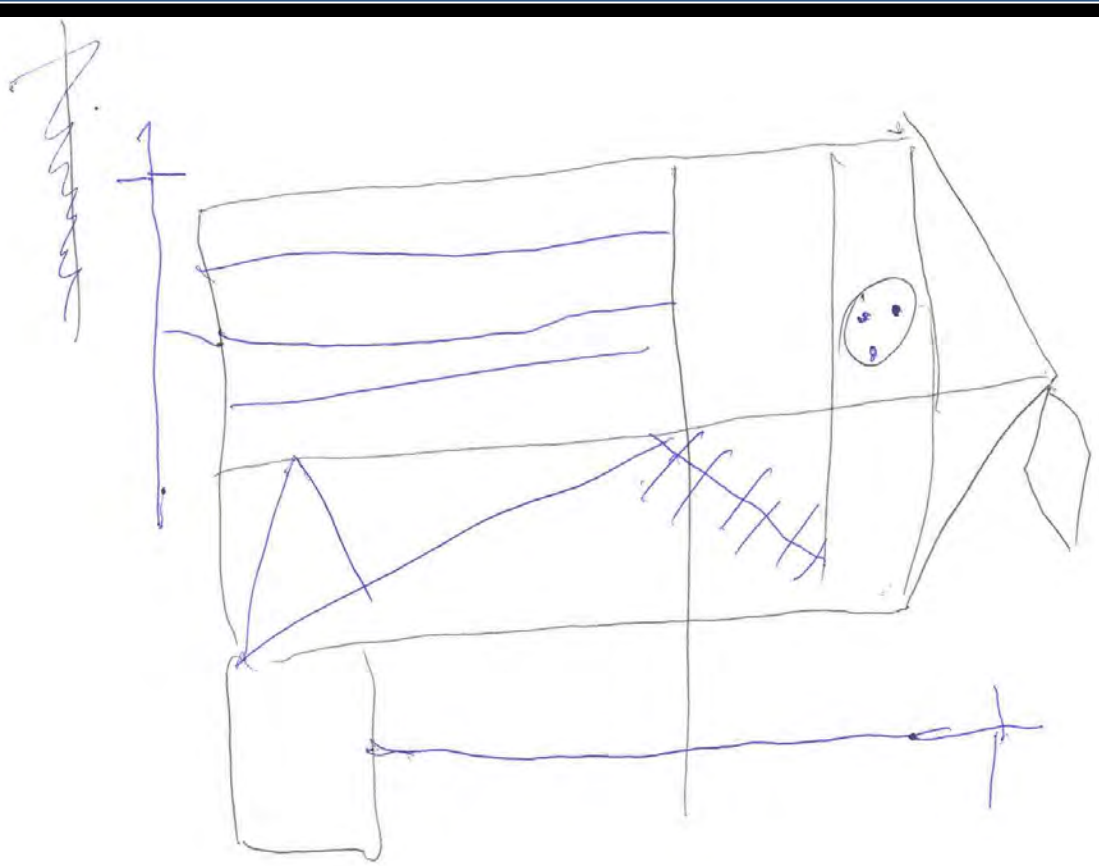
ECO TSA: nella norma

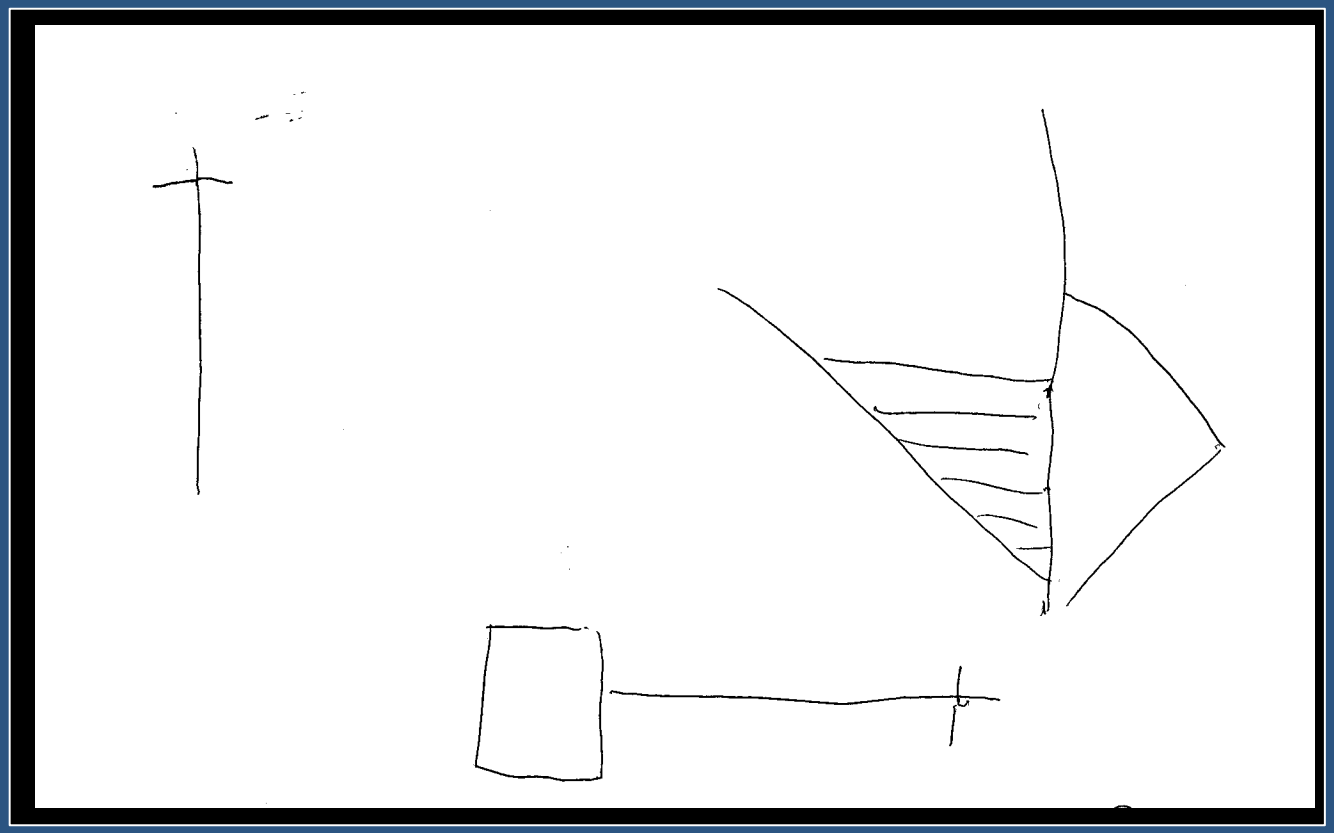
ABPM: normali i valori di pressione arteriosa sisto-diastolica con la terapia in atto.

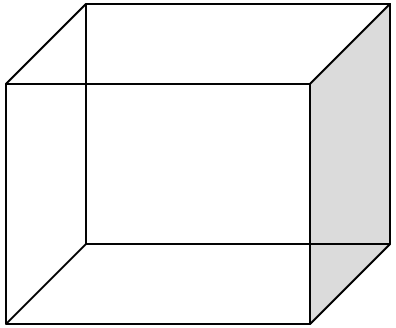
Tilt-table test: test positivo per modificazioni emodinamiche, non sintomi con risposta vaso depressiva vaso vagale

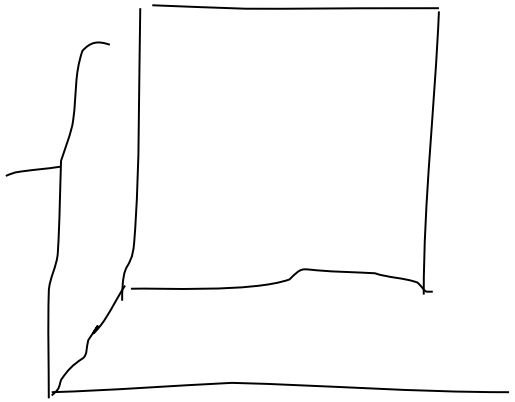
Valutazione Neuropsicologica 2003

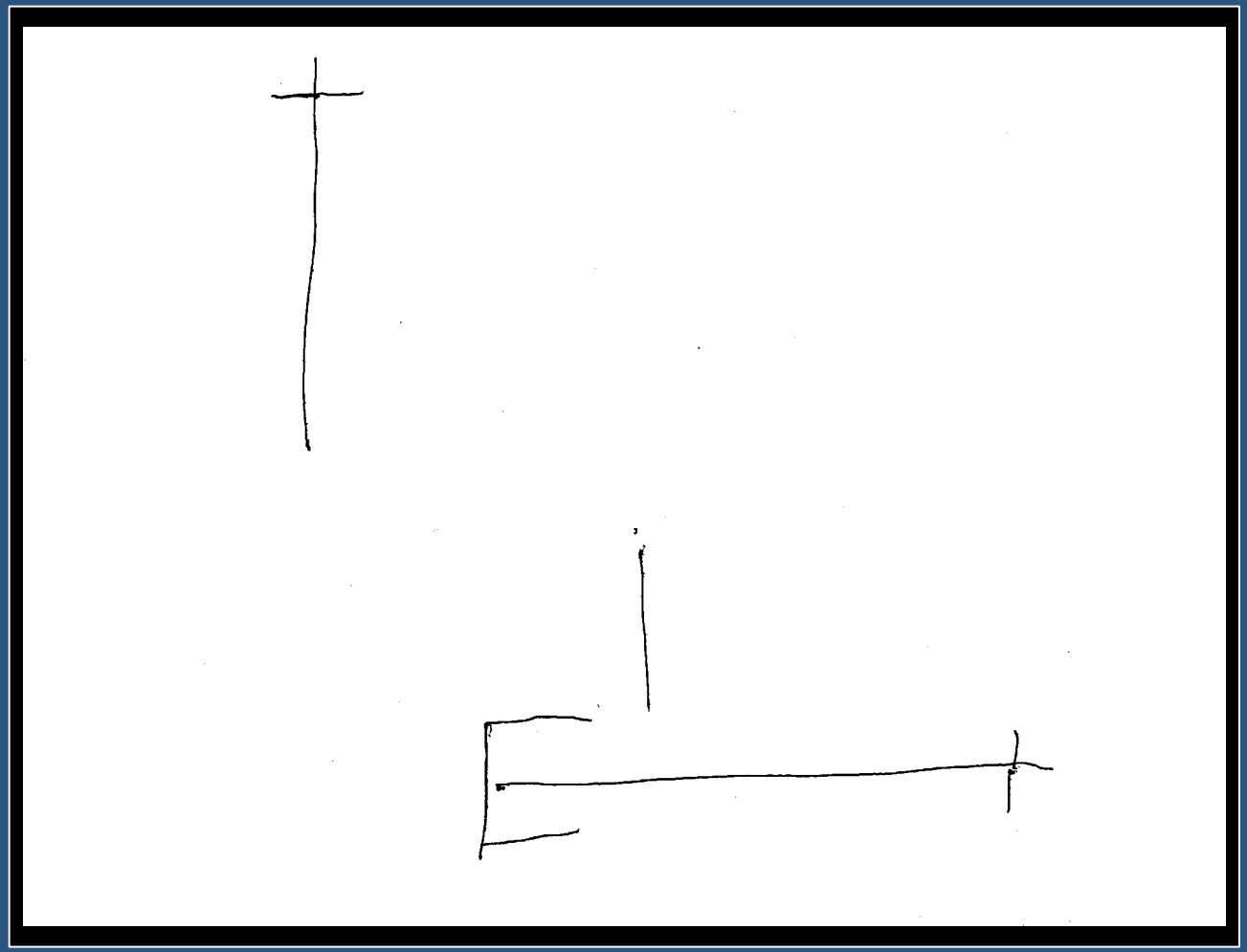
Memoria verbale e non verbale	
Apprendimento lista di parole	normale
Raccontino	normale
Figura di Rey recall	patologico
Abilità visuo-spaziali	
Matrici colorate di Raven	normale
Pianificazione spaziale e attenzione	
Trail Making A	normale
Trail Making B	normale
Linguaggio	
Fluenza per lettera	normale
Fluenza per categoria	normale
Funzioni esecutive-visuo costruttive	
Clock-test	normale
Figura di Rey copia	patologico











Petersen et al. Arch Neurol, 1999

(i) presence of a subjective memory complaint;

(ii) preserved general intellectual functioning (as estimated in this study by performance on a vocabulary test);

(iii) demonstration of a memory impairment by cognitive testing;

(iv) intact ability to perform activities of daily living;

(v) absence of dementia.

Revised Criteria for Mild Cognitive Impairment: Validation within a Longitudinal Population Study

Artero, Petersen, Touchon, Ritchie

Dement Geriatr Cogn Disord 2006;22:465–470

(i) presence of a cognitive complaint from either the subject and/or a family member;

(ii) absence of dementia;

(iii) change from normal functioning;

(iv) decline in any area of cognitive functioning;

(v) preserved overall general functioning but possibly with increasing difficulty in the performance of activities of daily living.

Dimissione

Decadimento cognitivo lieve in paziente con sintomatologia extrapiramidale, disautonomia ed encefalopatia vascolare

Ipertensione arteriosa sistemica

Ipertrofia prostatica

Disturbo d'adattamento con umore depresso

Terapia alla dimissione

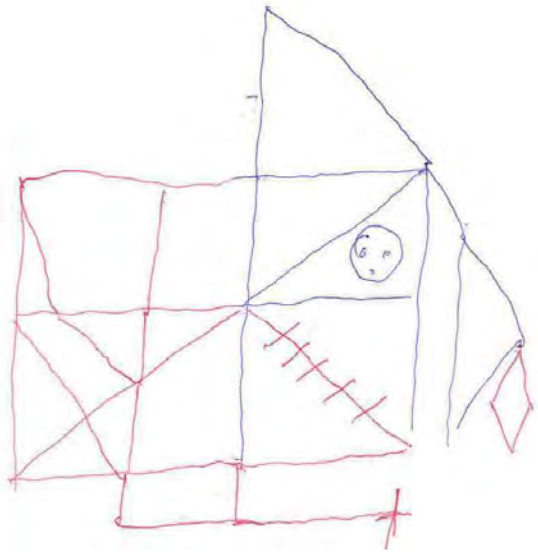
Sinemet cr 25/100	1cp x 3 die
Motilium	10 ml x 3 die
Norvasc	½ cp
Teraprost	½ cp
Elopram	10 gtt
Lexotan	10 gtt

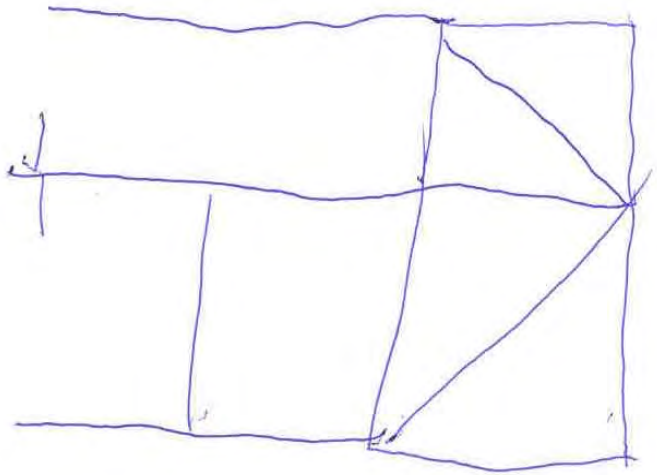
Valutazione Multidimensionale 2004

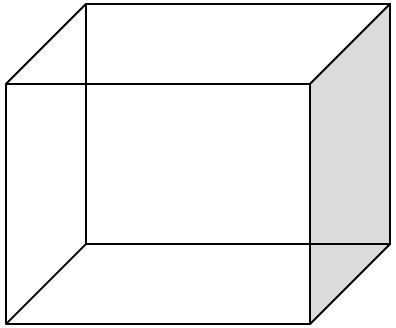
MMSE	27/30	26/30
Test orologio	9/10	9/10
ADAS Cog	12,6/70	7/70
CDR	0,5/5	0,5/5
IADL	1/6 funzioni perse	1/6
BADL	0/6 funzioni perse	0/6
Barthel index	100/100	100/100
Tinetti scale	21/28	20/28
UPDRS III	12/56	18/56
Hachinski	3/19	

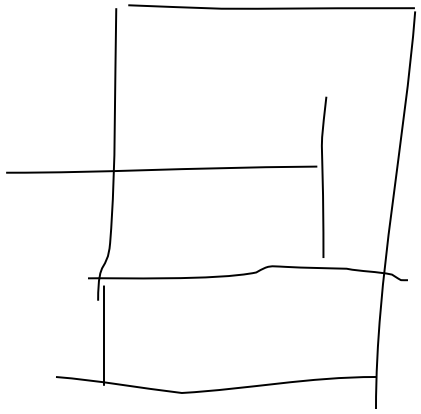
Valutazione Neuropsicologica 2004

Memoria verbale e non verbale		
Apprendimento lista di parole	normale	normale
Raccontino	normale	normale
Figura di Rey recall	patologico	ai limiti
Funzioni superiori		
Matrici colorate di Raven	normale	normale
Pianificazione spaziale e attenzione		
Trail Making A	normale	patologico
Trail Making B	normale	patologico
Linguaggio		
Fluenza per lettera	normale	patologico
Fluenza per categoria	normale	normale
Funzioni esecutive-visuo costruttive		
Clock-test	normale	normale
Figura di Rey copia	patologico	patologico









Valutazione Psicocomportamentale

GDS	10/15	12/15
Hamilton ansia	16/48	14/48
NPI	35/144	18/144
Deliri	3	0
Allucinazioni	0	0
Agitazione	2	2
Depressione	6	4
Ansia	6	4
Euforia	0	0
Apatia	6	4
Disinibizione	0	0
Irritabilità	6	2
Affaccendamento	4	0
Insonnia	2	0

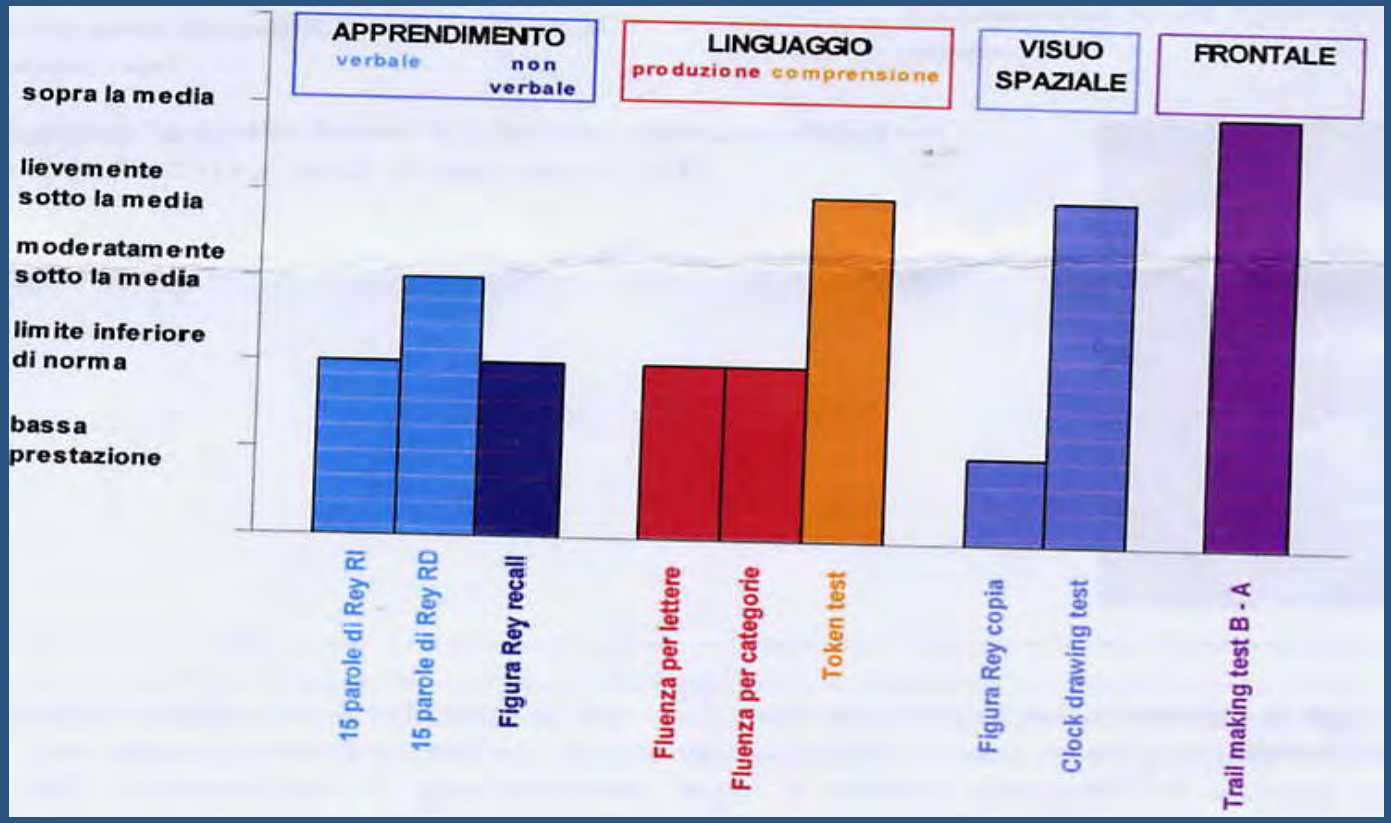
Ricovero presso “Ambulatorio per la depressione geriatrica”. 2005

Motivo della visita: relazione diagnostica

Il paziente è in carico presso l'ambulatorio della depressione geriatrica per sintomi ansiosi e depressivi (soprattutto apatia) esorditi circa 7 anni fa e peggiorati negli ultimi 2 anni, quando è comparso anche rallentamento nella deambulazione e piccoli passi, postura ricurva.

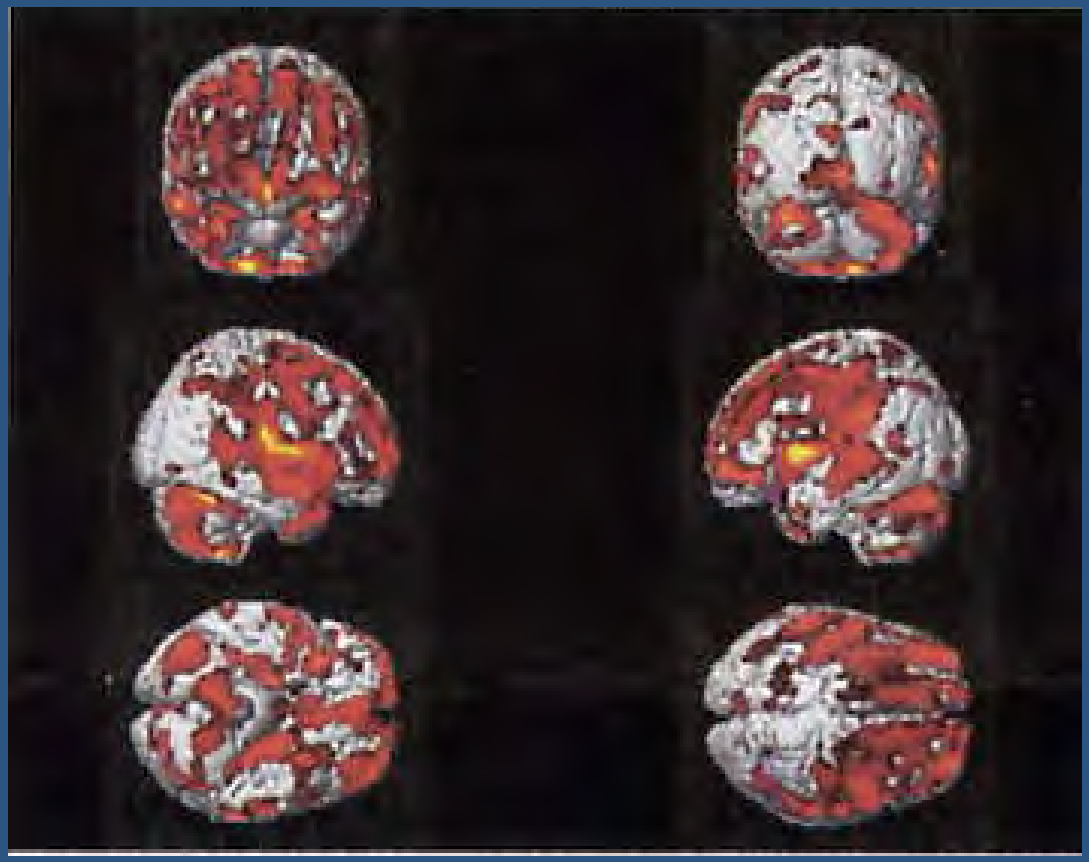
EON: ipertono plastico agli arti superiori, segno della glabella e muso positivi, lieve ipermetria e asinergia alla prova tallone ginocchio, ipotonia agli arti inferiori, deambulazione a piccoli passi strascicati, postura camptocormica, si gira su se stesso a passi discontinui con 3-4 passi. Ipotensione ortostatica. (170/100 in clino; 110/80 in orto immediato, 120/80 dopo 1 e 3 minuti.

Valutazione Neuropsicologica



Risonanza magnetica ad alta definizione

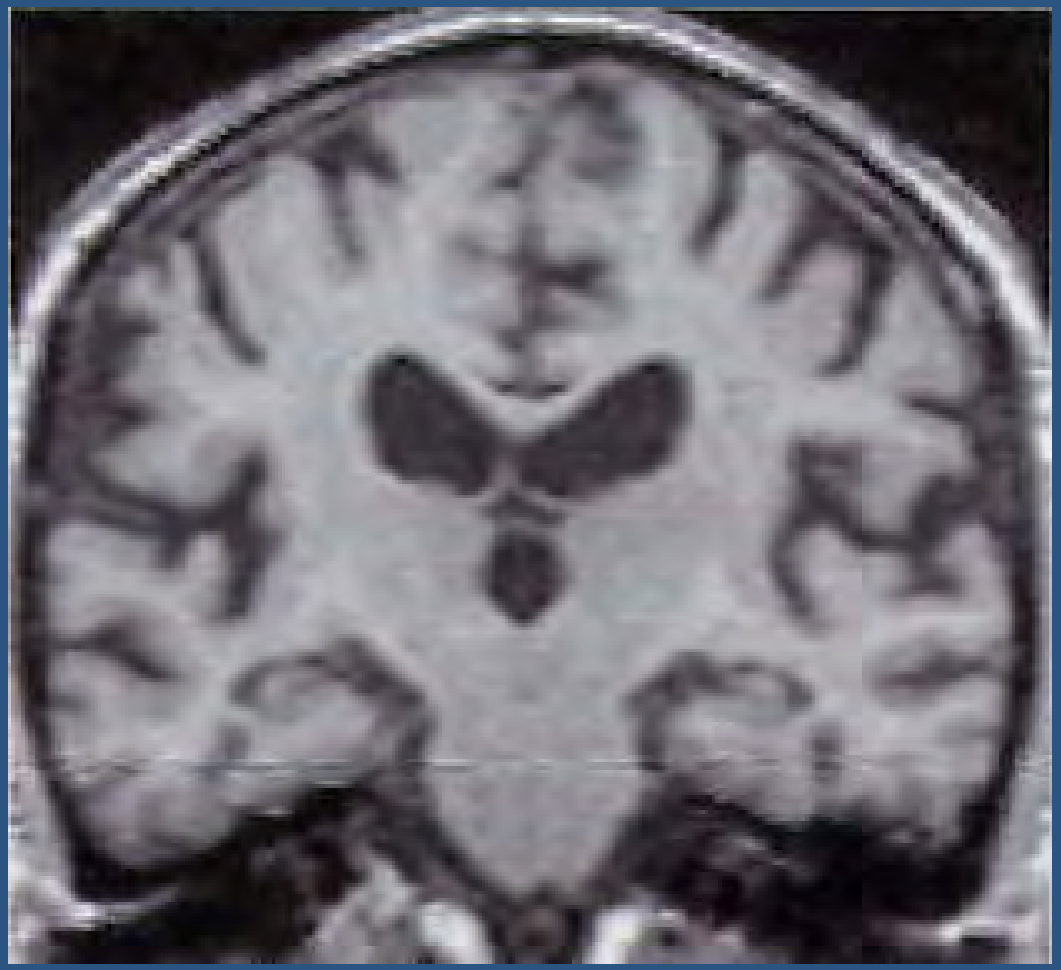
Atrofia corticale frontotemporale e parietale bilaterale, dx>sx, in assenza di danno vascolare sottocorticale.



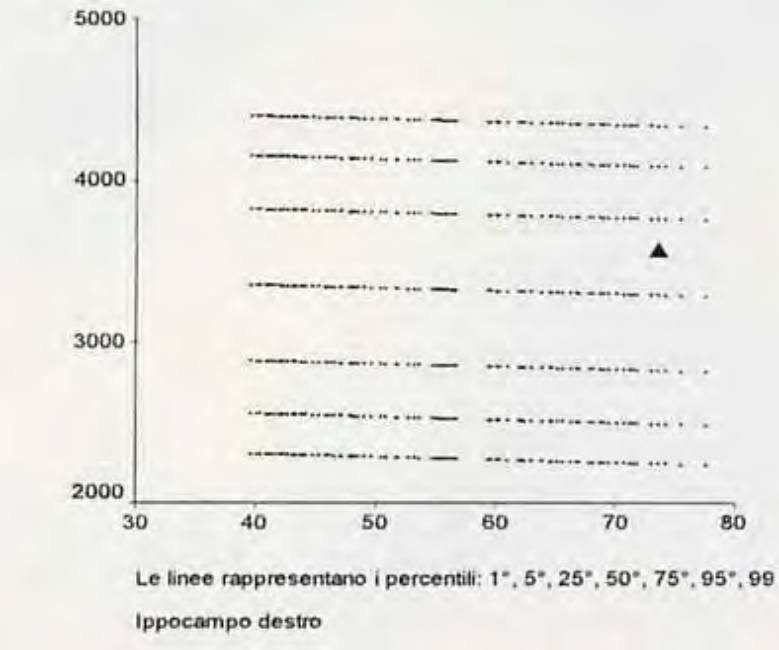
Risonanza magnetica ad alta definizione

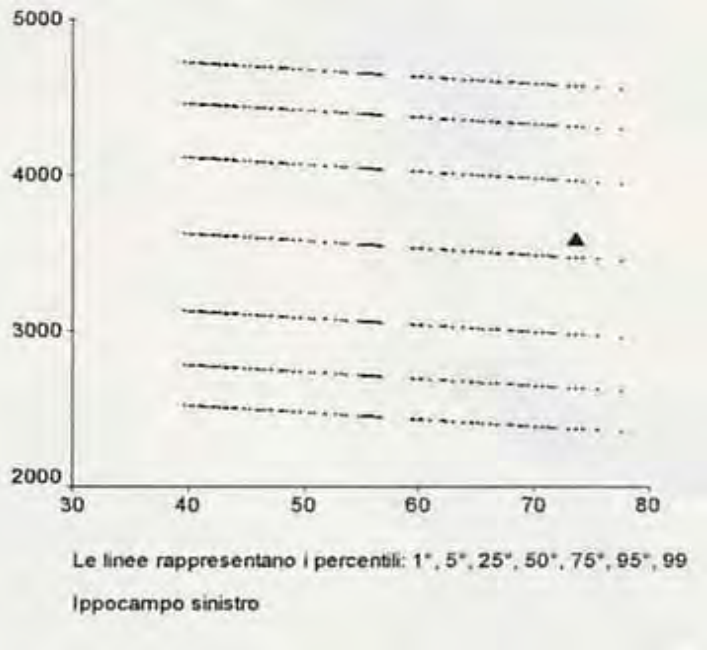
Atrofia ippocampale con scala qualitativa.

Lieve atrofia temporale mesiale:2/4 alla scala di valutazione visiva di Sceltens (v.n.0-1, patologici 2-4)



Atrofia ippocampale con volumetria:la volumetria dell'ippocampo (vol in cc normalizzato per volume intracranico in litri) è nella norma (25-50 percentile)

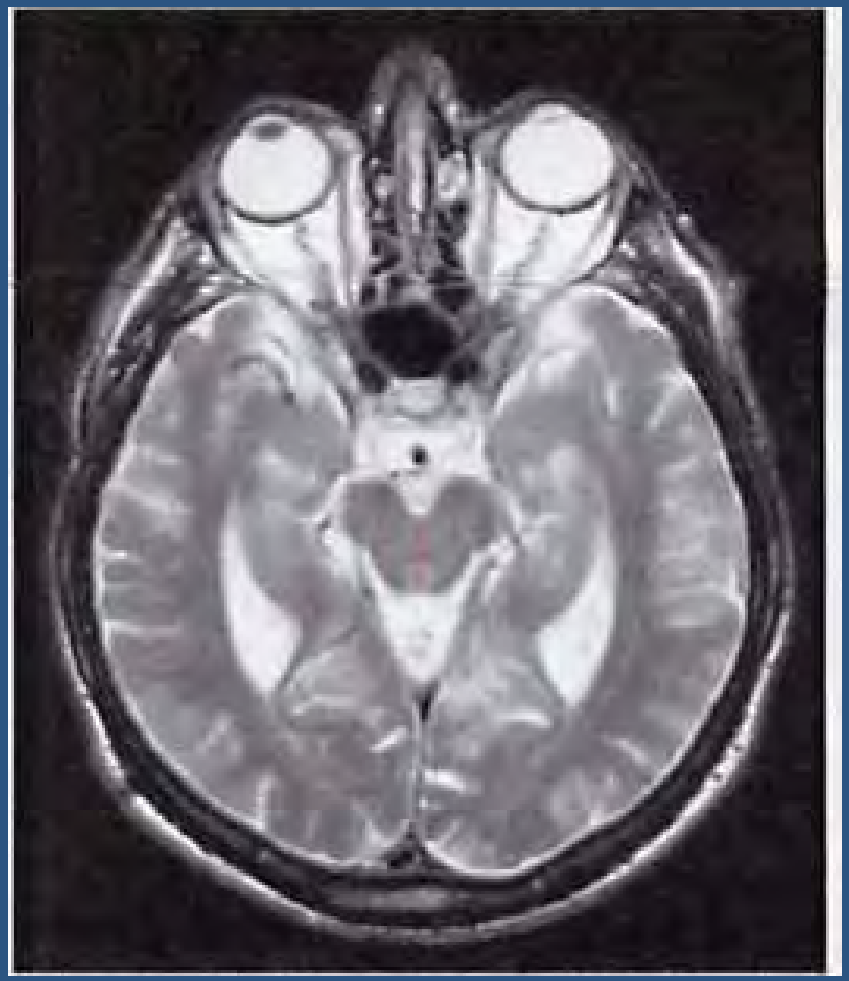




Risonanza magnetica ad alta definizione

Atrofia mesencefalica.

La misura lineare del diametro antero posteriore del mesencefalo è di 16,5mm (v.n. medi 18 mm; range 17-20).

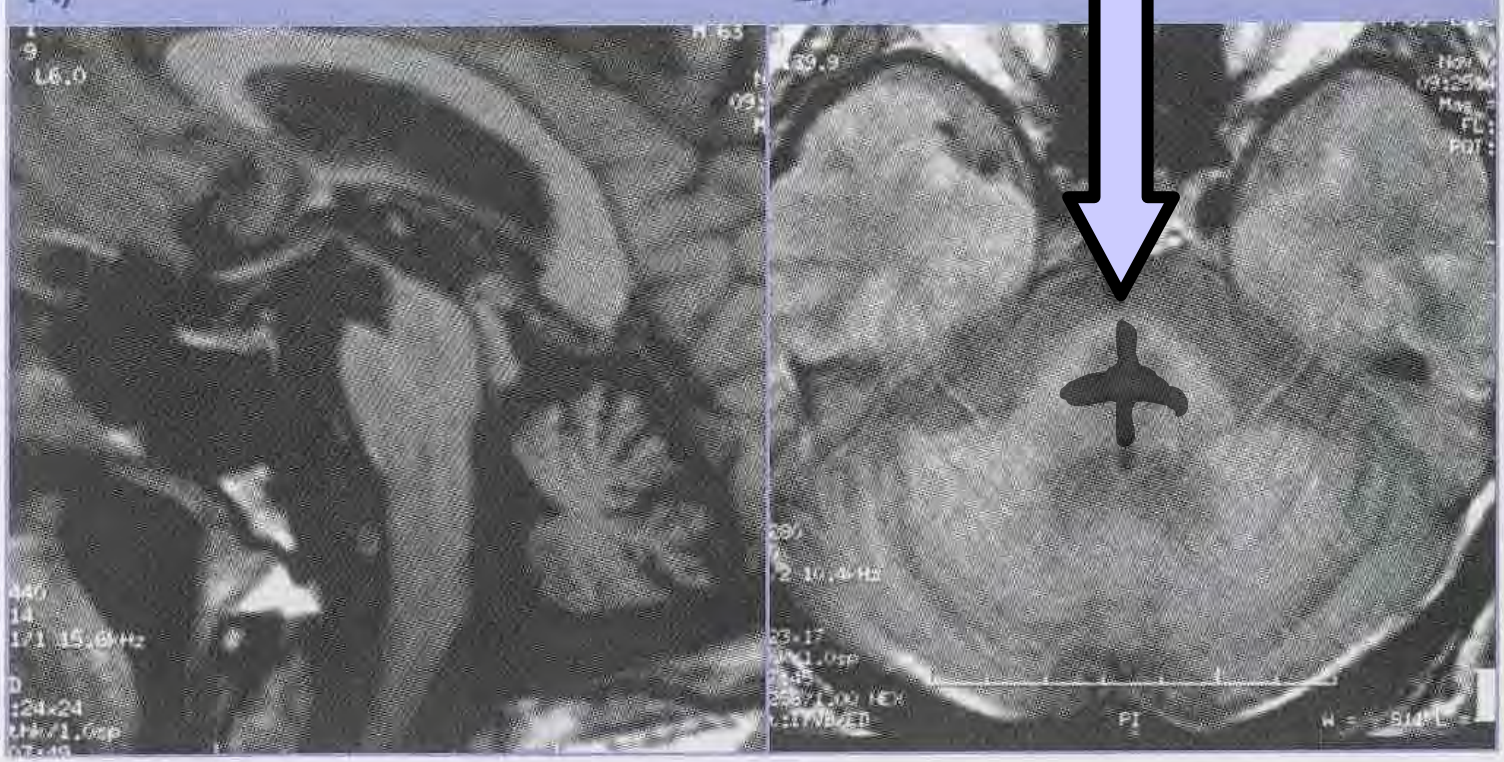


Diagnosi

Il quadro complessivo è indicativo di atrofia multisistemica di tipo cerebellare (MSA P). Si tratta di una malattia neurodegenerativa causata dall'accumulo di una proteina neurotossica (alfa sinucleina) e caratterizzata dalla combinazione di parkinsonismo, segni e sintomi autonomici variabili e segni cerebellari e piramidali. Il decorso è progressivo ed invalidante. Non vi è terapia specifica e il trattamento è sintomatico (la risposta del parkinsonismo alla L-dopa è generalmente incompleta e transitoria).

Figura 3. Sezione sagittale SE T… …ica posteriore che evidenzia atrofia … …an-golo bulbo pontino.
Sezione assiale DP pesata (b) ch… …no della croce di Savoiardo a sede p…
Il paziente affetto da MSA-C pre… …pi-co aspetto RM della atrofia… …A).
L'associazione di tali segni RM all… …nu-clei della base suggerisce la diagnosi di MSA-C.

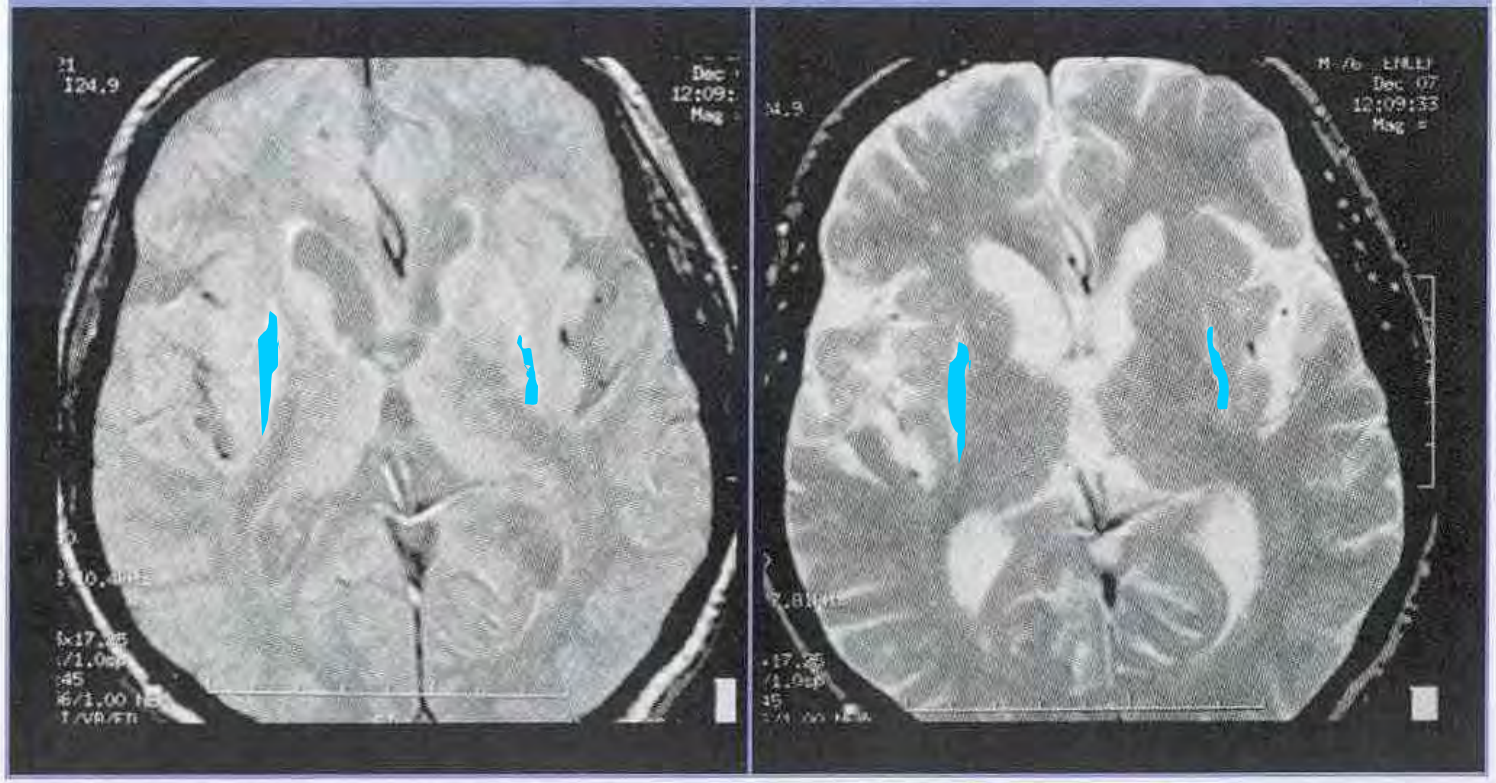
Degenerazione di fibre trasverse del ponte con risparmio dei fasci piramidali

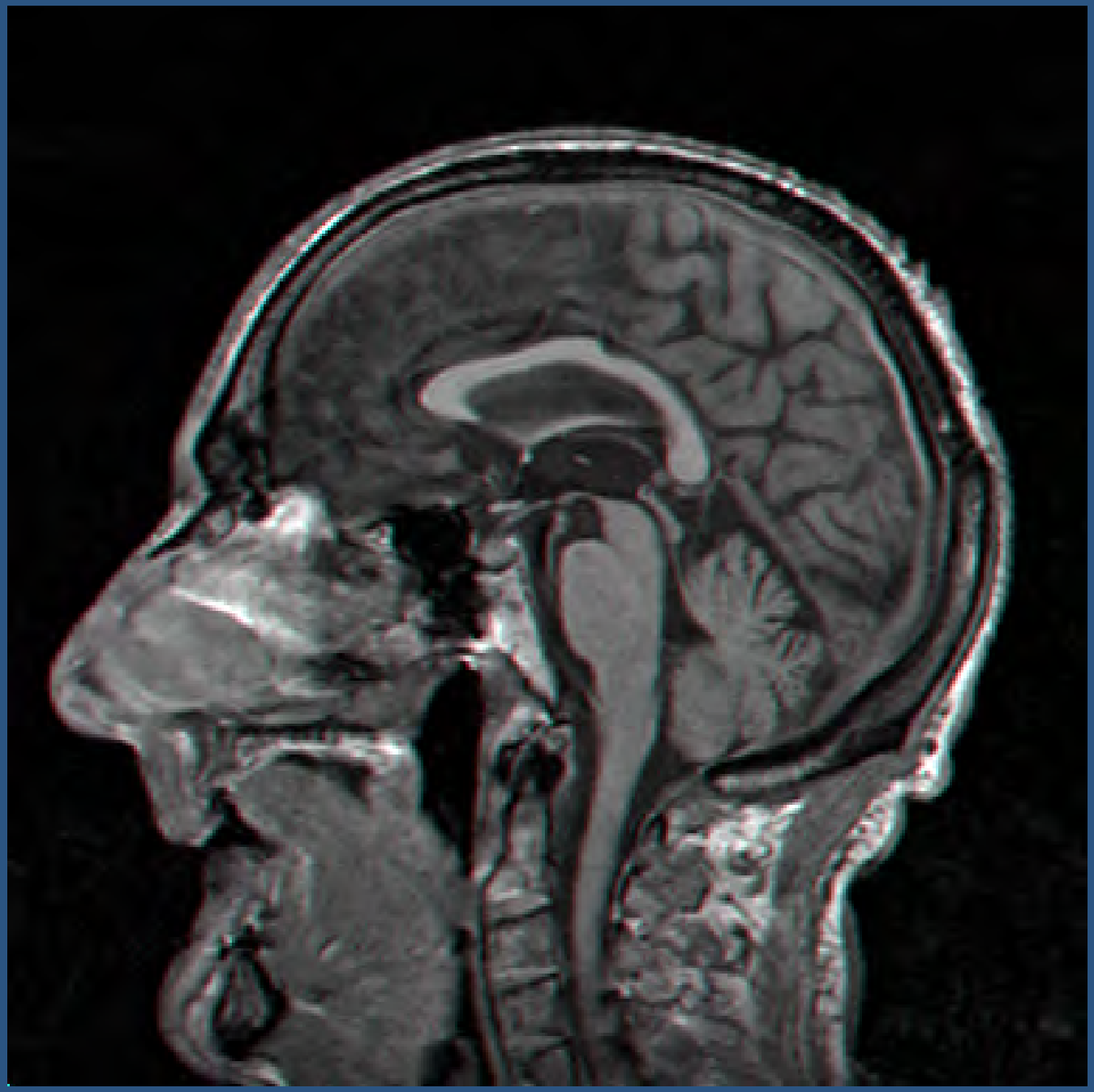


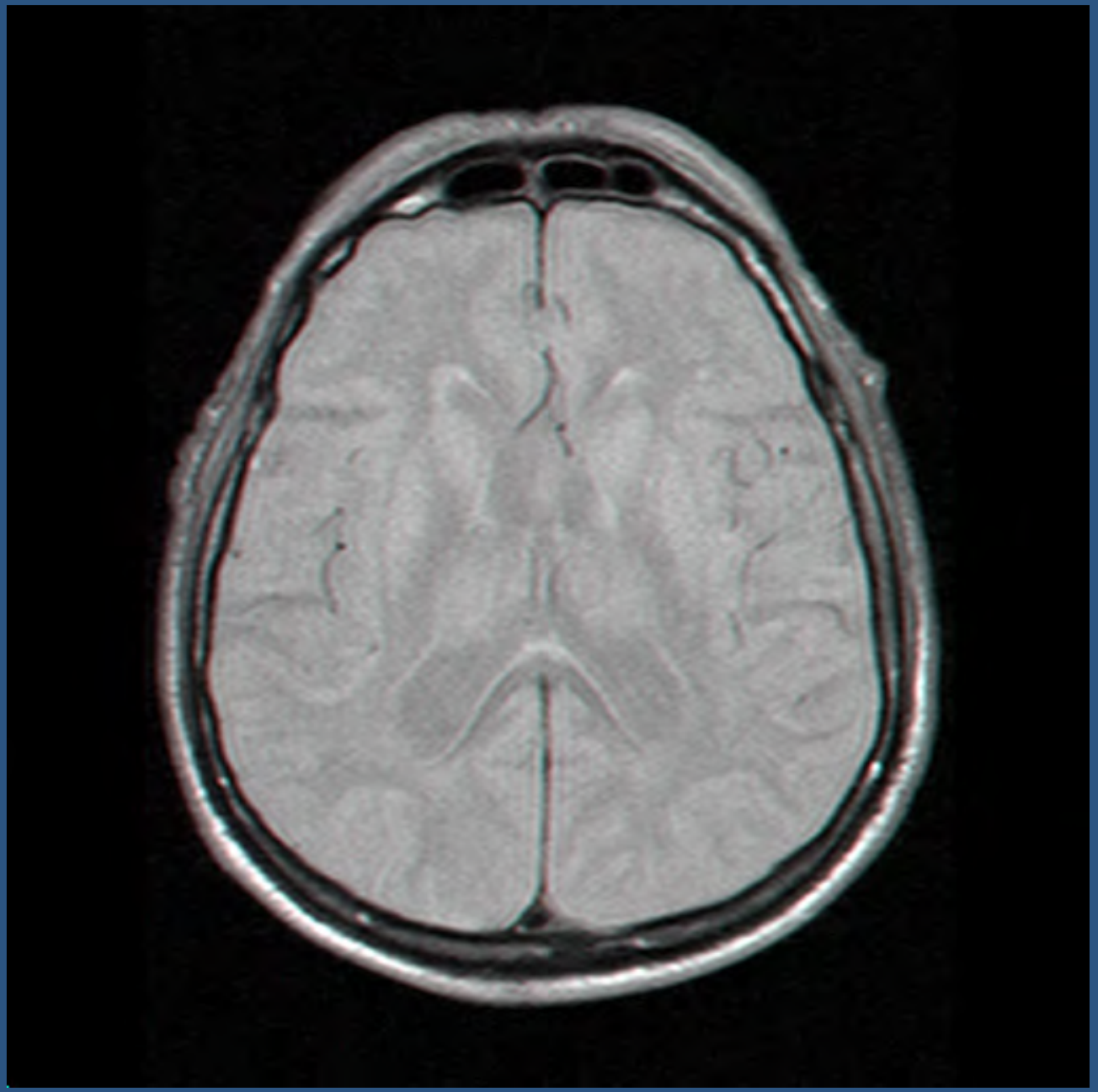
Fasi avanzate

Figura 2. Sezione assiale SE DP pesata (A) e T2 pesata (B) a livello dei nuclei della base eseguita con un apparecchio a media intensità di campo di un paziente affetto da MSA-P. Si noti l'iperintensità del bordo esterno del putamen bilateralmente associata a marcata atrofia dei putamen prevalente a destra. Tali reperti sono rispetto all'ipointensità putaminale ottenuta ad alto campo molto più specifici e con alto valore predittivo positivo nella diagnosi di MSA.

A) B)







2006, luglio

Stato Mentale	Vigile, psiche lucida, sensorio indenne, collaborante, parzialmente orientato nel tempo e nello spazio; MMSE 16/30
Nervi Cranici	Nella norma; MOE nella norma con riduzione di movimenti di verticalità; pupille isocoriche, normoreagenti allo stimolo luminoso ed all'accomodazione consensuale; riduzione dello sguardo verso l'alto, ipoacusia; non diplopia, non nistagmo. Lingua normoprotrusa. Ipoacusia bilaterale
Motilità e Tono Muscolare	Non deficit stenico in Mingazzini ed alle prove segmentarie AS e AI bilateralmente; lieve ipertono plastico agli arti superiori dx>sx; sequenze motorie e movimenti alternati rallentati; trofismo nella norma. Tremore fine attitudinale alle mani bilateralmente
Sensibilità	Nella norma la sensibilità superficiale AI bilateralmente.
Andatura e Postura	Deambulazione impossibile senza aiuto; stazione eretta: camptocormico il paziente potrebbe cadere se non sorretto dall'esaminatore.
Funzione Cerebellare	Prova indice-naso: dismetria ad occhi aperti e chiusi. Adiadococinesia presente.
Riflessi Osteo-Tendinei	Riflessi vivaci agli arti superiori e agli arti inferiori; non Hoffmann, Babinski a destra.
Riflessi Primitivi	Glabellare esauribile, palmo-mentoniero bilaterale, muso presente; prensione assente.

Sintesi: sindrome piramido- extrapiramidale con segni cerebellari e di liberazione frontale

Multiple System Atrophy
Definition

The concept of multiple system atrophy (MSA) as a unitary diagnosis encompassing several clinical syndromes has a long history.

In 1996 and 1998, the Consensus Committees representing the American Autonomic Society and the American Academy of Neurology defined MSA as a sporadic, progressive, neurodegenerative disease of undetermined etiology, characterized by extrapyramidal, pyramidal, cerebellar, and autonomic dysfunction in any combination.

Panel 1. Consensus statement for the clinical diagnosis of MSA: clinical domains, features, and criteria used in the diagnosis of MSA

I. Autonomic and urinary dysfunction

A. Features

1. Orthostatic hypotension (by 20 mm Hg systolic or 10 mm Hg diastolic)
2. Urinary incontinence or incomplete bladder emptying

B. Criteria

Orthostatic fall in blood pressure (by 30 mm Hg systolic or 15 mm Hg diastolic) or urinary incontinence (persistent, involuntary partial or total bladder emptying, accompanied by erectile dysfunction in men) or both

II. Parkinsonism

A. Features

1. Bradykinesia (slowness of voluntary movement with progressive reduction in speed and amplitude during repetitive actions)
2. Rigidity
3. Postural instability (not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction)
4. Tremor (postural, resting or both)

B. Criteria

Bradykinesia plus at least one of features 2–4

III. Cerebellar dysfunction

A. Features

1. Gait ataxia (wide based stance with steps of irregular length and direction)
2. Ataxic dysarthria
3. Limb ataxia
4. Sustained gaze-evoked nystagmus

Criteria

Gait ataxia plus at least one of features 2–4

IV. Corticospinal tract dysfunction

A. Features

1. Extensor plantar responses with hyper-reflexia

Criteria

Corticospinal tract dysfunction in MSA: no corticospinal tract features are used in defining the diagnosis of MSA

Reproduced with permission from Elsevier.[19]

Panel 4. "Red flags": warning features of MSA

Motor signs

Parkinsonism poorly responsive to levodopa[2]

Cerebellar ataxia[2]

Pyramidal signs[2]

Early instability and falls[28]
Within 3 years of disease onset

Rapid progression (wheelchair sign) despite dopaminergic treatment[28]
Within 5 years of disease onset

Orofacial dystonia or dyskinesias
Atypical spontaneous or levodopa-induced dystonia or dyskinesia mainly affecting orofacial muscles, occasionally resembling risus sardonicus of cephalic tetanus.

Axial dystonia
Pisa syndrome (subacute axial dystonia with a severe tonic lateral flexion of the trunk, head, and neck) or early severe camptocormia

Disproportionate anterocollis
Chin on chest, neck can only be passively and forcibly extended to its normal position with difficulty; despite severe chronic neck flexion, flexion elsewhere is minor.

Jerky tremor
Irregular myoclonic postural or action tremor of the hands or fingers

Dysarthria

Atypical quivering, irregular and severely hypophonic or slurring high-pitched dysarthria, which tends to develop earlier and be more severe than in PD and is associated with more notable dysphagia.

Non-motor signs

Severe dysautonomia[1]

Abnormal respiration

Nocturnal (harsh or strained, high pitched inspiratory sounds) or diurnal inspiratory stridor, involuntary deep inspiratory sighs and gasps, sleep apnoea (arrest of breathing for >10 s), and snoring increased from premorbid level, or newly arisen

REM sleep behaviour disorder

Intermittent loss of muscle atonia and appearance of elaborate motor activity (striking out with arms in sleep often with talking or shouting) associated with dreaming

Cold hands or feet

Coldness and colour change (to purple or blue) of extremities not caused by drugs, blanching on pressure and poor circulatory return

Raynaud's phenomenon

Painful "white finger" provoked by ergot drugs

Emotional incontinence

Crying inappropriately without sadness or laughing inappropriately without mirth

Definition

When autonomic failure predominates, MSA sometimes is termed *Shy-Drager syndrome*.

When extrapyramidal features predominate (80%), the term *striatonigral degeneration or MSA-P* sometimes is used. (SND)

When cerebellar features predominate (20%), MSA sometimes is termed *sporadic olivopontocerebellar atrophy or MSA-C. (OPCA)*

Epidemiology

Incidence	0,6 per 100 000 >50 ys: 3 per 100 000
Prevalence	1,9-4,9 per 100 000
Sex (m:f)	1,3: 1,0 (3:1)
Age (range)	33-78 (mean 54,3)
Mean survival	6-9 ys (bronchopneumonia 48%; sudden death 21%)

Pathophysiology

Progressive loss of neuronal and oligodendroglial cells in numerous sites in the central nervous system correlated with clinical symptoms.

No evidence of a genetic etiology.

Oligodendroglial cytoplasmic inclusions indicates that damage is primarily in the white matter.

In addition to the GCIs, extensive myelin degeneration occurs in the brain.

Chronic alterations in glial cells may impair trophic function between oligodendrocytes and axons and cause secondary neuronal damage.

Glial Ctytoplamic Inclusions (GCIs)

Unique biological hallmark of MSA

Multilayered tubular filaments containing ubiquitin, tau (classical cytoskeletal antigens) and α-synuclein (presynaptic protein)

α-synuclein accumulation in GCIs plays a central part in MSA, PD and LBD

Inability of oligodendrocytes to degrade α-synuclein normally produced or ectopic expression

CNS sites damaged

Basal Ganglia (motor neostriatum)

Putamen (caudal, dorsolateral); SN pars compacta

Motor cortex (primary and supplementary)

Olivopontocerebellar system

Basis pontis, transverse pontocerebellar fibers, middle cerebellar peduncles

Dorsal motor nucleus of the vagus nerve

Locus Coeruleus

Cathecolaminergic neurons of ventrolateral medulla

Pontomedullary reticular formation

Parasympathetic preganglionic nuclei of the spinal cord (Onuf's nucleus, S2-S3, inferior intermediolateral nucleus, S3-S4)

Sympathetic preganglionic neurons in the intermediolateral column of the spinal cord

Autonomic dysfunction

- Genitourinary (41-47% - 97%)
- Urinary incontinence (frequency, urgency)

Preganglionic cell loss in spinal cord (intermediolateral cell columns)
Related to detrusor hyperreflexia caused mainly by loss of inhibitory input to pontine micturition center (rather than to external urethral sphincter denervation alone)

- Urinary retention (incomplete bladder emptying)

Sacral intermediolateral cell columns (related to detrusor atonia)

- Erectile dysfunction or impotence

Autonomic dysfunction

- Orthostatic hypotension (68%)

Primary preganglionic damage of intermediolateral cell columns (baroreflex impairment and debuffering)

- Syncope (51% at least once, 15% recurrent)
- Post prandial hypotension
- Supine hypertension with orthostatic hypotension (60%)

Parkinsonism (46% - 91%)

GCIs in basal ganglia

- Akinesia and Rigidity

  Putamen, Globus Pallidus
- Postural Tremor or at rest (29%)
- Postural Instability (early, unusual recurrent falls)
- Orofacial or craniocervical dystonia associated with quivering, high-pitched dysathria
- Poor response to levodopa (28% good response early in the disease especially in younger patients, only 13% maintened this response)

Striatal cell loss. Loss of D1and D2 receptors in Striatum or impaired functional coupling of D1 and D2 receptors

Cerebellar Dysfunction (5% - 54%)

Cell loss in inferior olives, pontine nuclei, and cerebellar cortex

- Gait ataxia (wide-based stance with steps of irregular length and direction)
- Limb kinetic ataxia
- Ataxic dysartrhya
- Sustained gaze-evoked nystagmus

Pyramidal signs (49%)

Pyramidal tract demyelination

- Extensor plantar response
- Hyper-reflexia

Other symptoms based on mixed dysfunction

- Laryngeal Stridor - Vocal cord paralysis

Severe cell loss in nucleus ambiguus or biochemical defect causing atrophy in posterior cricoarytenoid muscles

- Sleep apnea

A neurogenic and abstructive mixed form

Clinical Presentation

Clinical domains	*Initial symptoms (%)*	*Incidence during lifetime (%)*
Autonomic and Urinary disfunction	41-74	97 (68 orthostatic hypotension)
Parkinsonism	46	87-91
Cerebellar Dysfunction	5	54
Corticospinal tract Dysfunction	-	49

Consensus statement on the diagnosis of MSA

Gilman et al., J Neurol Sci 1999

Developed diagnostic criteria based on *4 clinical domains*. These findings allowed subclassification of patients into different levels of diagnostic certainty such as *possible, probable, and definite*. The conference also recommended that MSA be subdivided into 2 categories based on the prevalent neurosystem involved.

Autonomic and urinary dysfunction

Features

- Orthostatic hypotension (by 20 mmHg systolic or 10 mmHg diastolic)
- Urinary incontinence or incomplete bladder emptying

Criteria

Orthostatic falls in blood pressure (by 30 mmHg systolic or 15 mmHg dyastolic) or urinary incontinence (persistent, involuntary partial or total bladder emtying, accompained by erectile dysfunction in men) or both

Parkinsonism

Features

- Bradykinesia (slowness of voluntary movement with progressive reduction in speed and amplitude during repetitive actions)
- Rigidity
- Postural instability (not caused by primary visual, vestibular, cerebellar or propioceptive dysfunction)
- Tremor (postural, resting or both)

Criteria

Bradykinesia plus at least one of features 2-4

Cerebellar Dysfunction

Features

- Gait ataxia (wide based stance with steps of irregular lenght and direction)
- Ataxis dysarthria
- Limb ataxia
- Sustained gaze-evoked nystagmus

Criteria

Gait ataxia plus at least one of features 2-4

Corticospinal tract dysfunction

Features

- Extensor plantar responses with hyper-reflexia

Criteria

No corticospinal tract features are used in defining the diagnosis of MSA

Consensus statement: diagnostic categories of MSA

Possible MSA

One criterion plus two features from separate other domains

When criterion is parkinsonism, a poor levodopa response qualifies as one feature (hence only one additional feature required)

Probable MSA

Criterion for autonomic failure and urinary dysfunction plus poorly levodopa-responsive parkinsonism or cerebellar dysfunction

Definite MSA

Pathologically confirmed by presence of high density of GCIs in association with degenerative changes in nigrostriatal and olivopontocerebellar pathways

Imaging

- MRI (olivopontocerebellar and putaminal atrophy) To differentiate from cerebellar ataxia, PD, PSP,CVD
- T2 weighted images. Hyperintensities within the pons and the middle cerebellar peduncles (hot cross bun); putaminal hypointensity associated with a slit-like hyperintensity band lateral to the putamen
- Diffusion weighted images. High putaminal regional apparent diffusion coefficients in MSA-P reflect ongoing striatal degeneration.
- MRI based volumetry. Significant reductions in mean striatal and brainstem volumes. MSA-C and MSA-P also have a low cerebellar volume.

Imaging

- Functional imaging

Recently, SPECT and PET ligands that enable study of cardiac sympathetic innervation have become available. They seems to be helpful tools that may support an early clinical diagnosis of MSA, discriminating from PD and pure autonomic failure

Treatment

Parkinsonism

- Levodopa (plus decarboxylase inhibitor) up to 1000 mg/day (30-70%; declines after few ys; diskinesias)
- Dopamine agonist (bromocriptine and lisuride not efficacy)
- Amantadine (anecdotal benefit in single case)
- Anticholinergics useful for hypersalivation
- Medial pallidotomy (not improve motor disturbances)
- Bilateral subthalamic nucleus high-frequency stimulation (beneficial in four patients)

Treatment

Orthostatic hypotension (to treat when disabling)

- Avoiding aggravating factors (large meal, alcohol, exposure to warm environment)
- Wearing of elastic stockings
- Head-up tilt of bed at night
- Increase salt intake
- Fludrocortisone and desmopressin (>plasma volume, <natriuresis) 0,1-0,3 mg/die
- Midodrine (increases peripheral resistance) 2,-10 mg x3/die
- Controlled trials comparing the different drugs not available
- Supin hypertension does not rquiring drug treatment if systolic bp < 200mmHg, elsewhere short acting calcium antagonist at night

Treatment

Genitourinary dysfunction

- Desmopressin at night for nicturia (tablets100-400 ug)
- Peripherally acting anticholinegic drugs (induce retention)
- Sildenafil for erectile dysfunction (exacerbate OH)

Other therapies

- Physiotherapy
- Speech therapy
- Occupational therapy and psychological support
- Wheelchair?
- Tracheostomy?
- Nasogastric o PEG?

Anatomical evidence for cerebellar and basal ganglia involvement in higer cognitive function.

Kim et al. Science. 1994;265:949-951

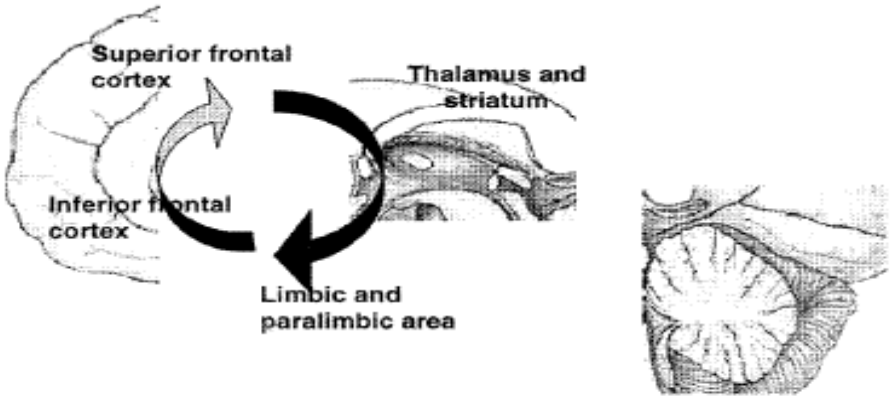
Evidence for cerebellar-frontal subsystem changes in children treated with intrathecal chemoterapy for leukemia.

Lesnik et al. Arch Neurol. 1998;55:1561-1568

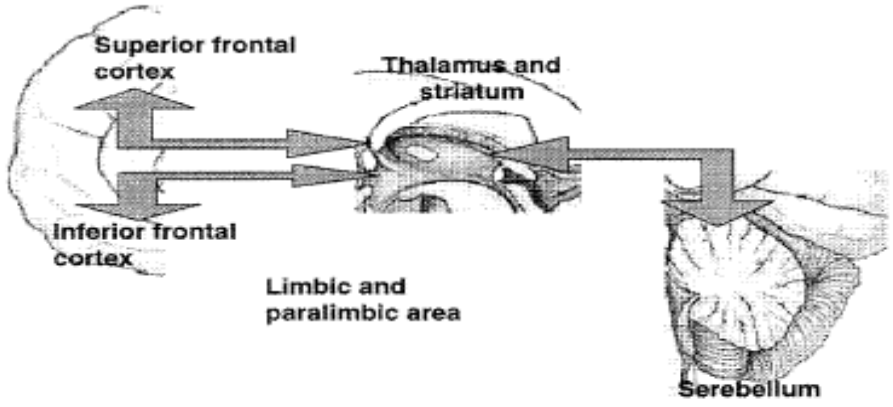
CORTICO-STRIATO-CEREBELLAR CIRCUIT DYSFUNCTION IN PSYCHOTIC (DELUSIONAL) DEPRESSION

New Frontiers in Psychiatry / Psikiyatride Yeni Ufuklar

Figure 1: Circuits Playing role in the pathogenesis of major depression with psychotic and non-psychotic features.



limbic-cortical- striatal-pallidal-thalamic circuits (LCSPT), previously defined by Drevets



Cortico-striato-cerebellar circuit in psychotically depressed patients

Parkinsonian signs in subjects with mild cognitive impairment

Barbara Vicini Chilovi, Luca Rozzini, Alessandro Padovani

Neurology 2006;67;182-183

To the Editor: We read the article by Boyle et al. with interest.
The authors report that mild cognitive impairment (MCI) is accompanied by extrapyramidal signs (EPS) that are related to the severity and type of cognitive impairment independent of vascular risk factors.
The association between mild parkinsonian signs (MPS) and MCI has previously been described, specifically the relationship between MPS and the amnestic type (aMCI).Furthermore, rigidity rather than tremor or bradykinesia were most strongly associated with MCI.
These findings confirm the assumption that MCI is associated with parkinsonian signs, the severity of which is related to the severity and differential pattern of both cognitive and behavioral dysfunctions. The association between EPS and specific behavioral disturbances included in the core features of DLB suggests that Lewy body pathology might be the major contributing factor to both EPS and BPSD.
In addition, neuropsychological data showed that MCI subjects had a greater deterioration of visuospatial skills primarily compromised in DLB. Further studies are needed to follow up those MCI patients with EPS to determine whether they have a more rapid progression to dementia.

Parkinsonian signs and psycho-behavioural symptoms in subjects with Mild Cognitive Impairment.

Background: Mild Cognitive Impairment (MCI) may be accompanied by extrapyramidal signs (EPS), which are related to the severity and type of cognitive impairment. Moreover mild parkinsonian signs are mostly associated with MCI of the amnestic type (aMCI). It has been hypothesised that MCI and EPS may share similar pathogenesis though it is unknown whether this involves Alzheimer-type pathology, Lewy bodies or vascular changes in the basal ganglia.

Aim of the study: further elucidate the relationship between MCI and EPS and to characterize the neuropsychiatric features of MCI patients with EPS.

Table 1. Clinical and socio-demographic characteristics of two groups of 132 MCI subjects with different severity of extrapyramidal symptoms (UPDRS part III).

	MCI without EPS N° 97			MCI with moderate EPS N° 35			
	Mean	SD	%	Mean	SD	%	*P*
Age (ys)	71,2	7,7		72,4	7,3		NS
Sex (female)			63,9			68,6	NS
Education (ys)	7,9	3,8		7,3	3,2		NS
Comorbility ^	2,1	1,7		1,9	1,6		NS
Drugs (n)	2,7	2,1		2,6	1,7		NS
APO -E ε4 §			42,7			40,6	NS
WML #			23,3			25	NS
Vascular index ç			42,3			34,3	NS
CDR total	0,5	0,1		0,5	0,1		NS
MMSE	26,8	1,9		26,7	1,7		NS
ADAS -Cog total score	7,9	4,1		9,7	4,7		.03
ADAS -Cog memory items	16,1	4,1		17,2	3,8		NS
ADAS -Cog without memory items	3,5	2,5		4,6	3,1		.05
Short story (Novelli)	7,5	3,3		8,5	4,9		NS
Rey's figure copy	28,1	7,3		26,4	8,6		NS
Barthel index	98,5	3,6		98,1	3,9		NS
BADL (functions lost)	0,2	0,4		0,2	0,4		NS
% of subject s with ≥ 1 functions lost			15,5			20	NS
IADL (functions lost)	0,4	0,8		0,5	0,7		NS
% of subjects with ≥ 1 functions lost			27,8			34,3	NS
Tinetti scale	27,5	1,5		25,6	2,8		.000
UPDRS -part III	1,1	1,7		9,3	7,2		.000
Neuropsychiatric Inventory	12,4	11, 5		16,3	11,5		NS
Geriatric Depression Scale (15 items)	4,5	3,2		5,3	3,7		NS
Hamilton anxiety scale	9,3	6,7		11,1	6,2		NS

Table 2. Neuropsychiatric characteristics (NPI subitems) of two groups of 132 MCI subjects with different severity of extrapyramidal symptoms (UPDRS part III).

	MCI without EPS N° 97	MCI with moderate EPS N° 35	
	%	%	P
Delusion	10,3	17,1	NS
Hallucination	5,2	11,4	NS
Agitation	25,8	40	NS
Depression	39,2	57,1	.05
Anxiety	35,1	54,3	.04
Euphoria	8,2	11,4	NS
Apathy	24,7	42,9	.04
Disinibition	2,1	2,9	NS
Irritability	47,4	45,7	NS
Aberrant motor behaviour	3,1	11,4	NS
Sleep disturbances	32	54,3	.02
Eating disturbances	12,4	2,9	NS

Conclusion: data corroborate the assumption that MCI may be associated with parkinsonian signs, whose severity is related to the severity of cognitive impairment, in particular of non memory functions, and to a differential pattern of psycho-behavioural symptoms.