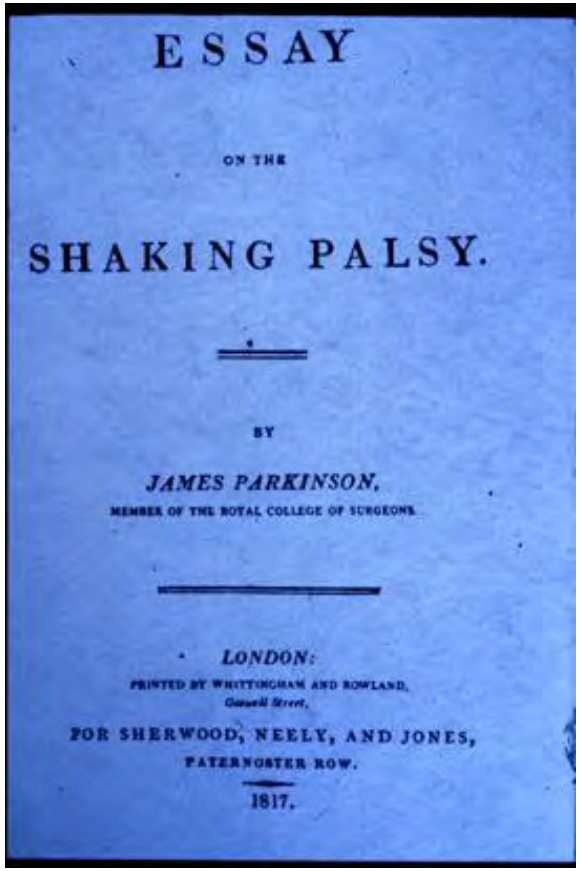
Parkinson


ESSAY
ON THE
SHAKING PALSY.
BY
JAMES PARKINSON,
MEMBER OF THE ROYAL COLLEGE OF SURGEONS.
LONDON:
PRINTED BY WHITTINGHAM AND ROWLAND,
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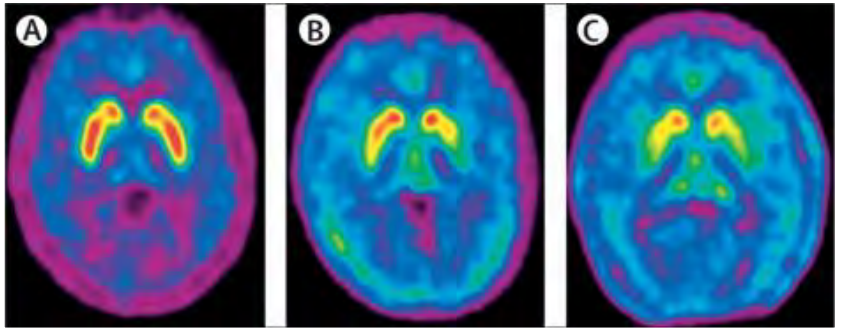

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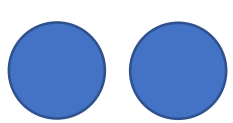
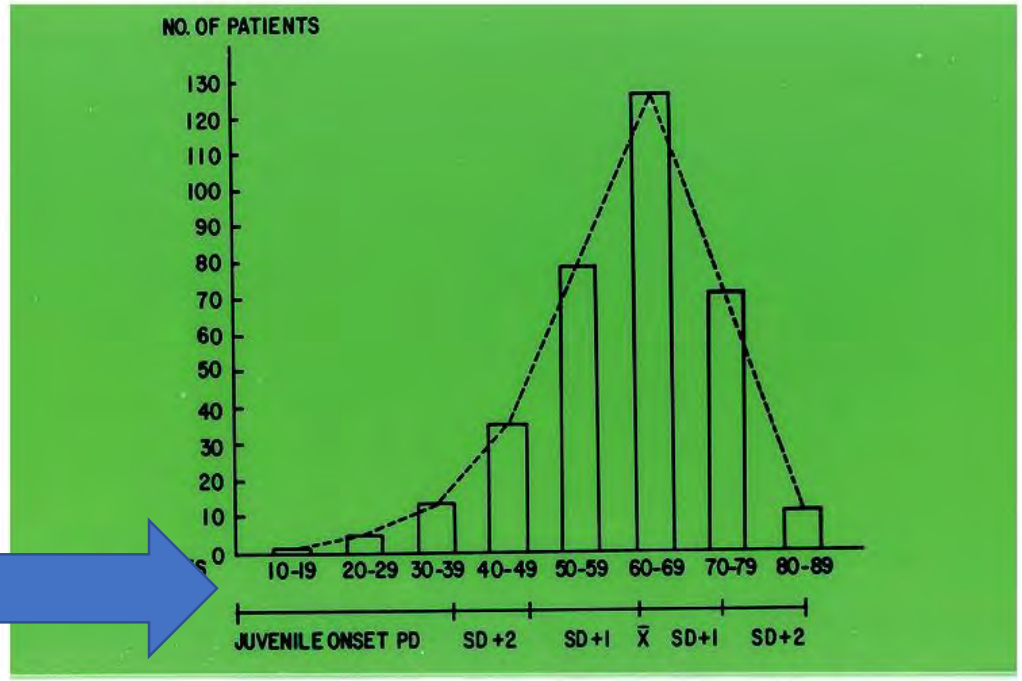




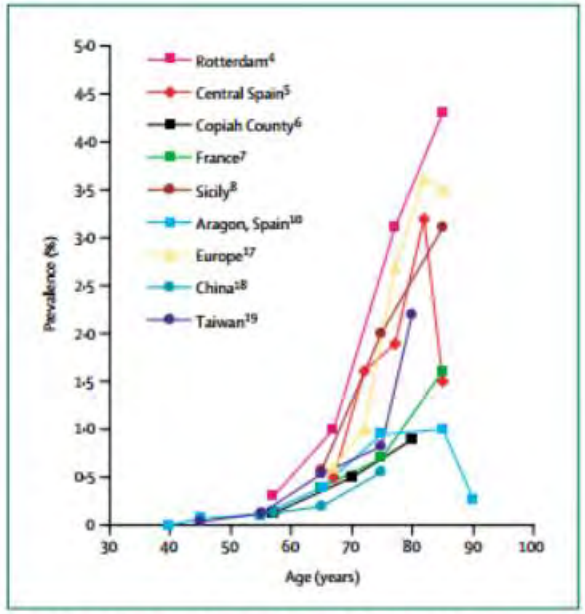


Figure 1: Population-based prevalence studies of Parkinson's disease

De Lau LM Lancet Neurol2006: 5: 525-535

1/1000

Causes et facteurs de risque

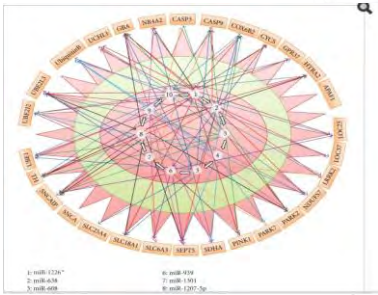
- Parkinsonisme postencephalitique 1920
- Environnement (pesticides, Mn…) 1970-80: existait avant les pesticides
- Parkinsonisme toxique (MPTP, Mn, CO..) 1980-90
- Cascade stress oxydatif-dysfonction des mitochondries-inflammation, excitotoxicité, apoptose
- Génétique depuis 10 ans: multiples gènes (expliquent 10-15%) et polymorphismes (variantes de la norme), mais 90% sporadique!!
- Voirie cérébrale : structure tridimmensionelle des proteines
- Exome, Protéome, lipidome, métabolome, channelome…: microarrays
- Inflammation
- Interaction environnement-génétique: épigénétique, RNA, histones
- Hypothèse aggrégation (prion)

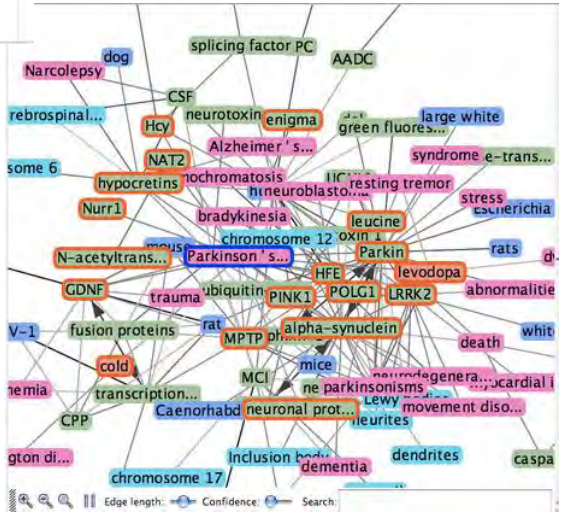
- Protecteurs: fumée (durée, quantité), café, ac urique

Table 1 – PARK, DYT and other main genotypes associated with prominent parkinsonism.
PARK DYT et autres génotypes principaux associés au parkinsonisme.

Disease (OMIM)	Map position	Gene	Transmission	PD phenotype	Main associated movement disorder
PARK coding					
PARK1/4 (163890)	4p21	*SNCA*	AD	Common	Typical PD with prominent non motor syndrome
PARK2 (600116)	6q25-q27	*Parkin*	AR	Common	Early onset parkinsonism, dystonia
PARK3 (602404)	2p13	Unknown	AD	Common	Typical PD
PARK5 (191342)	4p14	*UCHL1*	AD	Common	Typical PD
PARK6 (605909)	1p35-p36	*Pink1*	AR	Common	Typical PD
PARK7 (606324)	1p36	*DJ1*	AR	Common	Early onset parkinsonism, psychosis
PARK8 (607060)	12q12	*LRRK2*	AD	Common	Typical PD, benign course
PARK9 (606693)	1p36	*ATP13A2*	AR	Common	Kufor-Rakeb disease
PARK10 (606852)	1p32	Unknown	AD	Common	Variable
PARK11 (607688)	2q37	*GIGYF2*	AD	Common	Typical PD
PARK12 (300557)	Xq21-q25	Unknown	X-linked	Common	Variable
PARK13 (610297)	2p12	*Omi/HTRA2*	?	Common	Typical PD?
PARK14 (256600)	22q13	*PLA2G6*	AR	Common	Early onset dystonia-parkinsonism, myoclonus, epilepsy
PARK15 (605648)	22q12	*FBXO7*	AR	Common	Early-onset parkinsonism and pyramidal tract signs
PARK16 (613164)	1q32	Unknown	?	Common	Typical PD?
DYT coding					
DYT3 (314250)	Xq13	*TAF1*	X-linked	Common	Dystonia-parkinsonism
DYT5 (128230)	14q22	*GCH1*	AD	Common	Dopa-responsive dystonia
DYT12 (128235)	19q12-q13.2	*ATP1A3*	AD	Common	Rapid onset dystonia parkinsonism
DYT16 (612067)	2q31.3	*PRKRA*	AR	Common	Dystonia-parkinsonism
Other coding					
CHAC (200150)	9q21	*VPS13A*	AR	Common	Chorea, orofacial dyskinesias, parkinsonism
GD (606463)	1q21	*GBA*	AR	Exceptional	Both typical PD or atypical parkinsonism
HD (143100)	4p16.3	*IT-15*	AD	Common	Chorea, parkinsonism
PKAN (234200)	20p13	*PANK2*	AR	Uncommon	Dystonia
SCA2 (183090)	12q24	*ATXN2*	AD	Uncommon	Progressive cerebellar ataxia, dopamine-responsive parkinsonism
SCA3 (109150)	14q24.3-q31	*ATXN3*	AD	Uncommon	Progressive cerebellar ataxia, dystonia
SCA17 (607136)	6q27	*TBP*	AD	Uncommon	Progressive cerebellar ataxia, chorea, dystonia
WD (277900)	13q14.3-q21.1	*ATP7B*	AR	Uncommon	Tremor, dystonia

AD: autosomal dominant; AR: autosomal recessive; CHAC: choreoacanthocytosis; HD: Huntington's disease; PD: Parkinson's disease; PKAN: pantothenate kinase-associated neurodegeneration; SCA: spinocerebellar ataxia; WD: Wilson's disease.





Maladies répértoriées avec Synd.Parkinson

Familiales: 5-10%

Park1,4 (alphasynuclein), familial Lewy-body, park 2 (parkin) , Park 3, Park 5 (UCHL-1), Park 6 (PINK-1), Park 7 (DJ1), Park 8 (LRKK2), Park 9 (pallidopyramidal Kufor-Rakeb), Park 10 , Park 11, Park 12, Park 13, Omi/Htr A2, Synphilin-1, NR4A1, Nurr-1, POLG

DYT 2 (Lubag, X linked Philipino dystonia-parkinsonims),DYT 5 (Segawa) ,DYT 12 , RODP, PKAN (Hallervorden-Spatz)

SCA2 (Holguin, OPCA II, spinopontine, Cuban), SCA3 (Machado-Joseph, Azorean, nigrospinodentale, familial amyloidotic), SCA6, SCA 8, SCA 17,

OPCA I, II (Fickler-Winckler) III, IV (Schut-Heymaker, glutamate dehydrogénase), V, cérébelleo-oliviare

ETM1 (tremor essentiel et parkinson)

DFT: Tauopathies familiales: F-Pick, F-CBD, F-PSP, Chr 17, Alzheimer familial (PS1,2), DownF-grains argyrophiles, TDP-43 progranulopathies

Alzheimer familial (PS1,2), Down

FALS 1-5, FALSPDD Wihlhelmesen-Lynch), Kennedy bulbospinal

Paraparésies spastiques familiales SPG1-12

Mitochondriopathies, Kearns-Sayre, Kearns-Say, MERFF, MELAS, Leber (CPEO)

Calcifications des noyaux gris (Fahr syndrome)

Démences vasculaires familiales: CADASIL, HERNS, Nemoto..

Acanthocytose, HARP, Mc Leod

DRPLA (Haw River, Naito)

Syndrome de Perry (hypoventilation-dperession)

Wilson

Huntington forme rigide

Dégénérescences thalamiques

HDLS (herediatry fdiffuse leukoencephalopathy with axonal spehorids)

HDR (hypoparathyroidisme, surdité sneorielle, renal disease)

Prions familiaux

Dégénérescence stritaonigrée familiale MSA-F

Gliose sous-corticale progressive F-GSP

Maladie à inclusions neuronales hyalines, polyglucosan bodies, Hirano bodies, Bunina, Lafora

Familial pallidonigral

PD-ET: POLG1,2

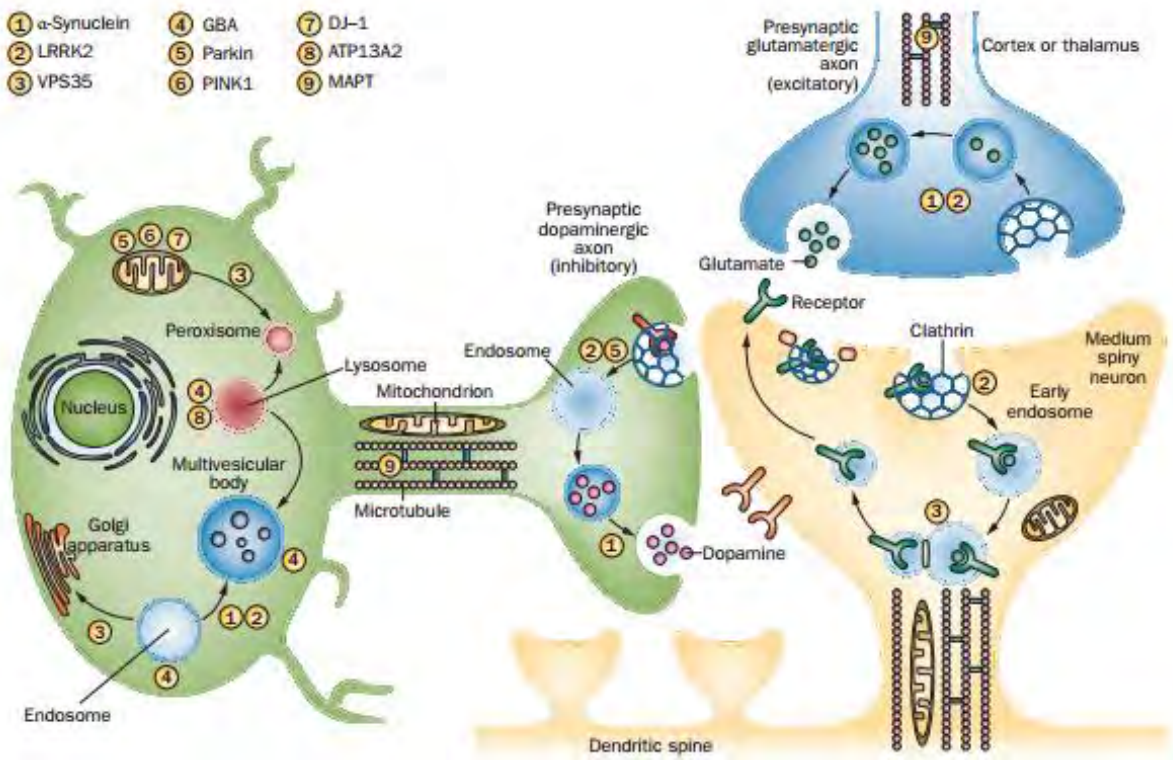
Hexosamininidase GM1, GM2, Tay-Sachs, Niemann-Pick C, D
Tay-Sachs, Sandhoff-Jatzkewitz
Gaucher forme adulte type III type Norbottnien
Alexander
Hemochromatose
Céroide lipofuscinose (Kuf's)
Paelizeus-Merzbacher
Seitelberger
Chediakh-Higashi
Smith-Magenis
AlcaptonurieAicardi-Goutières
Sclérose tubéreuse de Bourneville
Adrénomyéloneuropathie, adrénoleucodystrophie
Canalopathie KCNJ6
Coeliakie
Bulbopontin Vialette van Laere
Deficience fam.en folate, bioptérine, vit E,thiamine
Lipomatose multiple Launois-Bensaude
Sea-blue histiocyte

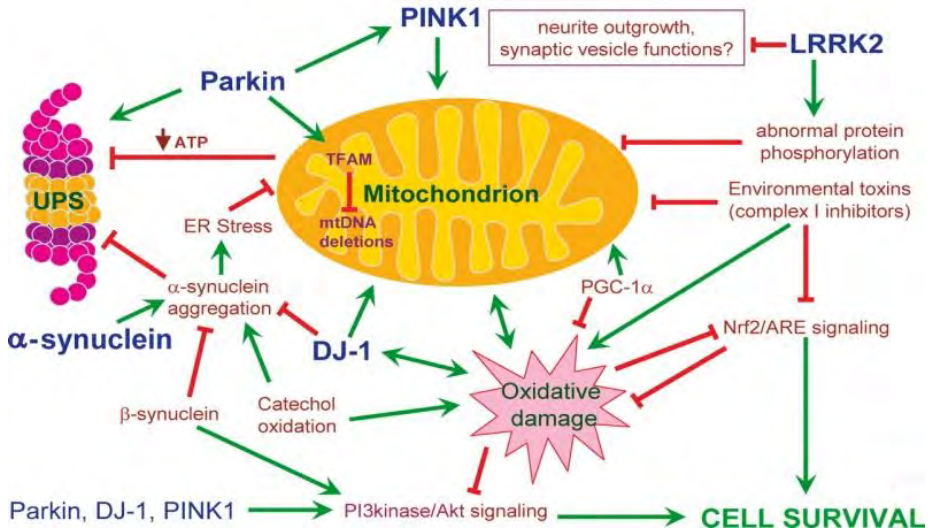
Sporadiques 90%

Atrophie multisystémique MSA SND,
MSA-OPCA, MSA-PD
Tauopathies: PSP (Steele-Richardson-Olszewsky)
CBDG
Synucléopathies:PDI?, DLBD, PAF, MSA SN
DFT (tauopathies, TDP-43, Chr 17, Pick, DLDH, AGD, NIFID, progranulopathies/ TDP 43, Motoneurone ALS-PD (D) DFTU,
Alzheier tardif

Symptomatique:
Endocrinien: hyperparathyroidisme, hypoparathyroidisme, psuedohypoparatyhroidisme
Thyroide
Secondaire ou symptomatique:
Parkinsonisme vasculaire (=demence vasculaire)
TCC, démence pugilistique
Toxique: Mn, Mg, solvants, DHBP, MPTP, methanol, pesticides, gaz, Cu
Anoxie, CN, CO
ALS PD Guam
Hémiparkinson-hémiatrophie
Hypoparathyroidisme
Herbes chinoises
Neuroleptiques, metoclopramide, anticalciques, cinnarhizine,
Antidépresseurs SSRI, amphotericine
Lithium, Valproate, phenytoine, disulfiram
Encephalite Japonaise, Influenza 1918, polyo, Western and Eastern Equine, St Louis, coronavirus
Mycoplasme, borrelia, toxo
Hydrocéphalie pression normale
Hématome sous-dural
Glioblastome, tumeur de ligne médiane
MAV, tumeur, hematome mésencéphalique
Insuffisance hépatique, rénale
Myélinolyse centropontique
Traumatisme electrique
Traumatisme thermique (coup de chaleur)
Radiotherapie
Chimiothérapie (VCR, ARAC)
Paraneoplasique
Sjogren, vasculites

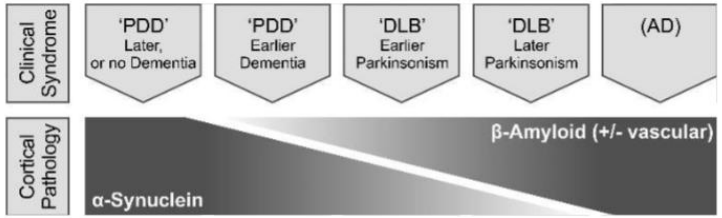
Synthèse génétique

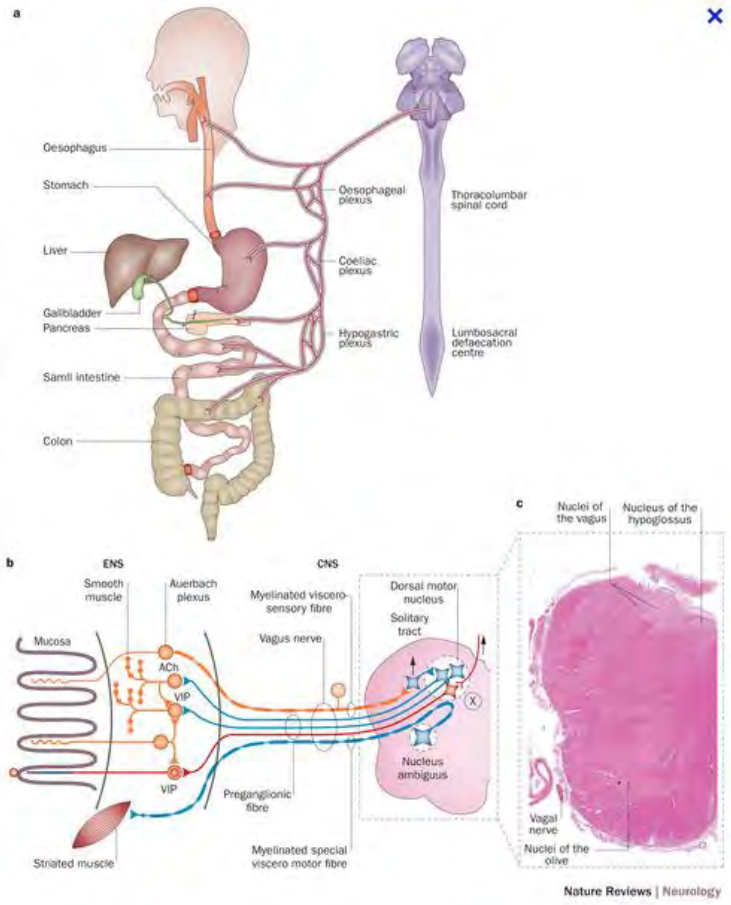


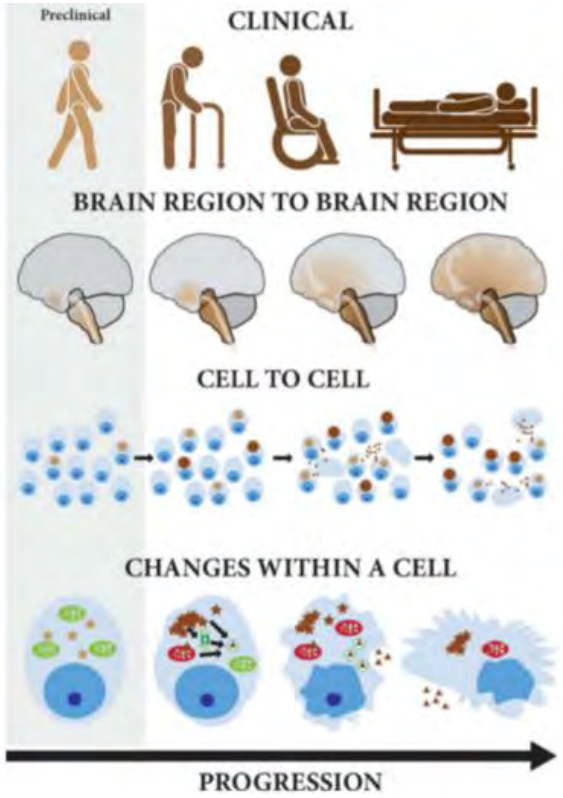


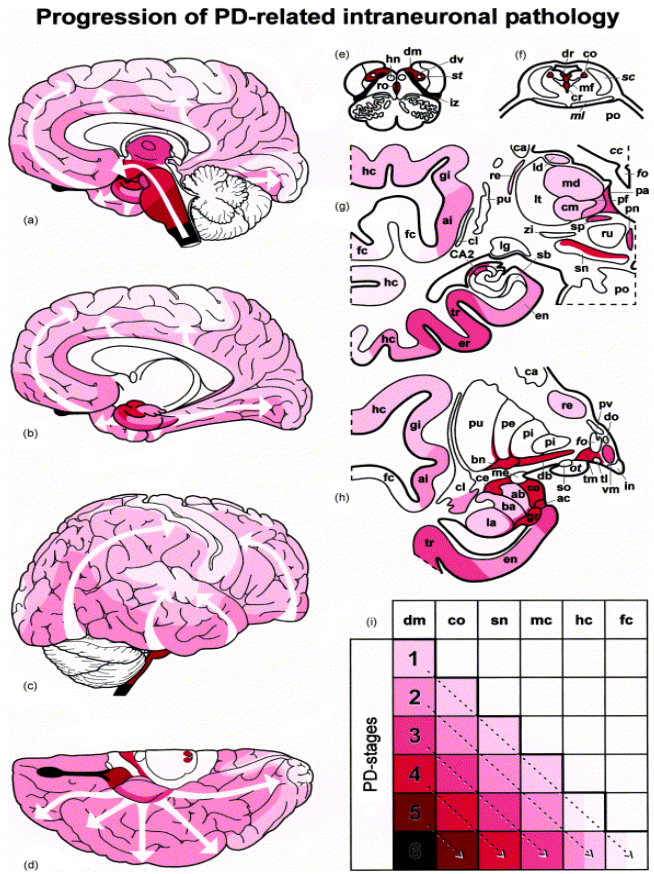
Trinh J Nat Rev Neurol 2013: 9: 445-454

Hypothèse de Braak









Stade présymptomatique

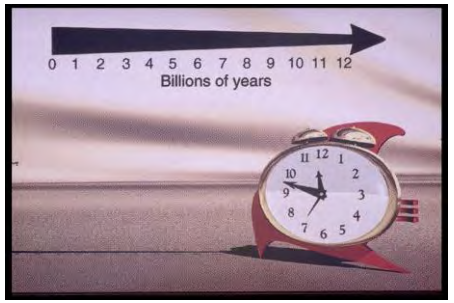
- Personnalité prémorbide > 20 ans
- Troubles comportement sommeil paradoxal: > 10-15 ans, insomnie, somnolence diurne
- Constipation > 10 ans
- Troubles olfaction 5 ans
- Fatigue 2-3 ans
- Douleurs atypique proximales, rachidiennes2-3 ans
- Troubles exécutifs, mnésiques, bradypsychsime 2-3 ans
- Dépression, anxiété: 2-5 ans
- Tremor interne, raideur 1-2 ans

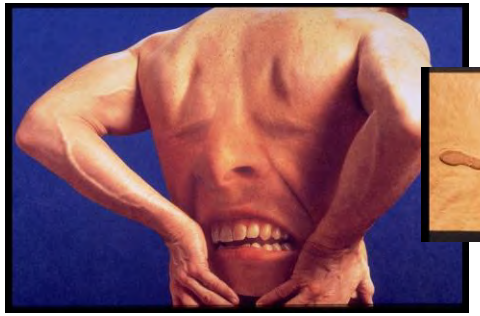
Syndrome parkinsonien moteur

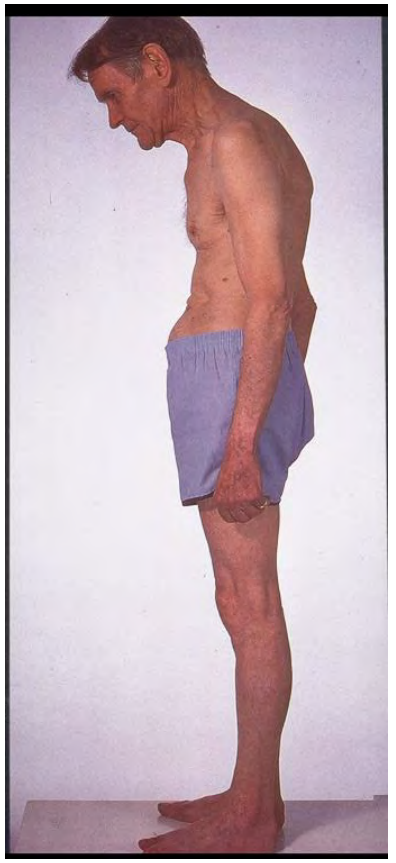
- **Bradycinesia: akinesia** (aspontanité, initiation difficile, perte automatismes: clignement, ballant..), **hypokinesia** (plus petit) , **bradycinésie:** plus lent (perte energisation)

Et au moins un de:

- **Rigidité (roue dentée si tremor)**
- **Tremblement de repos** asym. (**type I**), postural (**type II**), mixte **(type III**) , **monosmymptomatiqu**e: pill rolling 4-5 Hz
- **instabilité posturale et troubles de la marche** petits pas, traîne pieds, difficulté retournement, initiation, retropulsion, perte adaptations posturales et réflexes protecteurs, antéflexion du tronc
- Tardif: signes axiaux: dysphagie, marche, équilibre, freezing, voix, retropulsion, chutes
- Démence après 10-15 ans
- **Réponse à la L-dopa:** 70-100% dopasensible/doparésistant 1000. 15000 mg x3 mois

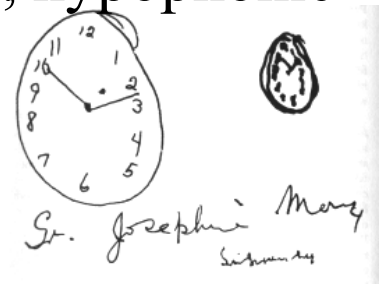






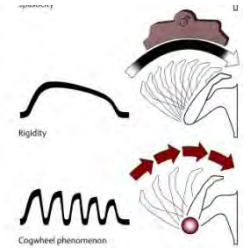
La clinique: les anciens canons du diagnostic clinique:

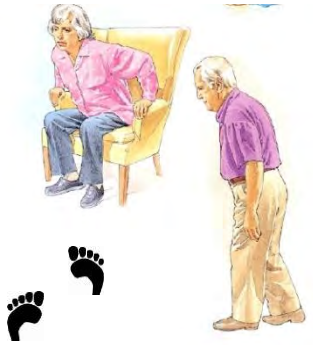
Bradycinésie micrographie, hypophonie



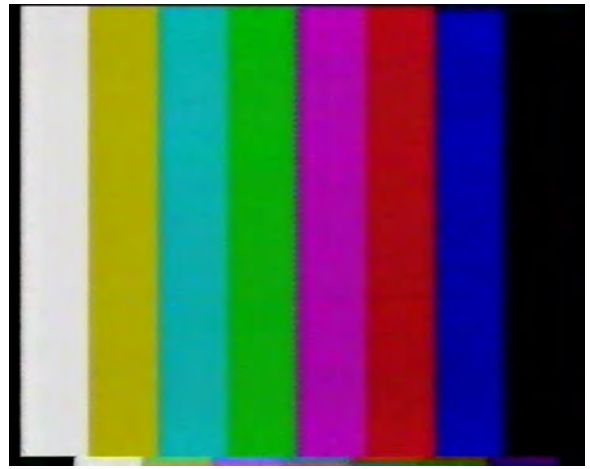
Tremblement

Troubles de marche et posture





Rigidité



Syndromes parkinsoniens: classification générale

- **Synucléopathies: PD** dopa sensible «idiopathique», presynpatique pur, /résistant/atypique
- **Démences à corps de Lewy, Maladie à corps de Lewy MCL, Démences avec Lewy bodies, MCI-démence du Parkinson, Syndromes Parkinson démence, PDD**
- **Atrophie multisystémique MSA**-P, MSA-C, MSA-SD,
- **Tauopathies: Paralysie supranucléaire progressive PSP**-R, **/PSPS:** PSP PD, PSP PA, PSP PPA, PSP DFT
- **Dégénéresence cortico-basale CBD/CBS**: CBD overlap PSP-CBD, CBD PPA, CBD DFT
- **Parkinsonisme des syndromes DFT: TDP43 (parkinson démence motoneurone), c9orf72, MAPT/tau/CHIMP2**
- **Parkinsonisme vasculaire PD vasc**
- **Troubles de la marche frontaux, parkinsonisme vasculaire, DFT**
- **PD tardif (neuroleptiques), médicaments** (metcolopramide, anticalciques, antiepi…)
- **PD hemiparkinson-hemiatrophie**
- **Formes réversibles**: toxique, infectieuses, inflammatoires, IGLON5, autoimmuns, paraneopl
- **Parkinsonismes secondaires: Mn, CO, anoxique, toxique, infectieux, drogues, médicaments, tumeurs, sous.duraux, HPN…**
- **Parkinsonismes familiaux, génétiques**
- **Parkinsonisme prions**
- **Parkinson atypique»**, overlap: **red flag signs**: dystonie, ataxie, pyramidaux, motoneurone, dysautonomie, oculomotricité, dyskinésies, tremor, tr cognitifs précoces, main étrangère,
- Corps de Lewy non nécessaire

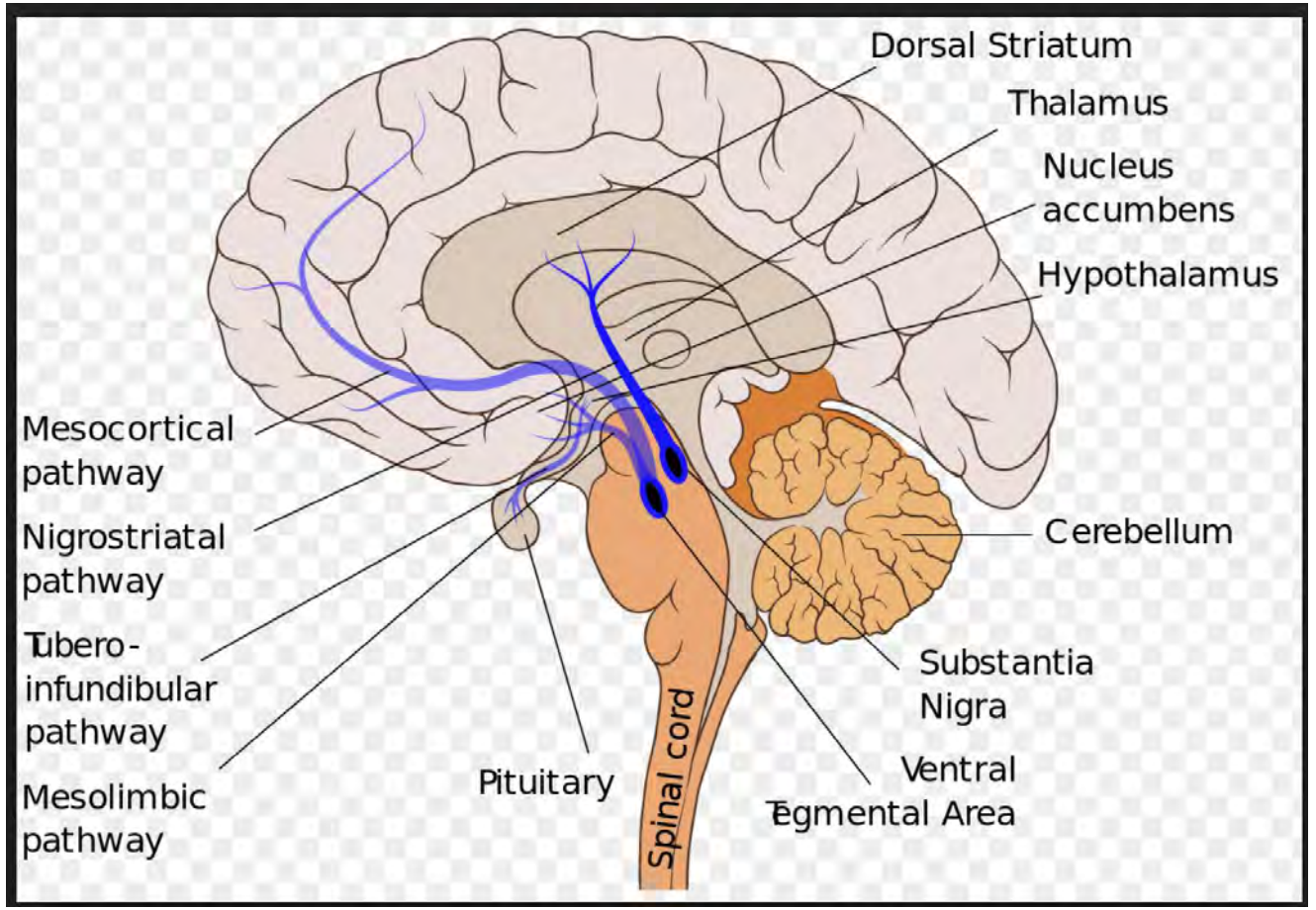
Syndromes parkinsoniens


Segment 2
Case 2
©1995 The Movement Disorder Society, Inc.

DD: bilan initial

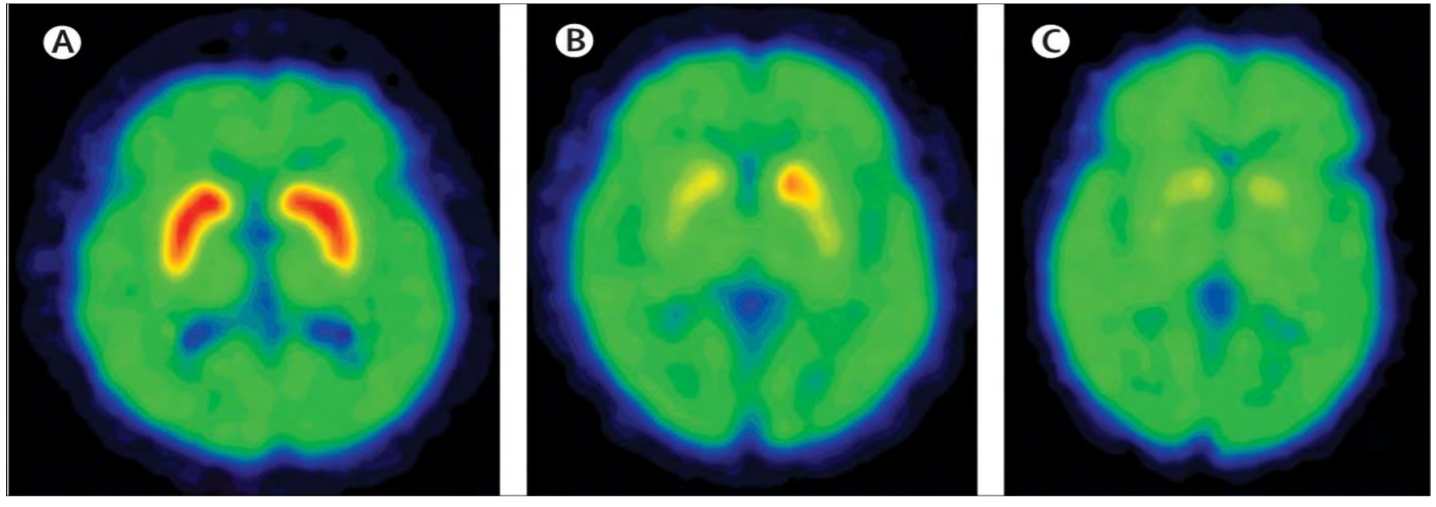
- Anamnèse, examen mais le montrer à un spécialiste (neurologue, consultation spécialisée)
- 2. IRM (Ct si calcifications), DAT scan si doute ou tremor atypique
- Si jeune <40 ans: conseil génétique, biologie moléculaire (caisse maladie!) , ceruloplasmine, cuivre sang, cuprurie, ex ophtalmo, Ca, Phopshate, PTH,
- PL anticorps antineuronaux (IgLON5), frottis nasal CJD
- SPECT MIBG (si LBD)
- Ex neuropsy

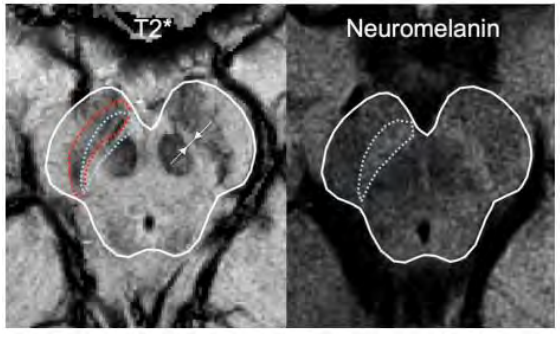
Parkinsonisme dopa-sensible: presynaptique: nigrostrié

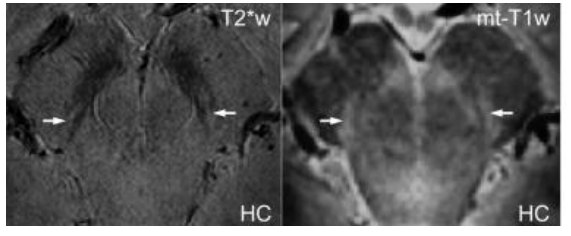


PET Scan F-Dopa/DAT Scan: parkinson presynaptique strio-nigré

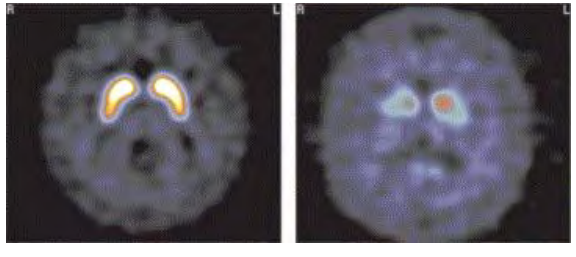
F-dopa PET

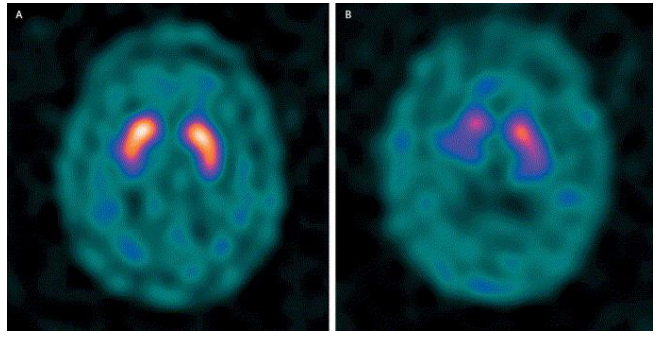


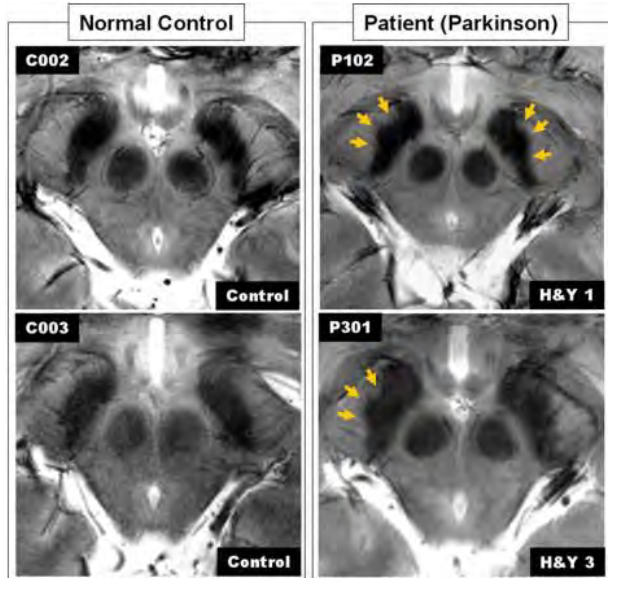




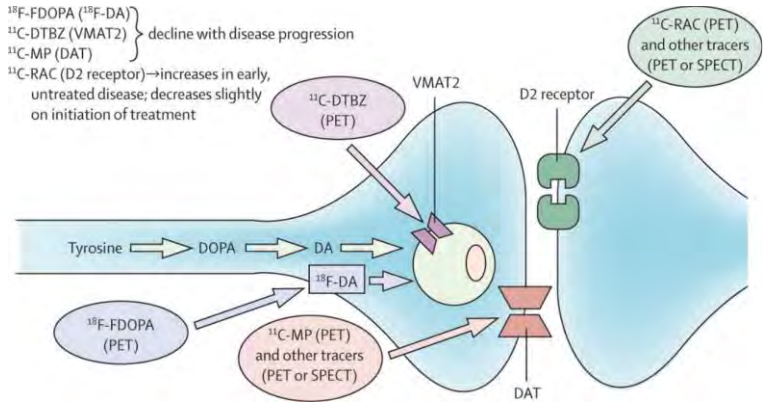
Beta CIT SPECT
DAT Scan

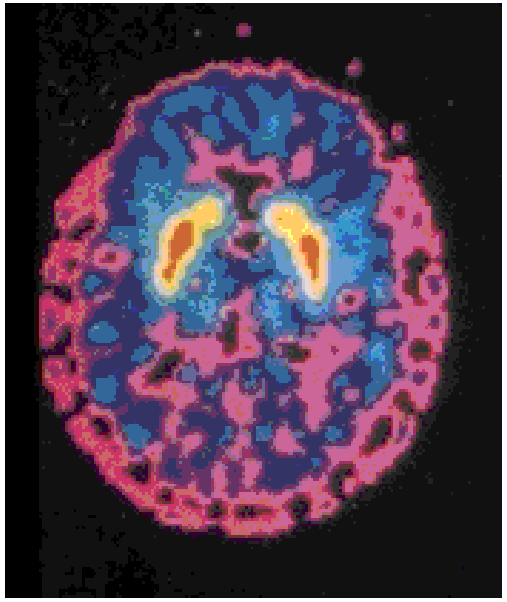




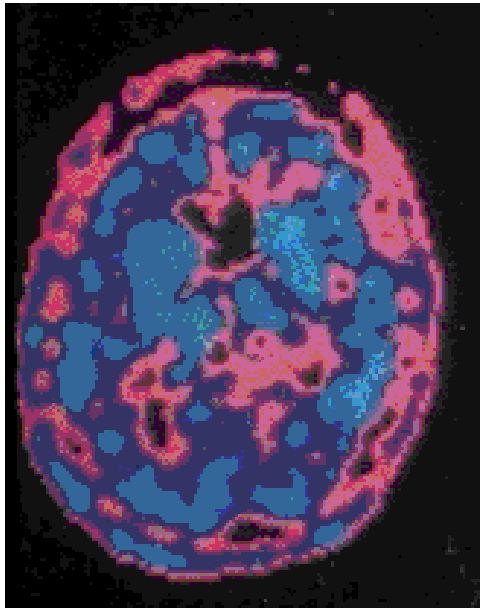


Parkinson dopa-résistant: postsynaptique





Parkinson



Parkinson dopa résistant

PET Raclopride

Red flags signs (neurologue)

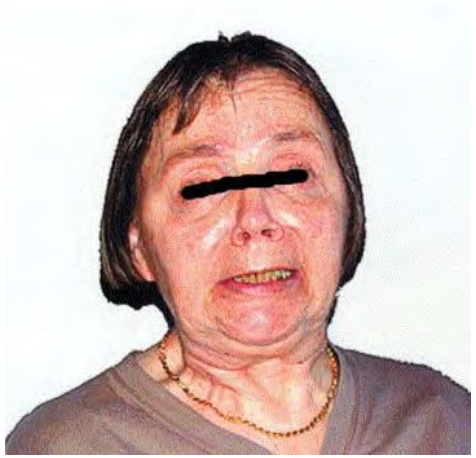
Anamnèse

- Absence de réponse à la L-dopa
- Prise de neuroleptiques (18 mois!!)
- Exposition à des toxiques (MPTP ou autres)
- Histoire de maladie cérébro-vasculaire avec microangiopathie
- TCC répétés
- Encephalite
- Crises oculogyres (neuroleptiques, encephalite)
- Traitement neuroleptique au début des symptômes
- Plus d'un membre de la famille atteint
- Rémission prolongée
- Strictement unilateral après 3 ans
- Progression rapide
- Pas de dyskinésies dopa-induites

Examen

- **Oculomotricité**: Paralysie oculomotrice supranucléaire, Signe de Collier (paupères écatées), signe de la Joconde, blépharoclonus, apraxie ouverture (dystonie), libération des réflexes oculocéphaliques, clinement persistant au réflexe photomoteur répété
- **Ataxie cérébelleuse**
- **Dysautonomie sévère précoce**, TA, sphincters, sexuels, retard du temps de reperfusion ou dyscoloration des doigts
- **Tr cognitivo-comportementuax précoces:** démence précoce avec troubles mnésiques, praxiques, langage, DFT, aphasie, Fluctuations cognitives, hallucinations, tr reconnaissance (Capgras), «Signes frontaux», dépendance à environnement, apraxie unilatérale, main étrangère, dépendance à environnement
- **Signes pyramidaux** de Babinski, clonus (sauf myélopathie)
- **Motoneurone périphérique**
- **Instabilité posturale précoce ou chutes initiales**
- **Dyskinésies** Dystonie: antecollis, laterocollis, retrocollis, dystonie MS, MI, camptocormie, dystonie faciale (asymétrique), myolconies, chorée, jerky tremor
- **Dysarthrophonie**, dysphagie sévère, hypophonie, festination du langage, signes pseudobulbaires, labilité émotionnelle, soupirs inspiratoires, stridor inspiratoire
- **Signe de la chaise roulante**
- **Impossibilité à aller à velo**

MSA



MSA-PD
MSA-C
MSA SD

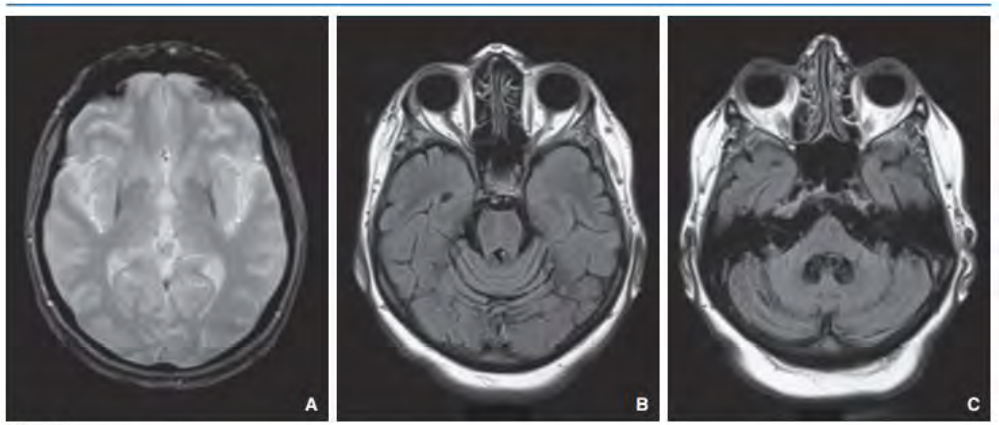
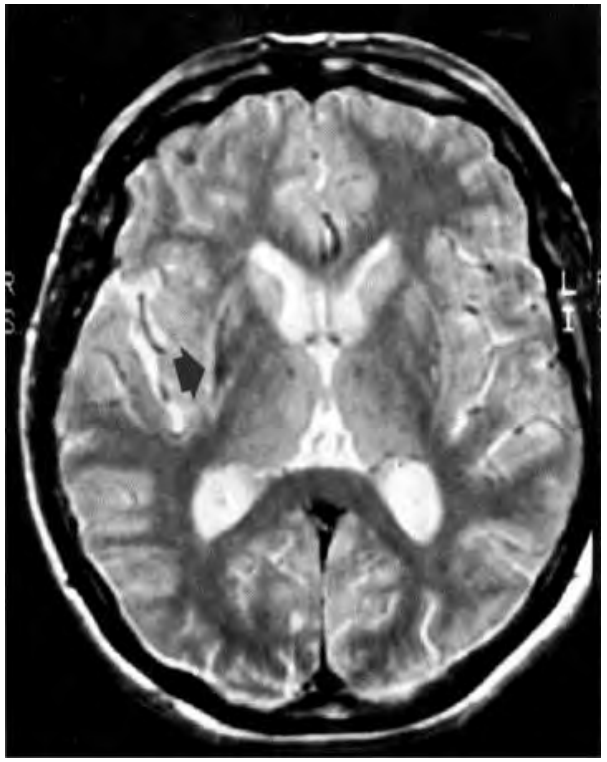
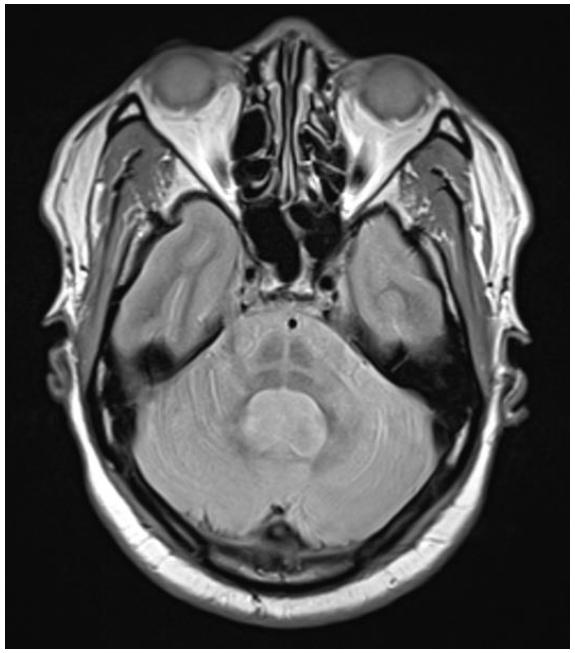
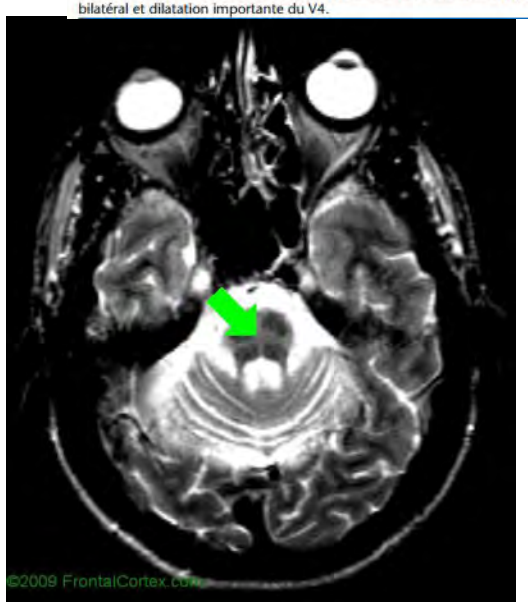


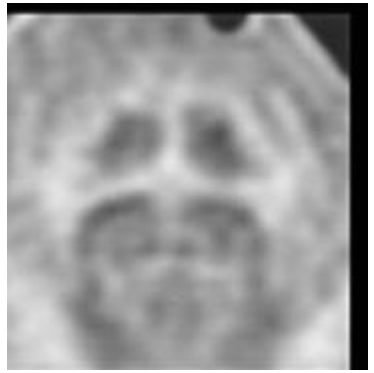
Figure 1.
A. Coupe transversale en séquence pondérée en T2 montrant un hyposignal bilatérale de la partie postérieure du putamen.
B. Coupe transversale en séquence *Fluid attenuated inversion recovery* (FLAIR) montrant un signe de la croix en regard de la protubérance, et atrophie cérébelleuse en regard.
C. Coupe transversale en séquence *Fluid attenuated inversion recovery* (FLAIR) montrant une atrophie des pédoncules cérébelleux moyens avec un hypersignal bilatéral et dilatation importante du V4.

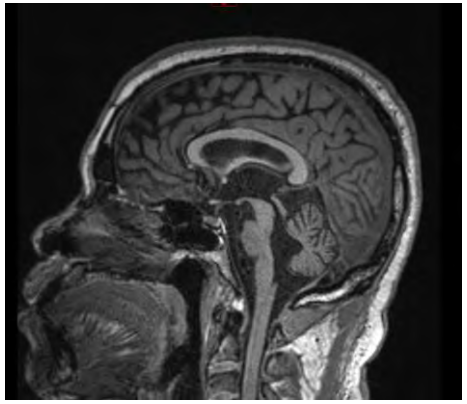




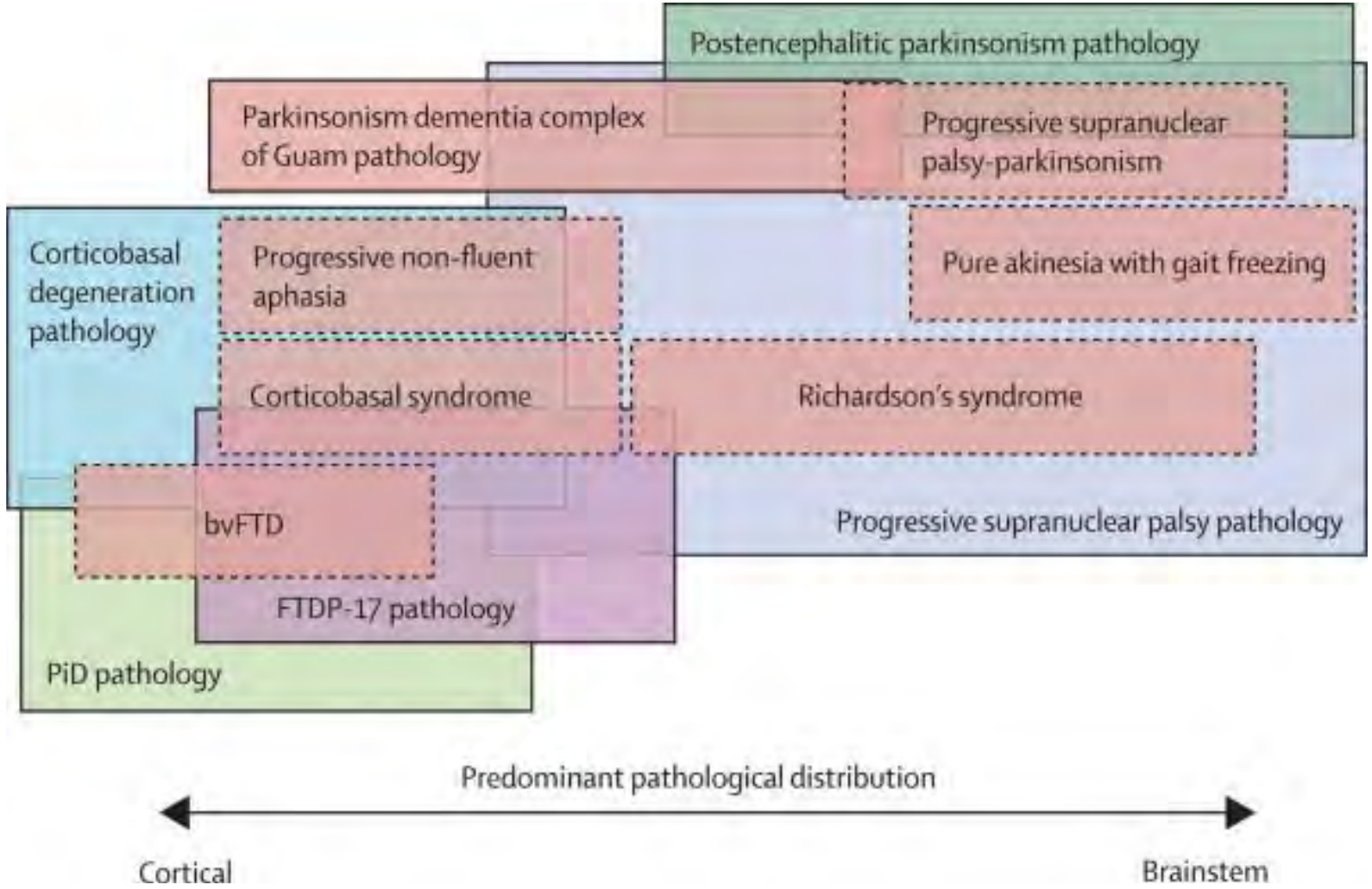
Cross bun sign



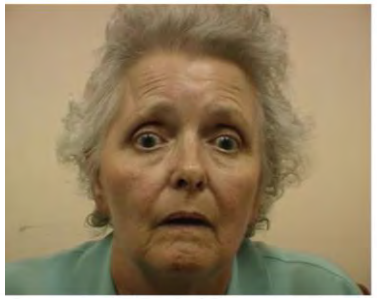




Tauopathies



PSP



Mickey

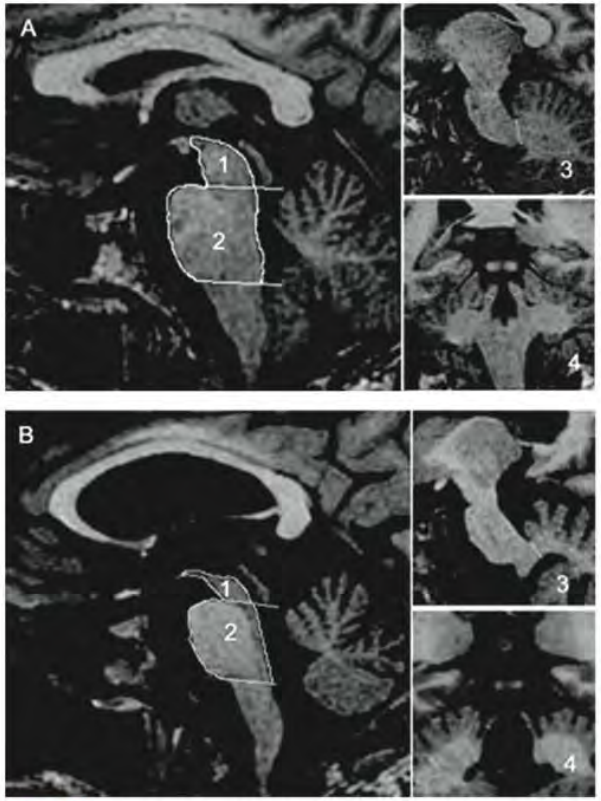


FIGURE 30.2 Sagittal and coronal T1-weighted volumetric spoiled gradient-echo MR images of **(A)** a patient with clinically unclassifiable parkinsonism with normal magnetic resonance parkinsonism index (MRPI) and **(B)** a patient with progressive supranuclear palsy (PSP). There is marked atrophy of both midbrain and superior cerebellar peduncle in the patient with PSP. (Reprinted from Morelli M, Arabia G, Novellino F, et al. MRI measurements predict PSP in unclassifiable parkinsonisms: a cohort study. *Neurology* 2011;77:1042–1047, with permission.)

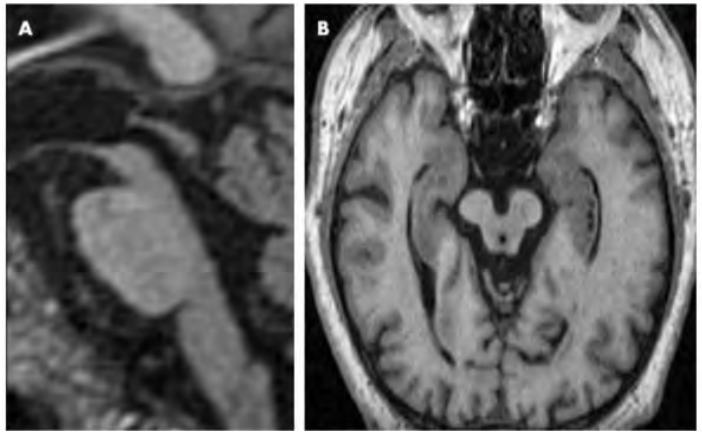
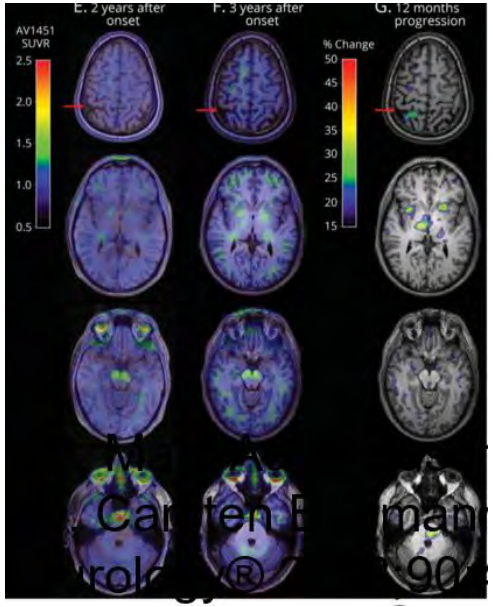
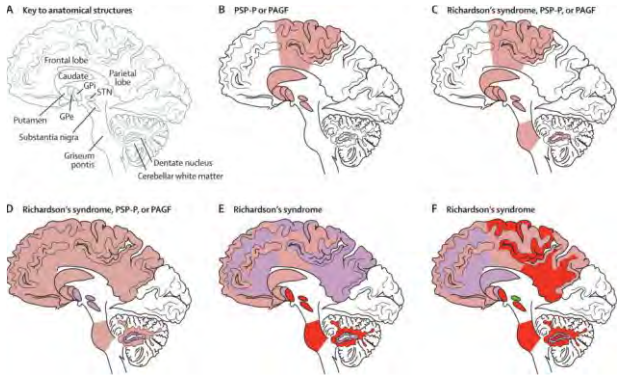


Figure 1
MRI of the brain in clinically definite PSP. (A) Sagittal T1-MRI through the brainstem demonstrating volume loss in the midbrain with relative preservation of the pons. The upper border of the midbrain has lost its normal convex appearance giving it the appearance of a hummingbird (or penguin) in side profile. (B) On axial T1-weighted imaging, the dorsal midbrain is markedly reduced in volume giving rise to a "Mickey Mouse" appearance.



Pet tau

Colibri



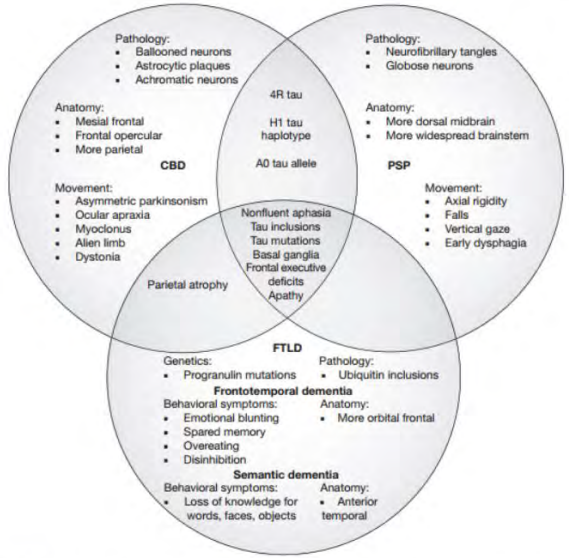
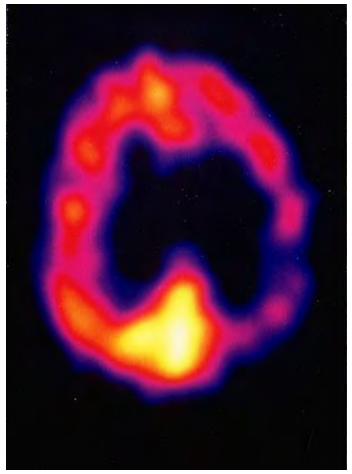
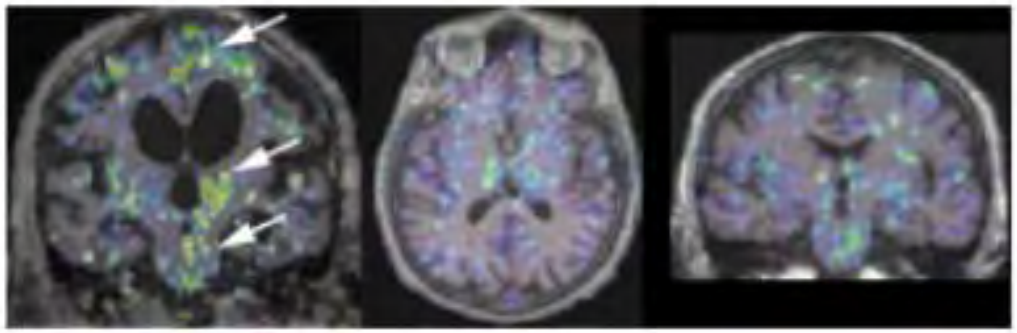
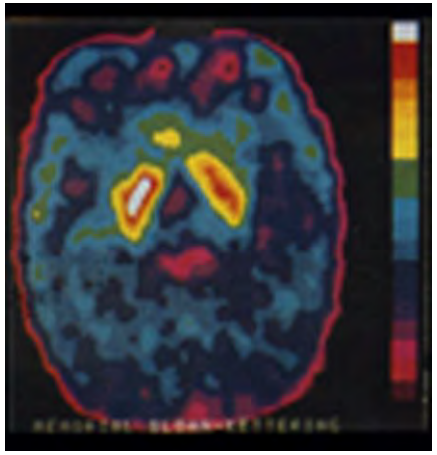


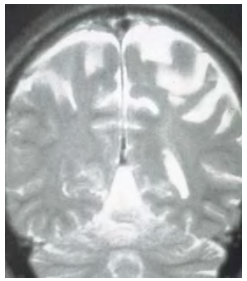
Figure 1 Venn diagram summarizing the similarities and differences between corticobasal degeneration, progressive supranuclear palsy and frontotemporal lobar degeneration. Abbreviations: 4R, four-microtubule repeat; CBD, corticobasal degeneration; FTLD, frontotemporal lobar degeneration; PSP, progressive supranuclear palsy.

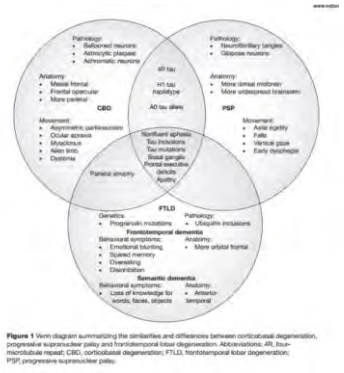
CBD /CBS











CBD
CBS: PPA, PSP overlap, DFT like

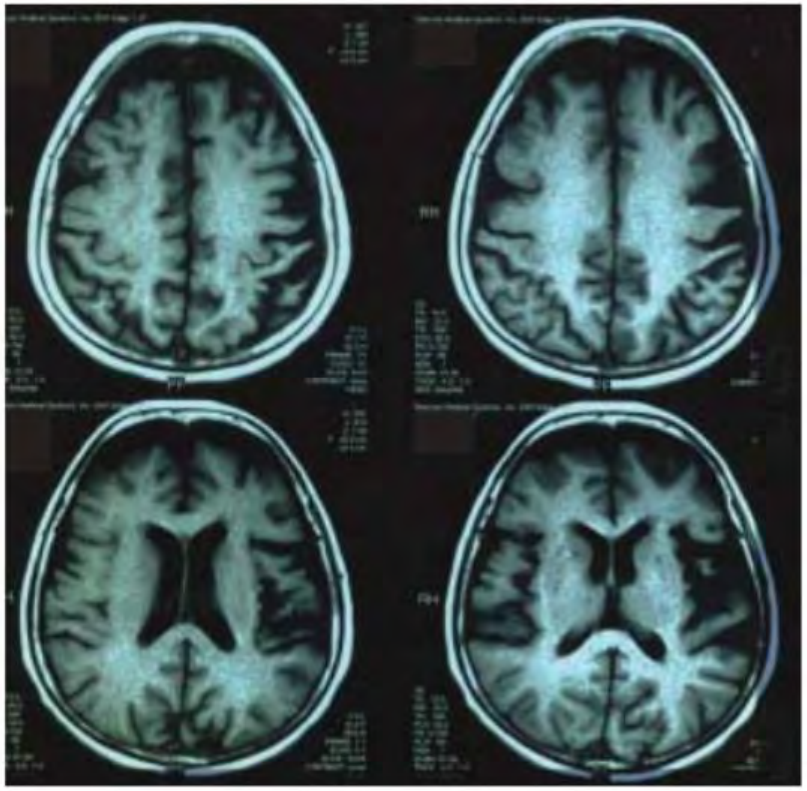


Figure 3 Case and image from Istanbul University, Department of Neurology materials.

Démence à corps de Lewy

Panel 1: Dementia terminology

Lewy body dementias
An umbrella term that includes clinically diagnosed dementia with Lewy bodies and Parkinson's disease dementia.

Dementia with Lewy bodies
Dementia that occurs before or concurrently with parkinsonism or within 1 year of onset of motor symptoms. However, not all patients develop parkinsonism.[2]

Parkinson's disease dementia
Dementia starting 1 year or more after well established Parkinson's disease.[1]

Mild cognitive impairment in Parkinson's disease
Cognitive impairment in patients with Parkinson's disease not sufficient to interfere greatly with functional independence.[1]

Lewy body disease
Pathological diagnosis. The distribution of Lewy body-type pathology and additional pathologies is often specified.

Major and mild neurocognitive disorder with Lewy bodies or due to Parkinson's disease
New terms proposed by DSM-5[4] corresponding to dementia with Lewy bodies and Parkinson's disease dementia.

DSM-5=Diagnostic and Statistical Manual of Mental Disorders, fifth edition.

Walker Z Lancet 2015: 386: 1683-1697

2e cause de démence : 23%
20-25% PD: PD-MCI
80% des Parkinson évoluent vers une démence, 50% à 10 ans, mais l'intervalle diminue avec l'âge
LBD pas rare avant 65 ans
Incidence: 31.6-112/100.000-an au-dessus de 65 ans
Les plus déments ont LBD et AD

Rares formes génétiques AD: LRKK2 et SNCA mutat, triplic
Facteurs de risque: GBA, ApoE4, SCARB2

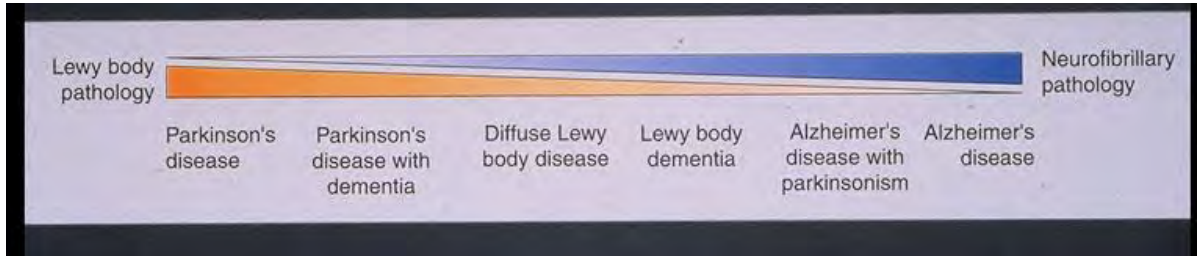


Table 1 Revised[1,2] criteria for the clinical diagnosis of probable and possible dementia with Lewy bodies (DLB)

Essential for a diagnosis of DLB is dementia, defined as a progressive cognitive decline of sufficient magnitude to interfere with normal social or occupational functions, or with usual daily activities. Prominent or persistent memory impairment may not necessarily occur in the early stages but is usually evident with progression. Deficits on tests of attention, executive function, and visuoperceptual ability may be especially prominent and occur early.

Core clinical features (*The first 3 typically occur early and may persist throughout the course.*)

Fluctuating cognition with pronounced variations in attention and alertness.
Recurrent visual hallucinations that are typically well formed and detailed.
REM sleep behavior disorder, *which may precede cognitive decline.*
One or more spontaneous cardinal features of parkinsonism: these are bradykinesia (defined as slowness of movement and decrement in amplitude or speed), rest tremor, or rigidity.

Supportive clinical features

Severe sensitivity to antipsychotic agents; postural instability; repeated falls; syncope or other transient episodes of unresponsiveness; severe autonomic dysfunction, e.g., constipation, orthostatic hypotension, urinary incontinence; hypersomnia; hyposmia; hallucinations in other modalities; systematized delusions; apathy, anxiety, and depression.

Indicative biomarkers

Reduced dopamine transporter uptake in basal ganglia demonstrated by SPECT or PET.
Abnormal (low uptake) ^{123}Iodine-MIBG myocardial scintigraphy.
Polysomnographic confirmation of REM sleep without atonia.

Supportive biomarkers

Relative preservation of medial temporal lobe structures on CT/MRI scan.
Generalized low uptake on SPECT/PET perfusion/metabolism scan with reduced occipital activity ± the cingulate island sign on FDG-PET imaging.
Prominent posterior slow-wave activity on EEG with periodic fluctuations in the pre-alpha/theta range.

Probable DLB can be diagnosed if:

a. Two or more core clinical features of DLB are present, with or without the presence of indicative biomarkers, or

b. Only one core clinical feature is present, but with one or more indicative biomarkers.

Probable DLB should not be diagnosed on the basis of biomarkers alone.

Possible DLB can be diagnosed if:

a. Only one core clinical feature of DLB is present, with no indicative biomarker evidence, or

b. One or more indicative biomarkers is present but there are no core clinical features.

DLB is less likely:

a. In the presence of any other physical illness or brain disorder including cerebrovascular disease, sufficient to account in part or in total for the clinical picture, although these do not exclude a DLB diagnosis and may serve to indicate mixed or multiple pathologies contributing to the clinical presentation, or

b. If parkinsonian features are the only core clinical feature and appear for the first time at a stage of severe dementia.

DLB should be diagnosed when dementia occurs before or concurrently with parkinsonism. The term Parkinson disease dementia (PDD) should be used to describe dementia that occurs in the context of well-established Parkinson disease. In a practice setting the term that is most appropriate to the clinical situation should be used and generic terms such as Lewy body disease are often helpful. In research studies in which distinction needs to be made between DLB and PDD, the existing 1-year rule between the onset of dementia and parkinsonism continues to be recommended.

McKeith I Lancet Neurol 2004: 3: 19-28

Avant : Sensibilité: 32%, spécificité 93%
Version révisée: sensib: 56%

Pas toutes les DLB développent un parkinson
DD AD

Critères valables seulement en début de LB
Fort potentiel:
RBD
Fluctuations au début
Hallucinations visuelles
Tr odorat
Tr dysautonomiques
EEG brady
SPECT MIBG, DAT

Lewy body dementia

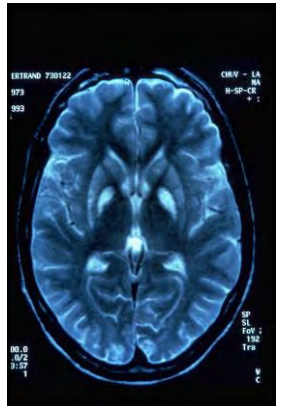
- MRI to evaluate pattern of atrophy and nondegenerative lesions (mimics)
- AD molecular biomarkers (CSF or PET) to test for mixed disease if atrophy patterns or clinical features are suggestive
- In-laboratory sleep study to evaluate for REM sleep without atonia; may also find evidence of dream-enactment behaviour on video recording

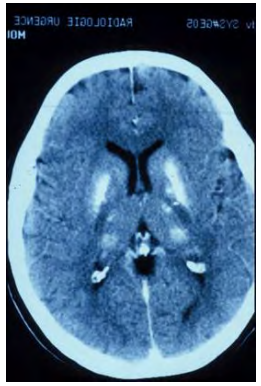
Mc Keith I Neurology 2017: 89: 88-100

Walker Z Lancet 2015: 386: 1683-1697

Imagerie CT, IRM:DD

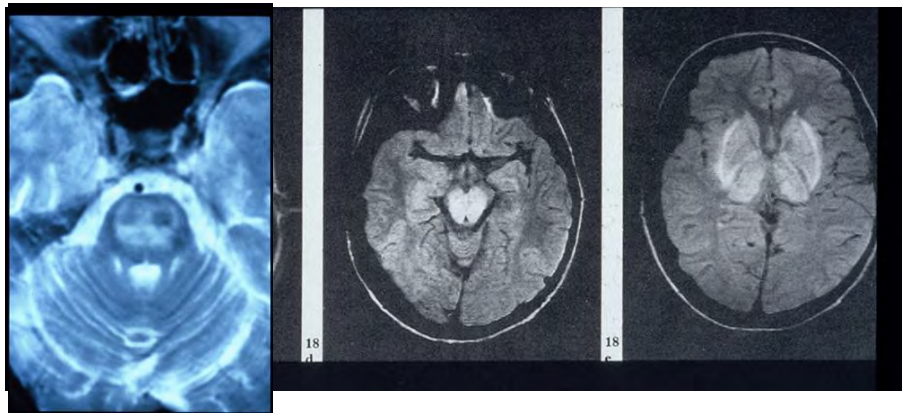
Anoxie CO



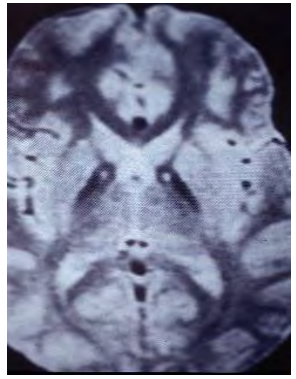


Hyperpara

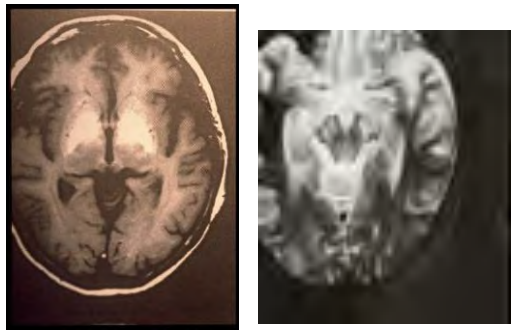
Hydrocephalie



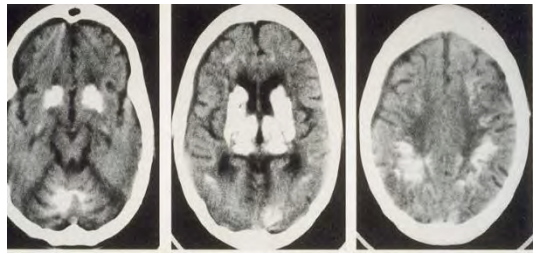
Wilson (panda)



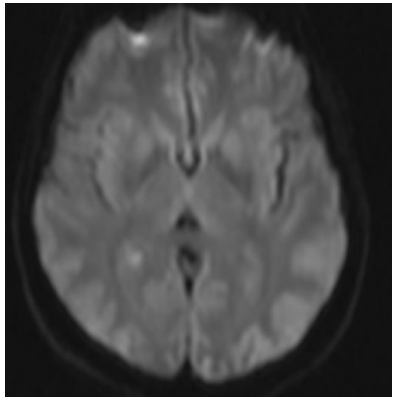
PKAN eyes of the tiger



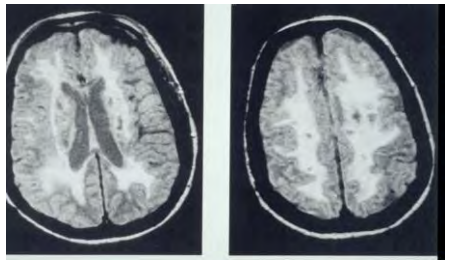
Mn



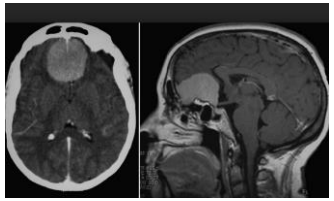
Fahr



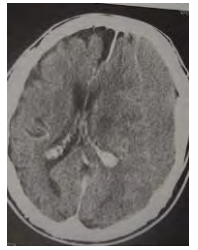
CJD



vasculaire

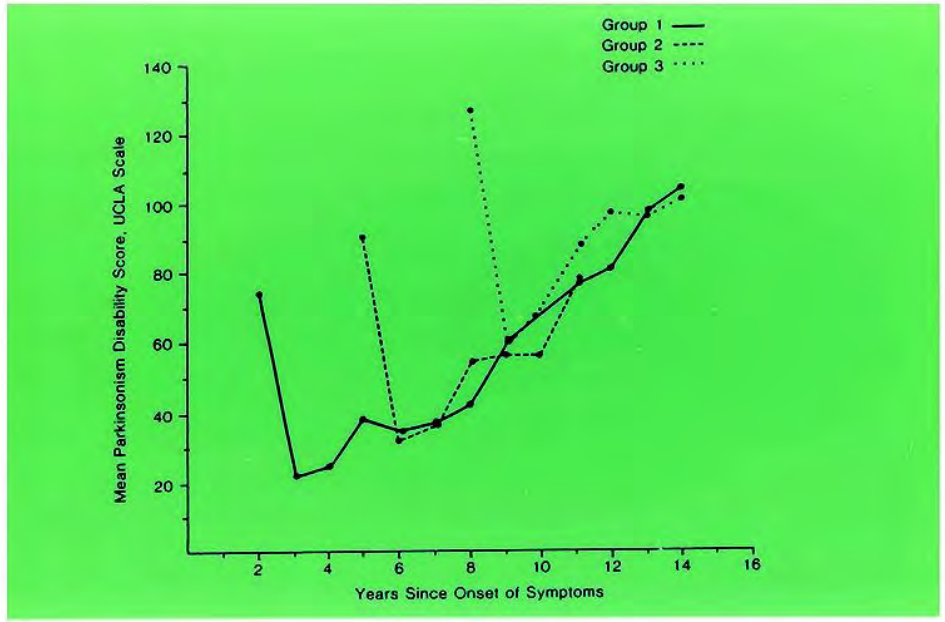


PEIC

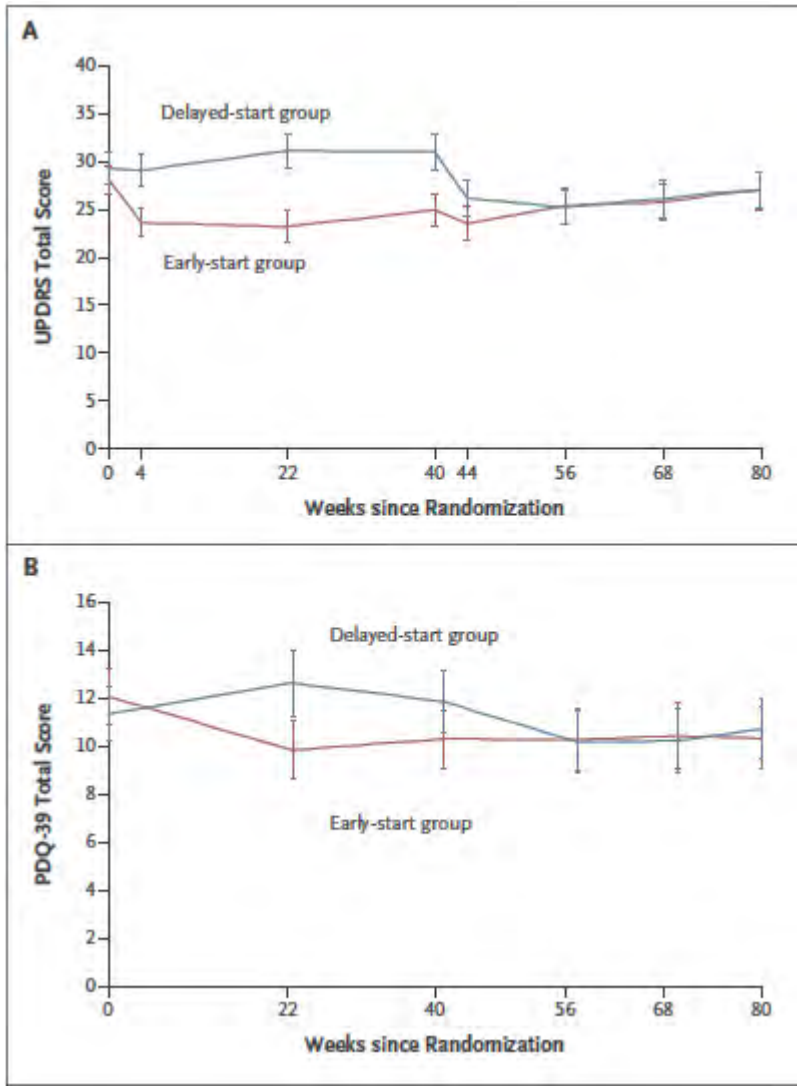


Sous-dural

Quand instaurer le traitement?



Markham and Diamond Neurology 1981



Lorsque gêné dans les AVQ ou style de vie

Verschuur al NEJM 2019

TRAITEMENT ANTIPARKINSONIEN

- **PREVENTIF** (neuroprotection): prévention primaire

- **RESTAURATEUR** (neurorestauration) : disease modifying causal

- **SUBSTITUTIF**: symptomatique

  DOPAMINE : PRECUSEUR: L-DOPA

  AGONISTE

  MODULATEUR METAB.

  NON DOPAMINERGIQUE

- **ELECTROCORRECTEUR**: (DBS): symptomatique

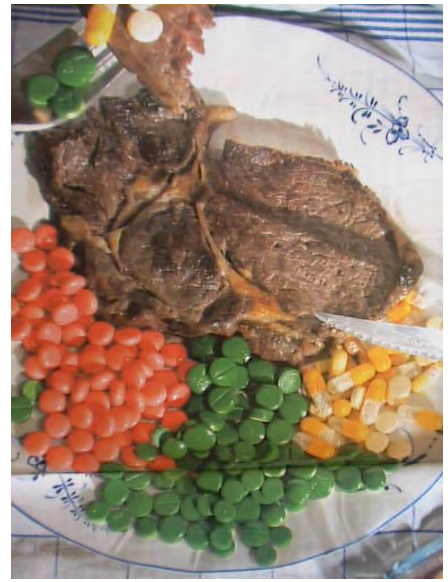
Neuroprotection?

Amantadine

Agonistes dopaminergiques

Anti-apoptotiques

•CEP1347 Mixed lineage kinase, TCH346: GAPDH :pas d'effet



DBS précoce

Coenzyme Q 10

Vitamine E

IMAOB
Rasagiline?

Traitement substitutif

IMAO B
(selegiline)
rasagiline

Antidyskinetiq
ues/freezing
Safinamide,
amantadineg

L-dopa
Formes standards L-dopa/bensérazide
L-dopa/carbidopa
Formes retard DR, CR
Formes dispersibles
Formes duodénales
Formes combinées avec IMAO B

ICOMT
tolcapone
entacapone

Agonistes de dopamine:
(Ergot: Pergolide, cabergoline, bromocriptine..)
Non ergot: Pramipexole ER
Ropinirole Modutabs
Rotigotine: patch

Amantadine

Par quoi débuter

- **<75 ans**: ttt mixte, L-dopa et petite dose agoniste dopa retard selon niveau d'activité, prévenir dyskinésies
- Rasagiline (Azilect) 1mg: pas suffisant
- Agoniste dopaminergique non dérivé de ergotamine: cave fortes doses, impulsivité

  Rotigotine (Neupro): patch

  Pramipexole (Sifrol)

  Ropinirole (Réquip)

  Rajouter au début domperidone (Motilium) contre effets secondaires

  Moins efficaces que L-dopa, mais moins de dyskinésies à long terme

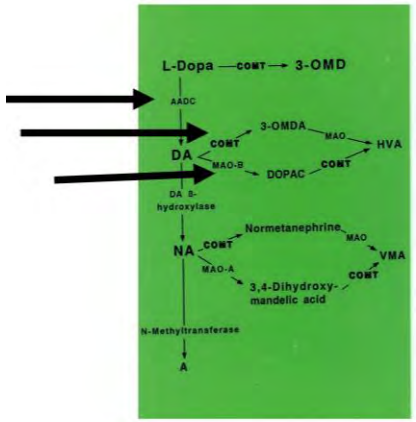
  Abandonnés ou echocardiographie annuelle obligatoire: cabergoline, pergolide, bromocriptine: dégénérescence des valves cardiaques
- Amantadine (Symmetrel, PK Merz, amantadine..) pue efficace seule

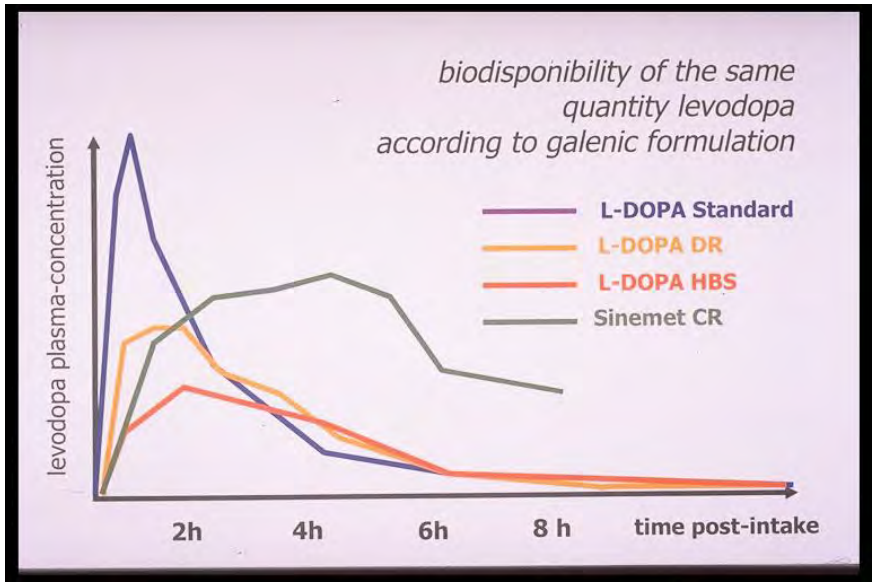
- Combinaisons (rasagiline+ agoniste dopamine, L-dopa+agoniste (jamais L-dopa seule)..

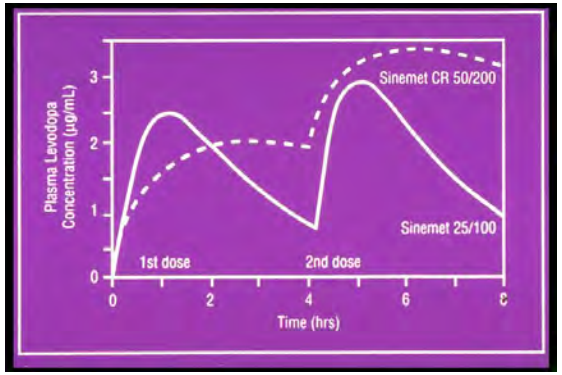
- **>75 ans**: L-dopa (formulation longue durée CR ou DR ? ou formules mixtes (Stalevo): L-dopa/carbidopa/entecapone
  Eviter les agonistes dopaminergiques si risque de confusion

L-dopa

- Larodopa: grammes!
- + benserazide (Madopar R) ou carbidopa (Sinemet R/levodpa-carbidopa)
- Formes slow release : Madopar DR, Sinemet CR
- Formes à libération rapide Madopar Liq
- Formes mixtes avec ICOMT: Stalevo: 50/100/150



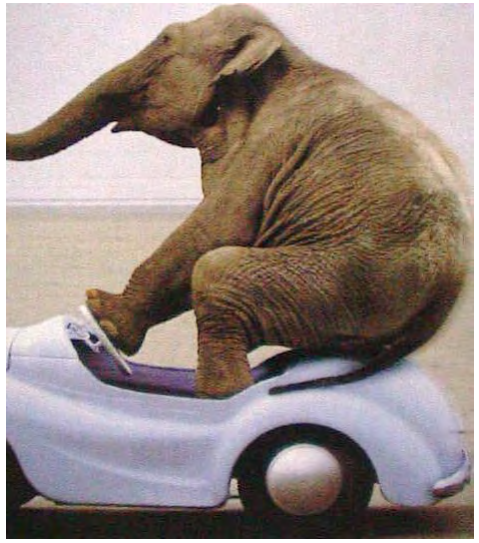


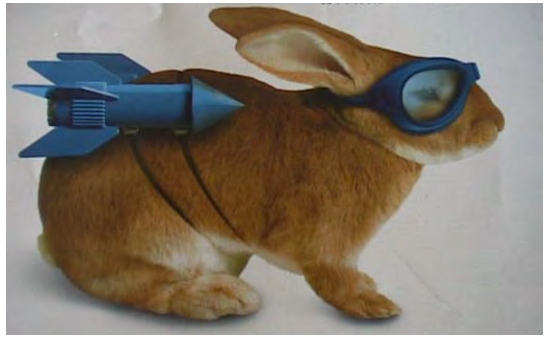


Effet tuile avec les retards

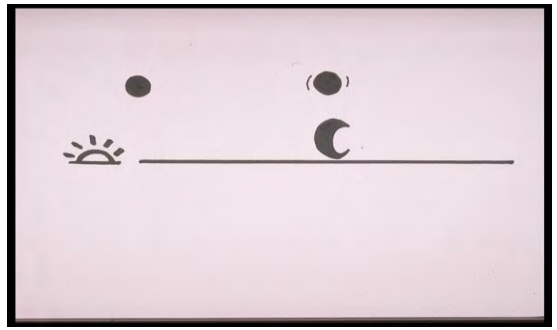
Non formattable: médecine personnalisée

Patient
Son ecosystème

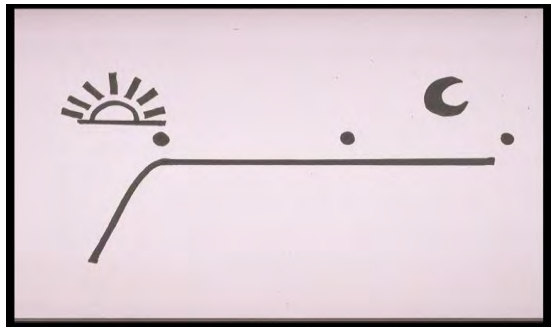




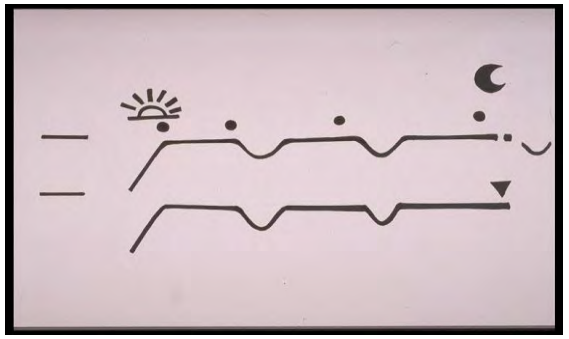
Fluctuations motrices/non motrices



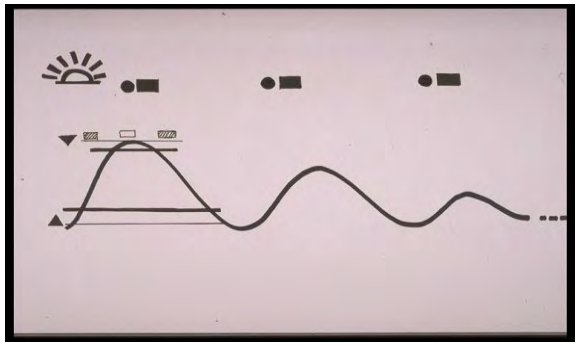
Honeymoon



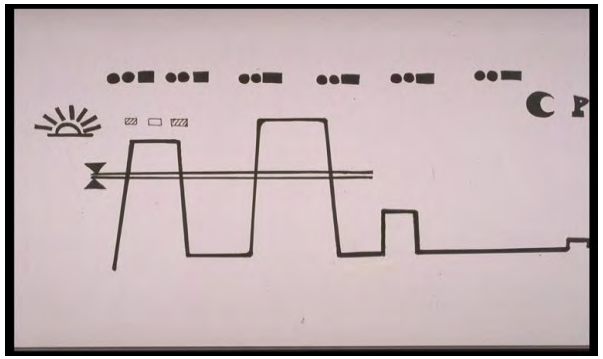
Akinésie matinale



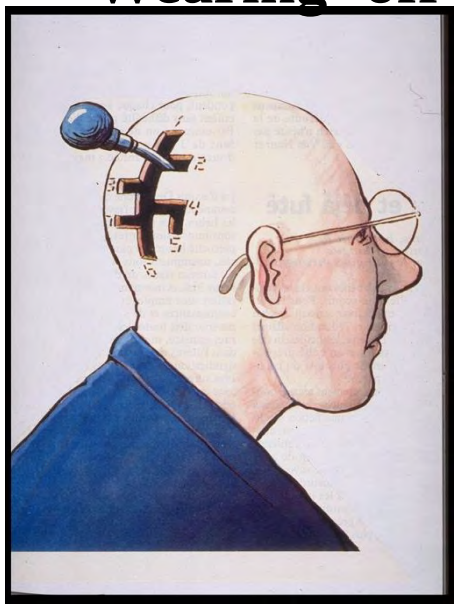
Wearing -off



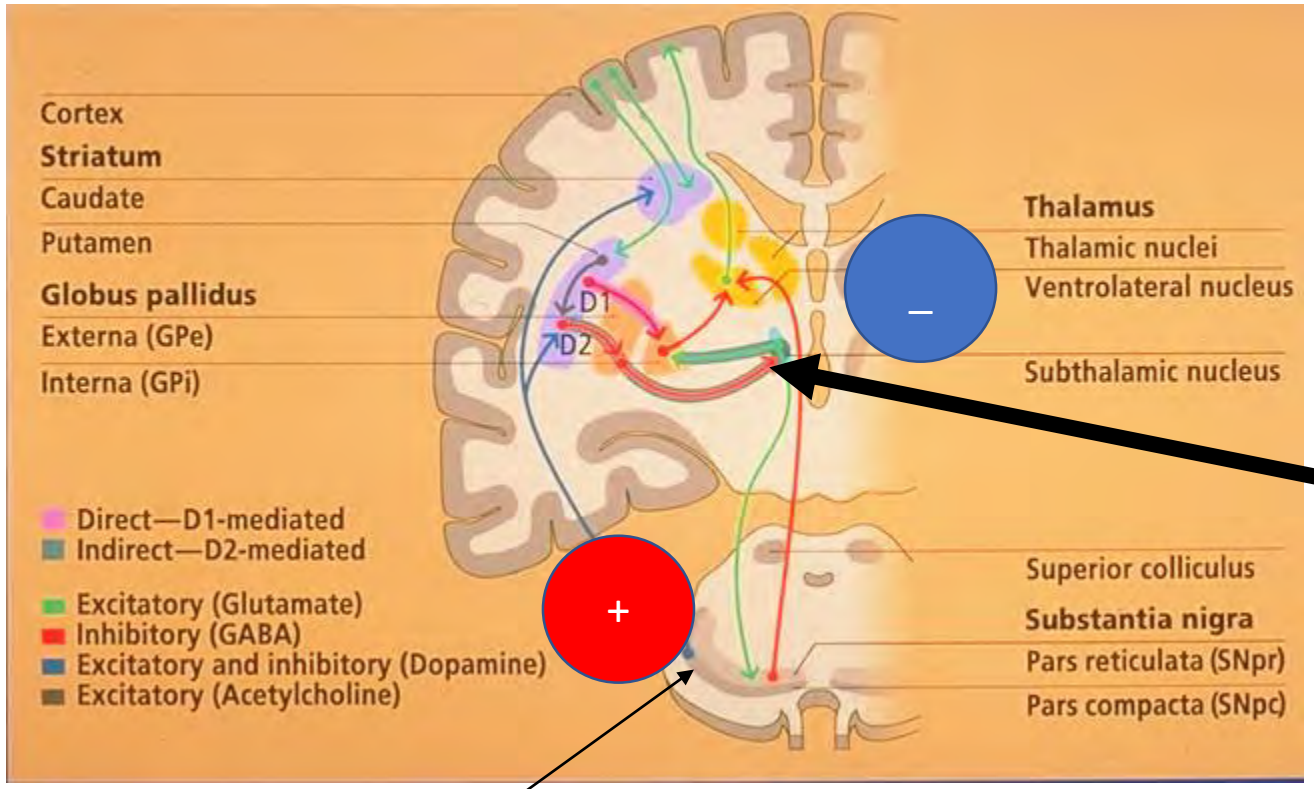
On-off



Yoyoing



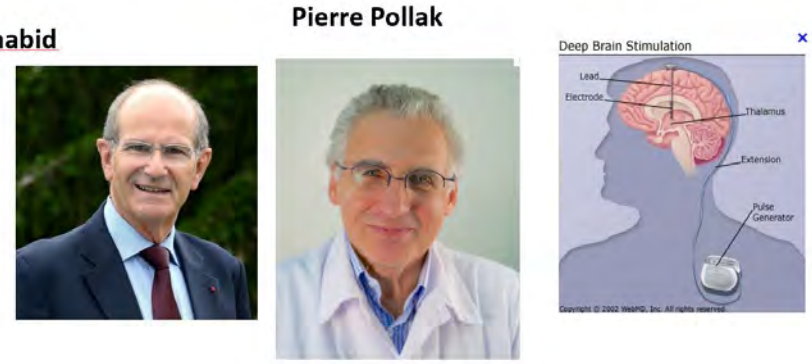
Noyaux gris



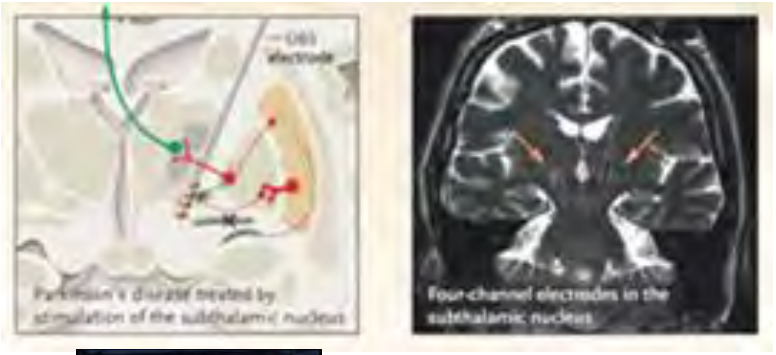
Noyau sous-thalamique:
frein des mouvements
« blocages »:
Hyperactif: arrêté par stimulation électrique (chirurgie)

Substance noire: « accelérateur » des mouvements
« dyskinésies »: dégénère progressivement: traitement substitutif (médicaments)

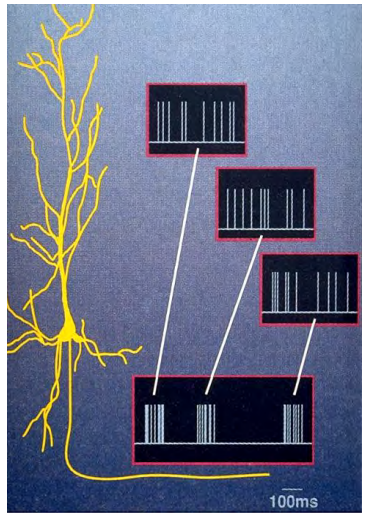
Chirurgie stéréotaxique



- **Indications**
- PD dopasensible (30% réponse) : predicteur de réponse, au stade fluctuations, Précoce?
- Non dément, pas de troubles psy (dépression, psychose)
- Pas de maladies graves
- Pas de troubles axiaux (marche, freezing on, dysrathrie sévère)
- Moins de 70 ans (plus jeune meilleure réponse)
- AVQ sévères moins bon pronostic
- Compliance

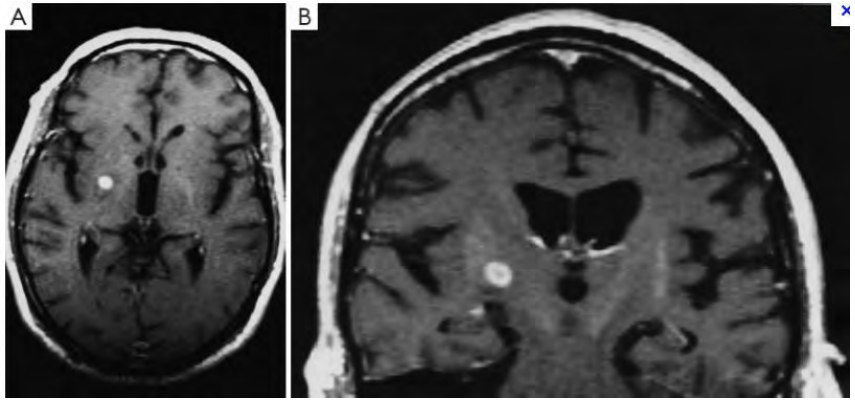


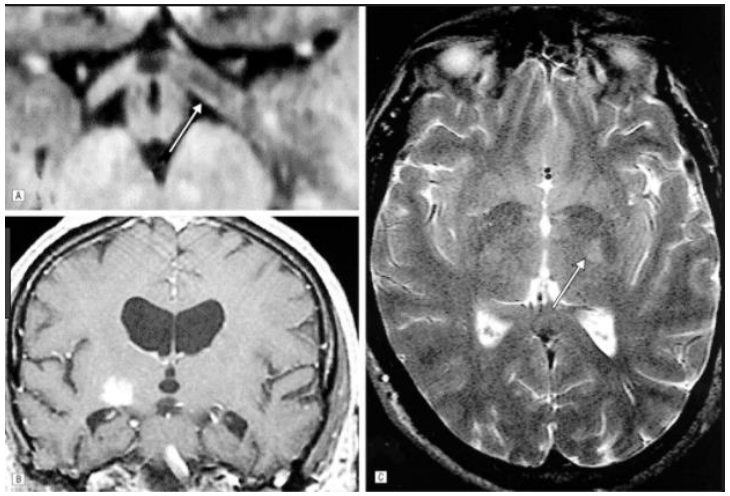
- **Effets secondaires:**
- **Graves:**
- Hématome: hemiplégie: 1-3%
- Infection: 1%
- Mortalité: 0.5 %
- **Morbidité:**
- Confusion postop. transitoire: 15%
- Dysarthrie: 9%
- Fuite LCR<1%
- Rupture matériel, migration, malfonction 5%
- Repositionnement 5%
- Dépression réversible 20%, suicide)
- Impulsivité (jeu pathologique, hypersexualité…)
- Troubles comportementaux: apathie
- Prise de poids 8%
- Tr cognitifs: si hematome ou infection ou démence
- Blepharospasme 3-4%, contractures faciales
- Impact sur le couple: redistribution



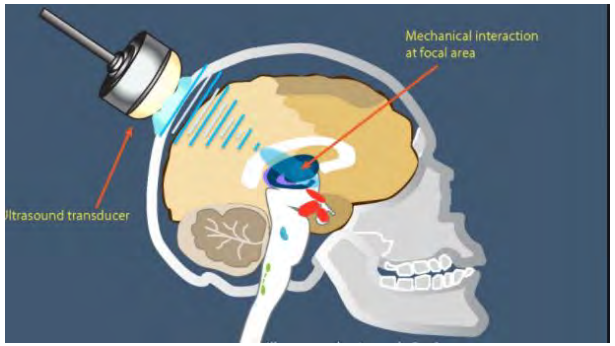
Ultrasons, gamma knife, lésions

Pallidotomie

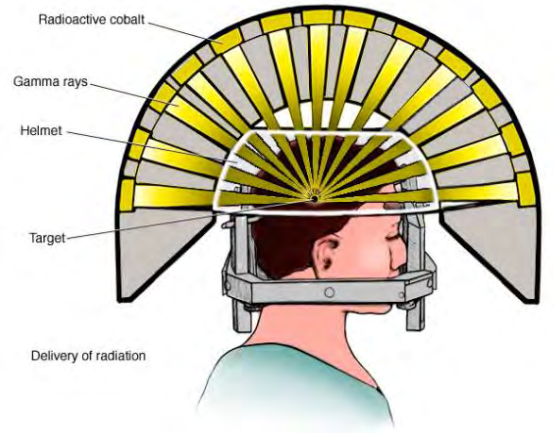




US



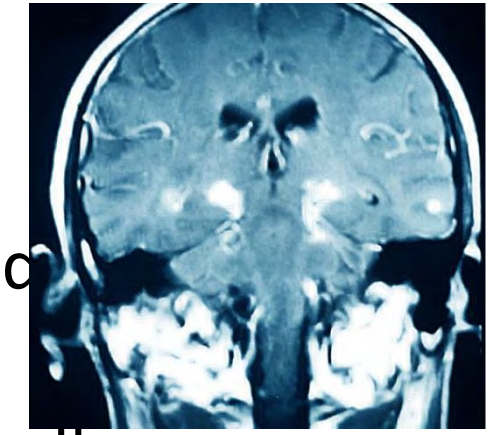
Gamma knife

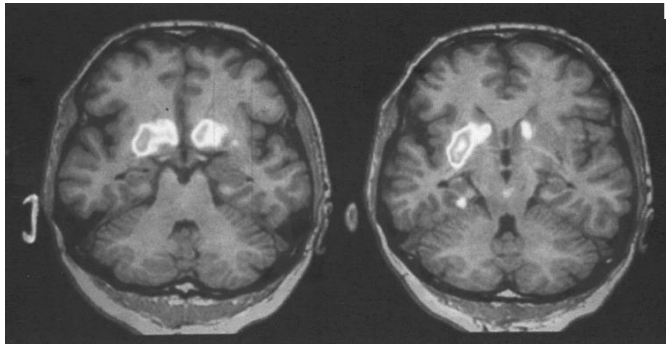


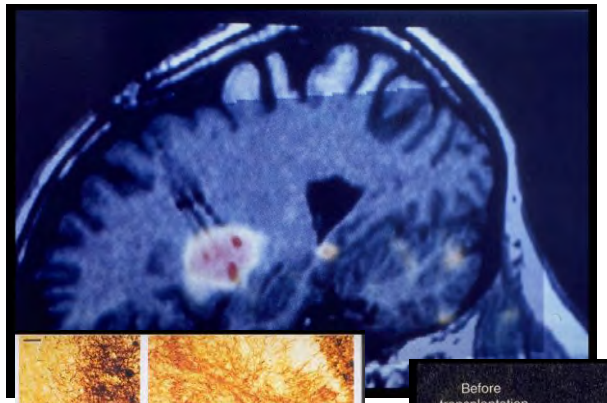
Greffes

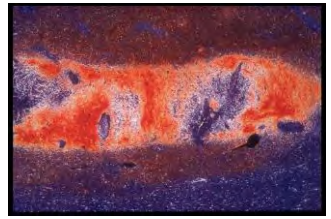
1970

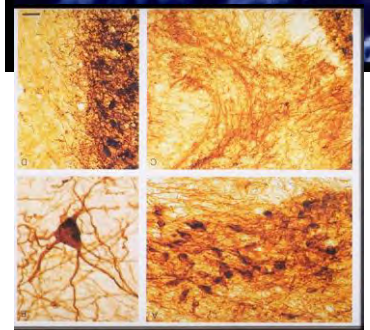
- Greffe de surrénale: Machado Mexique
- 1979: greffe fœtale: O Lindvall , A Björklund Lund
- USA: dyskinésies irrépressibles

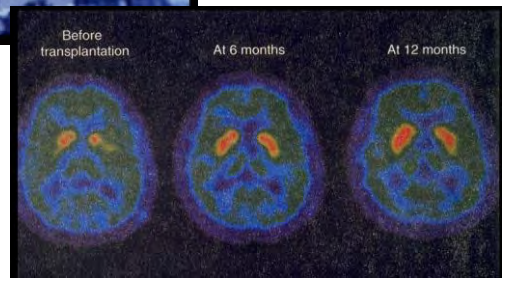


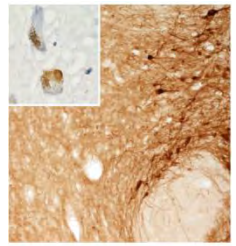




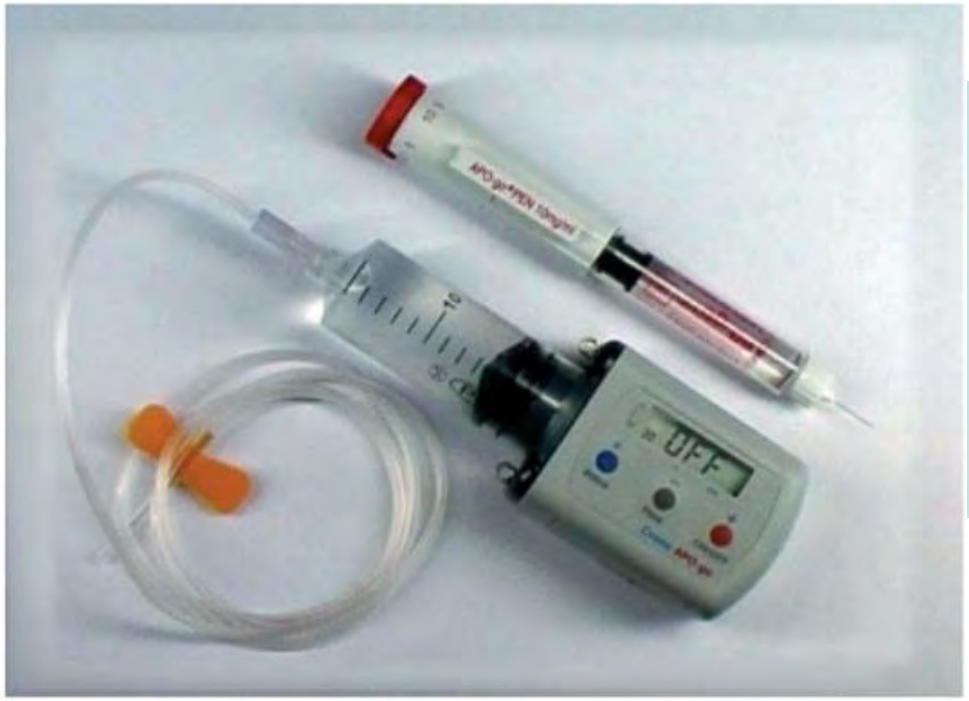








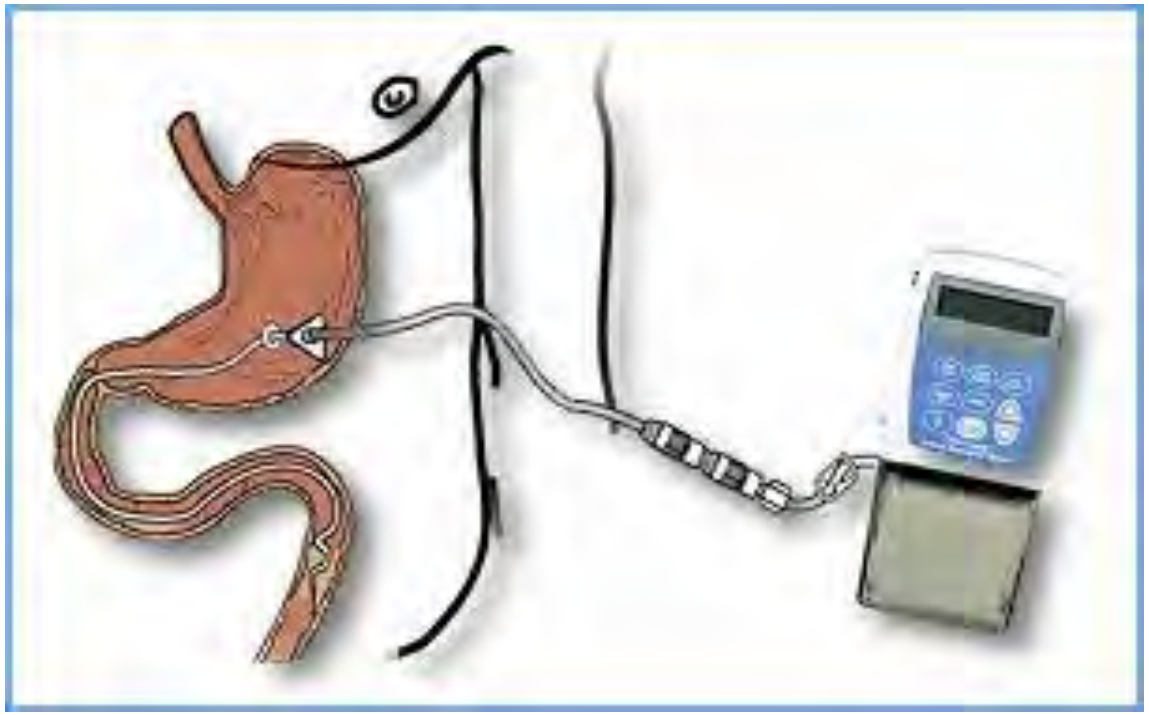
Apomorphine



Lees A Pratc Neurol 2002; 2; 280-287

Les alternatives lourdes

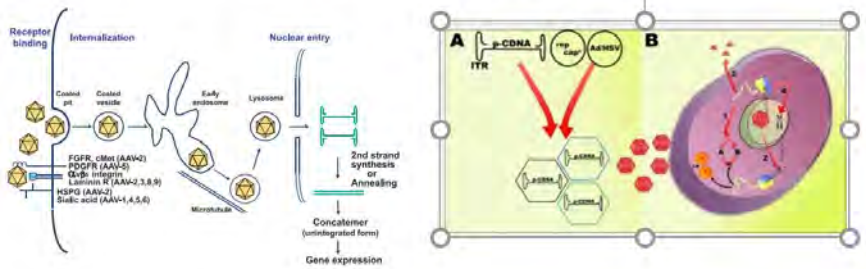
Apomorphine sc



Duodopa

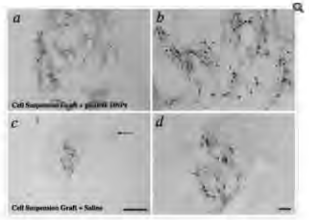
Futur

Transfection virales: lentivirus, AAV



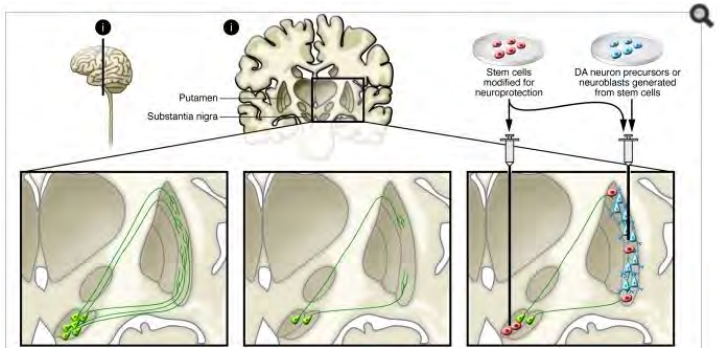
Nanomolécules

1-100 nm
Nanomatériaux
Agissent au niveau moléculaire



- Prévention?
- Image
- Ttt: délivrer médicaments de façon ciblée sur neurotransmetteurs… ?
- Biolabelling: dopamine loaded chitosan molecules : fluorecsence

Cellules souches



Inhibiteurs des proteasomes
SiRNA
Peptides anti aggrégation de molecules
Modulateurs de chaperones….

Dépression: 30-60% , anxiété

- **Eviter les tricycliques**: amitryptiline, nortryptiline, désipramine, **si troubles cognitifs**
- **Eviter trazodone (Tittico R)**

- **SSRI**: **le meilleur sertraline** le soir 50-100 (150 mg), fluoxetine 20-40 mg, paroxetin 20-40 mg, fluvoxamine

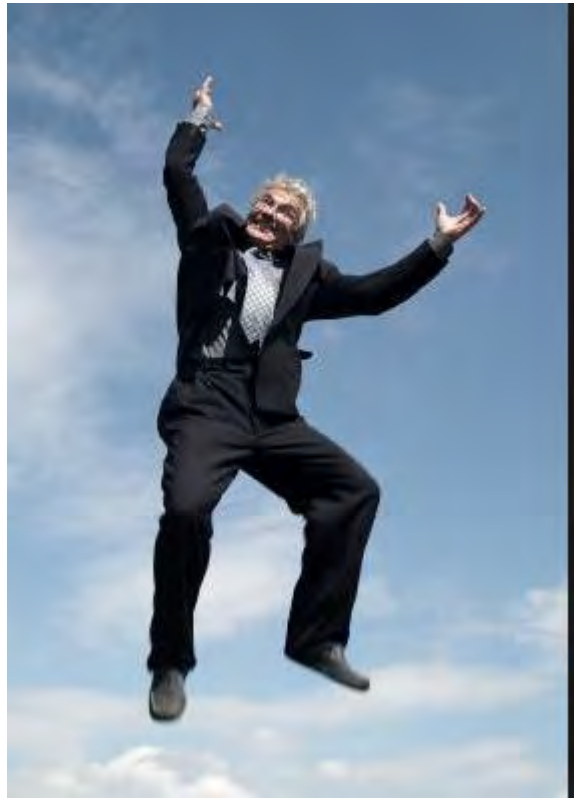
  Cave! SSRI + selegiline ou rasagiline : syndrome serotonergique crise hypertensive

- **SNRI** venlafaxine 2x 37.5-75 mg
- **Noradrenergic (alpha 2):** mirtazapine, reboxetine
- **Buproprion:** Wallbutrin R
- **ECT**
- **Swinging moods**: topiramate, vaproate, SNRI, SSRI
- Phobie sociale (sous estimée): SSRI, pregabaline, (moclobemide)
- Benzodiazépine (béta boquants)

Etats maniaques

- Surtout dans swinging moods, surdosage L-dopa

- TTT: Diminuer médication
- DBS
- Lithium ? Topiramate Valproate, lamotrigine

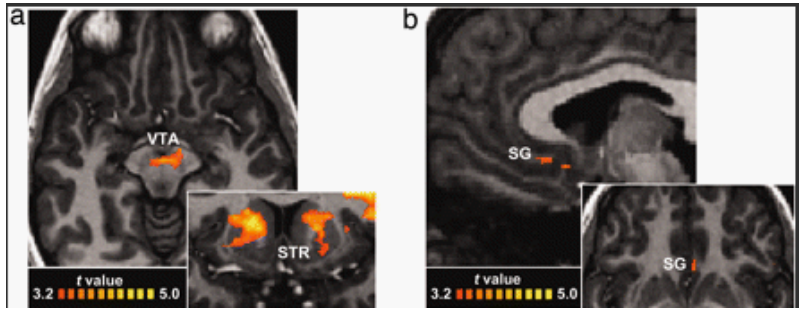


Dysfonction du système de récompense

- **Hypofonction**:
- Perte du plaisir (anhedonia)
- Emoussement affectif
- Apathie, depression.
- Personnalité: rigide,stoïque, persistant, ordré, obsessionnel, non toxico, ne recherche pas la nouveauté, sensation

Hyperfonction: **impulsivité** L Dopa, DBS: hypersexuality, jeu pathologique (hyperimpulsivité)…
Hypersexualité
Jeu pathologique
Achats compulsifs
TOC
Punding

TTT: Diminuer médication , DBS
SSRI, clozapine (Leponex)



Tr cognitifs: rivastigmine

- **PD MCI 30-80%**
- **Syndrome dysexecutif**: 20-40% planification, stratégies, maintien et shift attentionnel, attention divisée, fluence verbale, résolution de problèmes, rapidité mentale (bradyphrénie, inertie, rotation mentale, scanning, fluence et production), effort, sensibilité à la charge,
- **Mémoire**: immédiate et de travail diminuée, épisodique: difficulté de rappel, mot sur le bout de la langue, aidé par indiçage, verbale et visuo-spatiale, mémoire procédurale spécifiquement touche précocément, dyschronologie (anamnèse !)
- **Troubles visuo-spatiaux**: discrimination, reconnaissance, intégration, planification visuo-motrice, attention visuospatiale, mémoire visuo-spatiale
- **Perception et expression des signaux émotionnels**: prosodie, mimique, sémantique cerveau social)

Etat confusionnel,hallucinations, délire

- **Hallucinations, illusions (25-40%): bénignes:** « présence », »pourtour », « passage », illusions,
- **Hallucinations malignes:** visages, personnages, animaux…

Assoc: médicaments et démence débutante : PDD, LBD

- Délires construits
- Pensée désorganisée
- Comportement anormal
- Fausses reconnaissances, Capgras…

- Entrée dans la démence…
- Quetipaine, clozapine, aripiprazole (pamavansérine)

TT

Traiter infection déshydratation, électrolytes, corriger les troubles métaboliques

- **Enlever les médicaments aggravants** (sédatifs, anxiolytiques, anticholinergiques…)
- **Diminuer graduellement la médication antiparkinsonienne dans l'ordre**: anticholinergiques, amantadine, selegiline, rasagiline, agonistes de dopamine puis la L-dopa

- **Inhibiteurs de la cholinesterase :**donepezil, rivastigmine ou galanthamine

- **Neuroleptiques dernière génération** :Clozapine: 25-50 mg, quetiapine 12.5-50 mg, aripiprazole 5 mg

Symptômes non moteurs

- Cognitifs (PDMCI-démence) : 80%
- Dysautonomiques: 60% salivation, séborrhée, hypoTA, sudations, sphinctériens, sexuels
- Neuropsychiatriques: 40%
- Fatigue: 40%
- Sommeil: 35%
- Douleurs: 30%
- Dysphagie-dysarthrie: 25%
- Neurosensoriels 20%
- Tr sommeil 75%
- Gastrointestinaux: 80%: constipation, gastroparésie

Apathie

- 12-30%
- Amantadine, Dopamine agonists , L-dopa?
- SSRI
- Buproprione (Wellbutrin)
- Abilify

Fatigue: 40%

- Régler le sommeil, dépression, sédatifs
- Amantadine
- Agonistes de dopamine
- (amphétamines (Ritaline R, Modafinil, Xyrem)
- Buproprione? (Wellbutrin R)

Conclusion

- Parkinson dopa sensible ou doparésistant
- Typique ou atypique (red flags)
- Evolution simple
- Parkinson problématique
- Formes génétiques


That's all Folks!