4th International Congress on the Improvement of the Quality of Life on Dementia, Epilepsy, MS and Peripheral Neuropathies

PARKINSON'S DISEASE AND DEMENTIA - SPECIAL MANAGEMENT IN REHABILITATION

F. Gerstenbrand, W. Struhal

Dementia is not a regular complication in Parkinson's disease, mostly observed in a later state. As the origin of dementia in Parkinsons's Disease a primary lesion of ganglia cells and as a second factor vascular circulatory disturbances in connection with low blood pressure are discussed. A great number of Parkinson's patients are showing a special personality structure with the main sign of an obsessive personality, in the German literature called as an anancasm, irritating the management of treatment. Some leading historical personalities like Mao Tse Tung, Adolf Hitler, Generalissimo Franco and others, showing the typical anancastic traits with mental rigidity as the main symptom.

Worldwide four million patients are suffering by an idiopathic Parkinson syndrome, with a mean age of 62 and 65 years, and 5 % to 10 % patients lower than 40 years. Loss of dopamine neurons in the substantia nigra as pathogenetic basis generally is accepted. In the course of Parkinson disease a symptom free phase and the presymptomatic state, as the period of dopaminergic neuron deterioration, followed by the phase of onset of symptoms, undiagnosed or misdiagnosed up to 2 years. Since the dopa treatment era 3 phases can be differentiated, the phases of controllable symptoms (honeymoon period - 5 years), the phase of motor complications (5 years), the drug insufficient phase with upcoming of dementia (3 - 5 years). The therapeutic window is continuously diminished.

Principal objectives of the treatment in patients with Parkinson's disease are compensation of symptoms. In the treatment of Parkinsons's patients the three columns are substitution of the dopamine deficit (dopaminergic drugs etc.), a special physiotherapeutic program and a psychogenic guided management. The treatment of dementia has to be included in the therapeutic programme. Treating from the view of the patient leads in the successful therapeutic programme, minimum of side effects and avoidance of complica-

tions, extent of the controlled course of the disease, collecting reserves in treatable drugs and the hope to be cured or to be improved.

The motoric disabilities (wearing off symptoms, dyskinesia) bring severe molestation, the patient needs intensive psychological care including his relatives. In the third phase the system of the therapeutic community is a great help. The amelioration of quality of life is the ethical background.

With the start of decline in the drug influence and at the beginning of symptoms of dementia the aim is to continue the home care with the possibility of short treatment phases in special neurological departments. Only in the case of severe motoric disabilities and in decompensation of the mental state Parkinson's patients need a nursing home care or have to be brought in a neurological department with special experience.

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4th International Congress
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&
ABSTRACT BOOK

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Parkinson´s disease and dementia

Special management in rehabilitation

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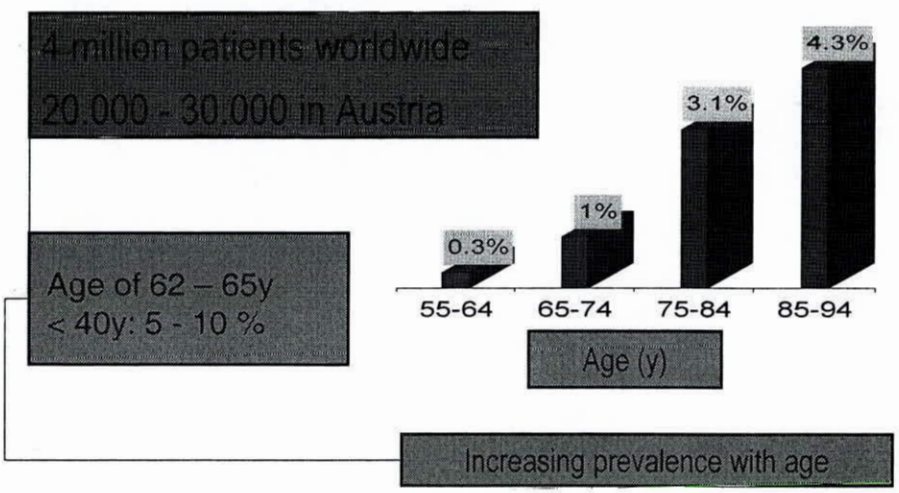
Epidemiology of Parkinson's disease



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Different clinical forms of PD

(Barbeau, 1982, Gerstenbrand, 1983)

- Acinetic-rigid type
- Equivalent type
- Tremor-dominant type

- Old-age type (Alters-Parkinson)

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Causes and Risk Factors of Ideopathic Parkinson Syndrome (IPS)

- Age
- Gene analysis
  - α - Synuclein, Parkin
- Neurotoxins
  - environment
  - Methyl - Phenyl - Tetrahydro - Pyridine (MPTP)
  - Carbonmonoxid, Mangan, Cyanid

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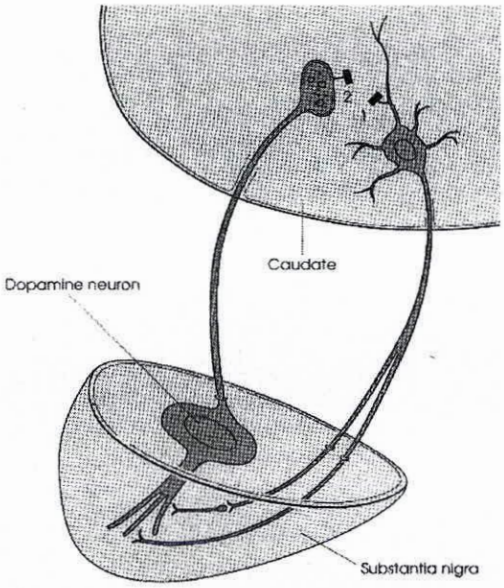
Pathogenetic basis



Loss of Dopamine

Post mortem:

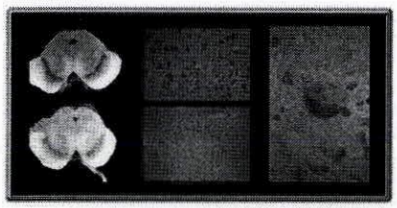
> 90 %

Main symptoms:

70 - 80 %

" asymptomatic " :

< 50 %



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Pathogenesis of Parkinson's disease

- Loss of dopamine in striatum
  - Asymptomatic (mot.): < 50 %
  - Cardinal symptoms: 70 - 80 %
  - Post mortem: > 90 %

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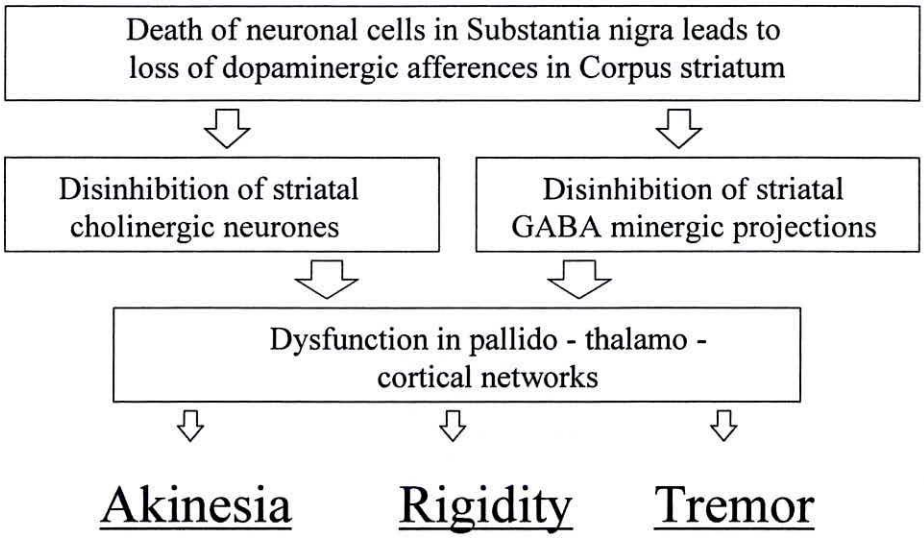
Pathogenesis of Parkinson - Syndrome



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Classification of Parkinson - Syndrome

- Idiopathic PS (80 - 85 %)
- Atypical PS (4 - 5 %)
  - MSA
  - PSP
  - CBGD
- Secondary PS (10 - 15 %)
- Pseudo-PS

modif. n. W. Poewe, 1996.

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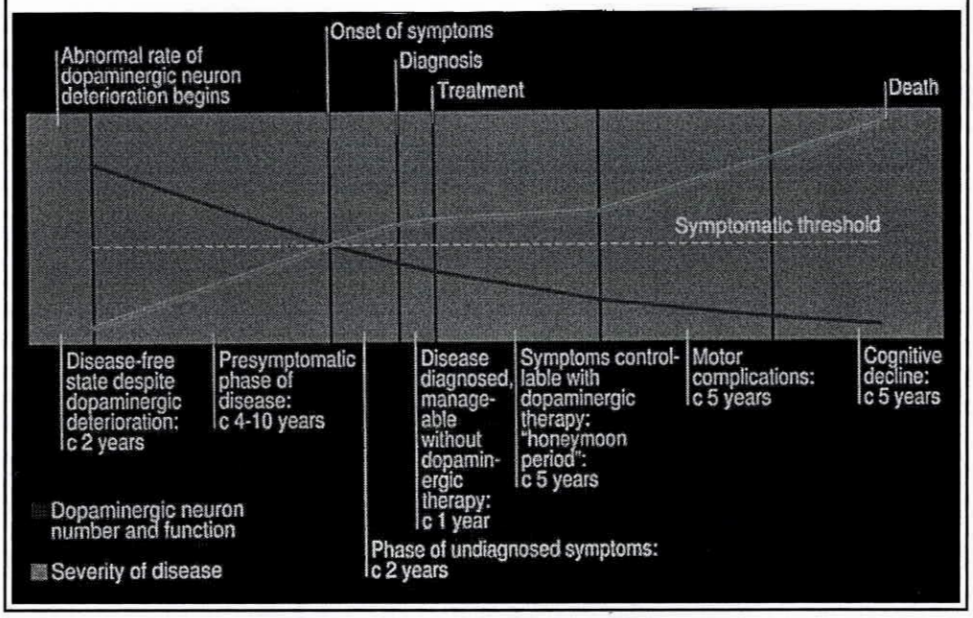
Phases and Course of IPS



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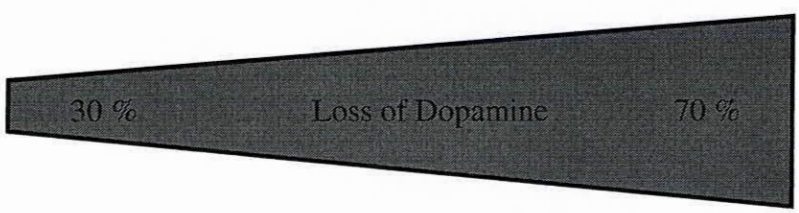
Clinical Aspects of IPS



Preliminary sympt.

Emotional lability
Memory dysfunction
Mood disorder
Performance brake

Sense of smell dysfunction

Anancastic personality

Early sympt.

Depression, fear

Vegetative disorder

Vigilance disturbance

Posture abnormality
Hypokinesia

Pain in vertebral spine, headaches

Full stage

Akinesia
Rigidity
Tremor

Bradyphrenia

Disturbance in postural reflexes
Disturbance of cognitive performance
Disturbance of autonomic NS

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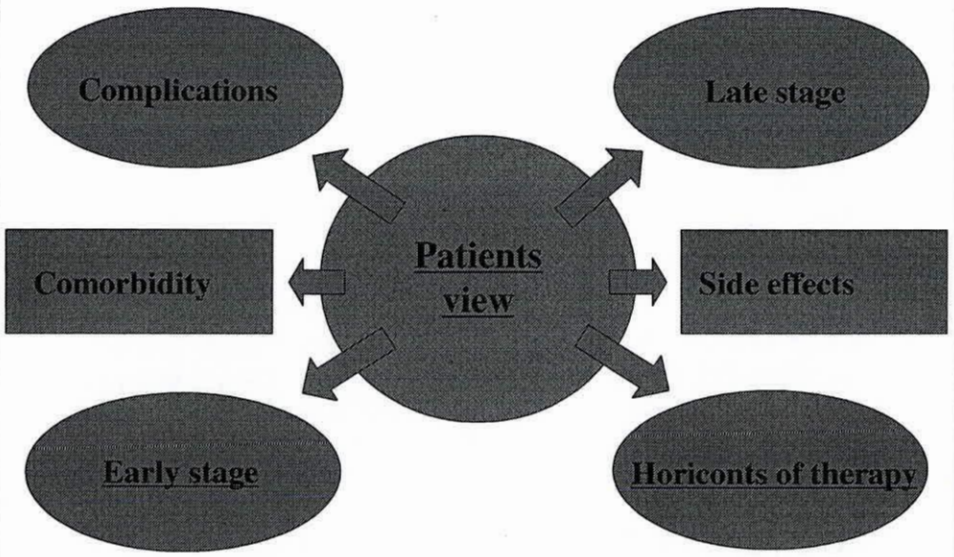
Decision in therapy program



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Principles of Therapy - Objectives

- Prevention
- Restauration of premorbid neuronal integrity and function
- Prevention of neuron decline (neuroprotection)
- Compensation of symptoms
- Amelioration of Quality of Life

modif. after W. Poewe, 1998

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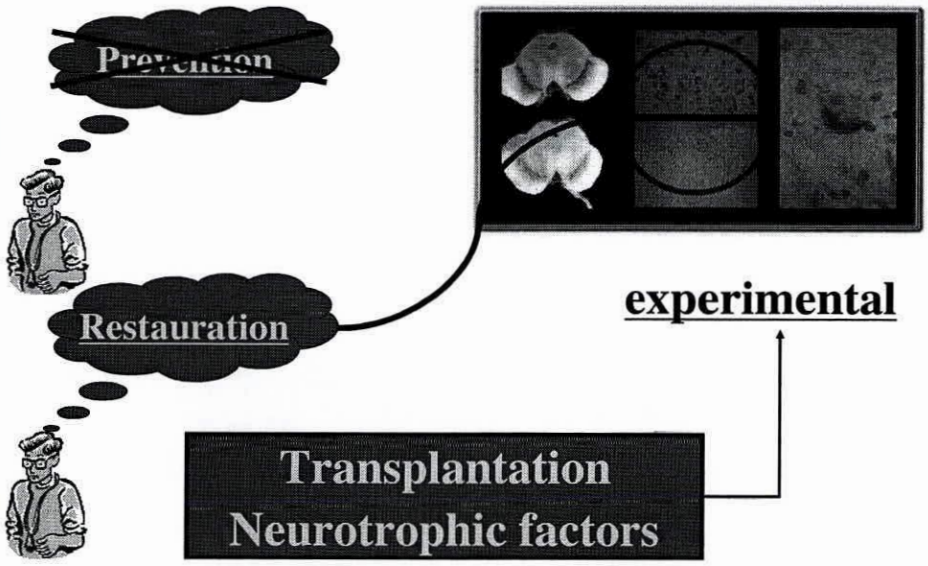
Principal aims of therapy



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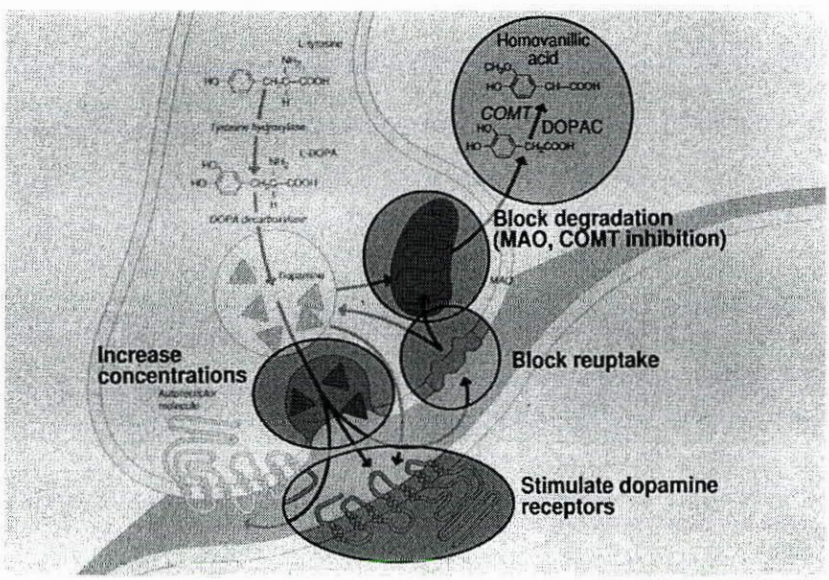
Strategies of medical treatment



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Classes of substances
Substitution therapies

- Dopaminergic drugs
  - L-Dopa
  - Dopamin-agonists (DA)
- COMT-Inhibitors
- MAO-B-Inhibitors
- Non-dopaminergic drugs
  - Amantadine
  - Anticholinergics

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L - Dopa & Benserazid / Carbidopa

- Advanteges
  - Gold standard
  - Good response of all patients
  - Influence to all main symptoms
  - Monotherapy
- Disadvantages
  - No neuroprotection
  - L-Dopa – long time syndrome
  - SE: nausea, vomiting, postural hypotension, psychotic symptoms, sleepyness

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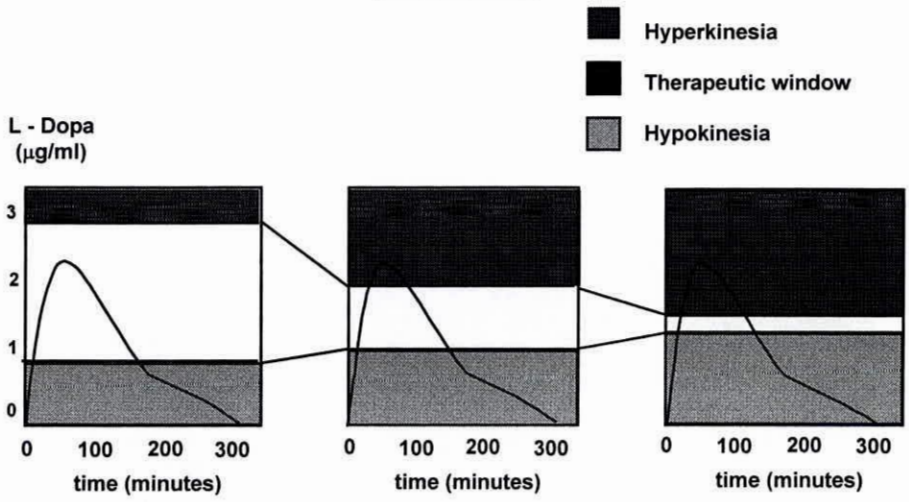
Effect of progression on the therapeutic window



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Disadvanteges of L-Dopa therapy

Loss of effectiveness in 75 % of the patients after 2 - 5 years

- Central pharmakodynamic mechanisms
- Peripheral pharmakodynamic mechanisms
- Wearing - Off
  On - Off
  Dyskinesias
- Delayed - On
  No - On

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Dopaminagonists

(J.P.Hubble, 2002)

	HT (h)	PD (m)	Dosage (mg/d)
Bromocriptin (**Umprel**)	6	70-100	7.5 - 30
Lisurid (**Dopergin**)	2 - 4	60 - 80	1 - 5
Cabergolin (**Cabaseril**)	65 +	60 - 80	2 - 6
Pergolid (**Permax**)	15-27	60-120	1.5 - 12
Pramipexol (**Sifrol**)	8 - 12	60-180	1.5 - 4.5
Ropinirol (**Requip**)	4 - 6	90	9 - 24

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Dopaminagonists (DA)

- Advanteges
  - neuroprotection (?)
  - Monotherapy
    - After 3y 30 - 40 %
    - After 5y 30 - 35 %
  - No L-Dopa longtime syndrome
  - + L - Dopa: Dyskinesia later and minor
  - + L- Dopa saving effect
- Disadvanteges
  - ? Minor effect compared to L-Dopa
  - Risk factors for incompatibility
  - SE: nausea, dizzyness, psychotic symptoms, sleepyness

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Neuroprotective (?) properties of dopamin-agonists

	PET	ß - CIT	time
L - Dopa[1,2]	- 20 %	- 25 %	3 years
Ropinirol[1]	- 14 %		3 years
Pramipexol[2]		- 11 %	3 years
Pergolid[3]	- 11 %		3 years

[1]REAL-PET $p < 0.02$; [2]CALM-PD $p < 0.01$; [3]PELMOPET $p < 0.08$;

Ref.: AAN, 2002.

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Amantadine

- Advantage
  - Possible parenteral application
  - Good effect on rigor, tremor, akinesia
  - High anti-dyskinesia potential
- Disadvantages
  - Livedo reticularis
  - Edema of the legs
  - Psychotic reactions

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Anticholinergics

- Advantages
  - Good effect against tremor
- Disadvantages
  - Antiparkinson effect only minimal
  - Cognitive dysfunctions
  - SE: hallucination, psychotic reaction

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Frequent problems in therapy of PD

Problem	Solution
Fluctuation of effectiveness	COMT-Inhibitors Dopamine-Agonists
On – Off	Apomorphine pause in therapy (?)
L–Dopa Dyskinesia	L–Dopa reduction Fraction of dosage Dopamine-Agonists Amantadine
Akinetic states	Amantadine - infusion
Resistent tremor	Beta-Adrenoceptor blockers Inderal ® Mild sedatives, Oxazepam, etc.

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Individual treatment program

- Age
- Profession, hobby, partner
- Characteristic of symptoms / Disability
- Dominant symptom(s)
- Costs (?)

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Therapeutical horizont in higher age

- Shorter treatment duration
- Diminished risk of long period complications of dopaminergic substances → L-Dopa
- Higher comorbidity risk
  - Drugs
  - Brain circulation disturbances

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Other forms of treatment program

- Stereotactic operation
  Pallidotomie
- Stereotactic neuromodulation
- Implantation

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RESULTS OF STN STIMULATION

- Reduction of Akinesia, Rigidity and Tremor
- Reduction of number and intensity of OFF-Phases
- Reduction of Drug Therapy
- Reduction of Dyskinesias
- Improvement of Quality of Life

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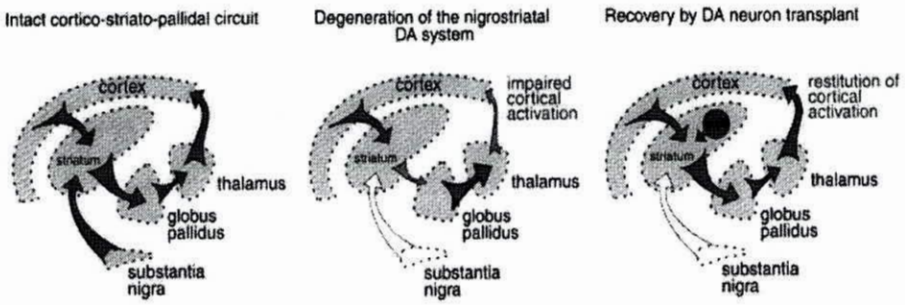
RESTORATION OF DOPAMINERGIC NEUROTRANSMISSION IN PARKINSON'S DISEASE

(Björklund and Lindvall, Nature Neuroscience, 2000)



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Summary in treatment of PD

- Pharmacological treatment the basis
  *) initial phase: Amantadine can be used
  *) basic regime: L-Dopa
  *) later phase combination with agonists, apomorphin-pump system
  *) Beta-blockers in resistant tremor
- Surgical treatment used in later course, especially to decrease side effects.
  *) Deep brain stimulation main method
- Implantation treatment may be successfull, but currently in experimental stage

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Non motoric symptoms of IPS, neuropsychiatric

- Cognitive Dysfunction
  - Visual spatial deficit
  - Memory disturbances
  - Frontal dysfunction
- Dementia
- Depression
- Symptoms of an anancastic personality

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Parkinson, 1817, Shaking palsy:

"The senses and intellects being uninjured"

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Premorbid and morbid traits in the personality of patients with PD

F. Gerstenbrand, E. Karamat, 1999

Clinical features

- Anancastic
- Pedantic
- Introverted
- Apprehensive
- Irresolute
- Undecided
- Wavering
- Hesitant
- Self-reproaching
- Skeptical
- Inner tension
- Restlessness

Social attitudes

- Ahedonic
- No tendency towards addictiveness
- Difficult relationship with women
- Loner
- Non-smoker
- Teetotaller
- Workaholic

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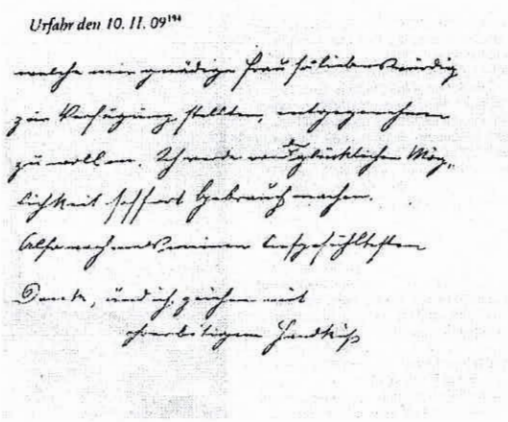
Typical handwriting of a Parkinson patient, 30 years before onset



Excessive rigidity, restrained motions, no garland, ruptured stroke, lack of flow and rhythm, no dynamic

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Typical painting of a Parkinson patient, 30 years before onset

Copy of a painting 18th century, Michaelerplatz, Vienna

photo-like, without feeling of motion, no dynamic, no curves

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Dementia & Psychosis in PD

- PSYCHOSIS
  - 16 - 37 %
  - Delirium states
  - Paranoid - hallucinatoric reaction
- DEMENTIA
  - 20 - 30 %
  - Subcortical
  - Dysexecutive syndrome

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Dementia in PD

- Multifactorial pathology
  - Lewy bodies
  - Fibrills
  - Vascular lesions

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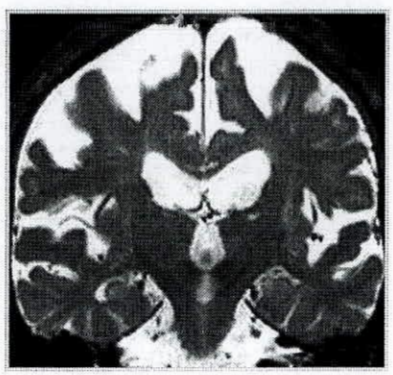
Cerebral MRI in dementia

Brain atrophy in dementia



Mixed dementia (cerebro-vascular lesions, Korczyn)

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Clinical types of dementia in PD

- Subcortical type
- Visuo-spatial & executive deficits
- Memory deficits

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Factors in development of dementia in PD

- Longlasting course of PD
- UPDRS mot. > 25
- Acinetic-rigide form of PD
- Early autonomic disturbances
- Increased tendency to psychotic reactions

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Risk factors

- Dopaminergic treatment
- Antidepressiva & sedativa
- Co-morbidity
- Surgical intervention (narcosis)

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ACh - Esterase inhibitors in dementia by PD

Substance	Dosis	Effect
Rivastigmin	3 - 12	Memory, halluc., behaviour
Donepezil	5 - 10	MMSE +, CIBIC +
Tacrin	8 - 120	ADAS - cog. + MMSE (+)
Memantine	20 – 30	Mood, memory

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Memantine for Dementia[1]

- 5 studies for analysis in AD, VD, MD
  - 20 - 30 mg / day
- Significantly in favour of Memantine
  - Cognition
  - ADL
  - Mood & behaviour
  - Global impression of change
- Trials small and protocols too short

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[1] Areosa et al; Cochrane Database Syst. Rev. 2003

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Incidence and treatment in PD

Psychosis

- 16 - 37 %
- Co-morbidity
- Risk factors
- Medicaments

atypical neuroleptica

- Clozapin
- (Quetiapin)

Dementia

- 20 -30 %
- Clinical profile

ACh - Esterase inhibitors

- Rivastigmin
- Donepezil
- Memantine

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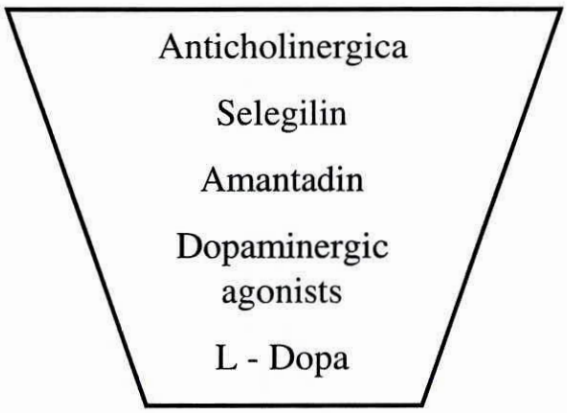
Dopaminergic medicaments inducing psychotic reactions



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Medicaments inducing psychotic reactions

- Muscle-relaxantia
- Spasmolytica
- Sedativa

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Treatment of psychotic reactions

- Dosis reduction
  Last in – first out
- Atypical neuroleptics
  Clozapin, (Quetiapin)

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Summary in treatment in PD

Therapy of the main symptoms

- Medicamental substitution
- Physiotherapy – special form
- Psychagogic guidance – special psychotherapy

Therapy of attendant neuro-psychiatric phenomens

- Dementia
- Psychotic reactions
- Anancastic personality