

(there is a concern that they may induce extrapyramidal symptoms and/or akathisia, and aggravate parkinsonism) and tricyclic antidepressants in the depression in PD is widespread in clinical practice. In patients with severe depression who are refractory to antidepressant medication, a series of ECTs may be useful. Nonconventional therapies such as transcranial magnetic stimulation are being investigated. Unfortunately, until well-designed clinical trials have been performed, the selection of antidepressant medication in PD will be largely driven by the differences in the side-effect profiles of the available drugs and by the personal experience of clinician, as well.

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### Effects of dual tasking on gait and fall risk: What's the role of executive function?

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Falls are a common, debilitating phenomenon among older adults that are especially frequent among patients with Parkinson's disease. New methods are needed to improve our ability to identify persons with the greatest fall risk and to intervene to reduce fall risk. In the past, efforts have focused largely on motor control aspects; however, recent work highlights the potential role of cognitive function, in general, and executive function, more specifically. Although gait and cognitive function are typically viewed, at least at first glance, as separate and more or less distinct processes, a growing body of literature suggests that there are strong interconnections and dependencies. Here we briefly review the influence of cognitive function, specifically executive function, on gait, dual task performance, and fall risk. We show that in patients with Parkinson's disease and in idiopathic elderly fallers, the ability to maintain a steady walk worsens as subjects perform secondary mental tasks of increasing difficulty. Moreover, this ability appears to be related to executive function capabilities. This association between executive function and gait variability suggests the possibility of cause and effect. Thus improving cognitive function, especially executive function and attention, might help to decrease gait instability and reduce fall risk in Parkinson's disease.

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### Familial dementia with Lewy bodies

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Dementia with Lewy bodies (DLB) is characterized by a unique dementia syndrome with associated fluctuations in cognition or arousal, recurrent and fully-formed visual hallucinations, spontaneous parkinsonism, and REM sleep behavior disorder. Most cases have been sporadic, but there is growing appreciation of kindreds with two or more affected individuals with DLB. Still other kindreds have a varying phenotype, with affected members having features of parkinsonism, dementia, "psychosis," and other neuropsychiatric manifestations. In this presentation, we will review the literature and our institutional experience on known and suspected genetic influences on the clinical phenotype of DLB and/or pathologic disorder of Lewy body disease. Data accumulated to date indicates that while some cases of familial DLB are associated with alterations in the synuclein and parkin genes, other genetic mechanisms not yet identified are likely at play.

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### Quality of life in Parkinson's disease patients with depression

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Objective: To assess the impact of depression on Parkinson's disease (PD) on patients in their quality of life (QoL), from their own point of view. Background: It has been found across numerous studies, using different assessment instruments, examining different patient subgroups, or investigating different contributing factors that severity of disease, as assessed by conventional methods of measurement, only correlated moderately with QoL. In contrast, presence and extent of depression, in addition to disability, have mainly contributed to QoL scores. Methods: One hundred and two consecutive (53.9% are males and 46.1% are females) PD patients were included in the study (mean age=58.4, S.D.=9.9). The diagnosis of depression was made according to DSM-IV criteria and severity of depression was measured with Hamilton depression rating scale (HAD). The two instruments for QoL were used in the present study: (a) Short-form Health Survey (SF-36) and (b) Parkinson's disease quality of life inventory (PDQ-39). Results: The depression was present in 46% of PD patients; with 18.6 fulfilled the criteria for major depressive disorder and 27.4 were dysthymic. The 65.5% in depressed PD group were females. The worse quality of life was evident in the major depressed PD patients in comparison to dysthymic ( $p=0.009$ ) and non-depressed PD patients ( $p=0.003$ ), even the motor competence was not significantly different. The greater difficulties in activity of daily living were present in PD with major depression. The depression was the most significant predictor of worsening of the QoL in PD, on both applied measurements for quality of life, in contrast to the other predictors e.g. severity of the disease, age, duration of the disease, medication, cognitive abilities. Conclusions: The early diagnosis and treatment of the depression in PD is inevitably important.

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### Premorbid and morbid personality in Parkinson's disease: Clinical features

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In James Parkinson's original definition of patients with the disease bearing his name, he stated that beside the neurological symptoms, 'the senses and intellects being uninjured' (Parkinson, 1817). After the increased interest on Parkinson's disease mostly started in the L-Dopa era growing awareness to mental changes like depression and intellectual impairment came up, in the last years dementia, characteristic premorbid and morbid features of patients with Parkinson's disease has received comparatively little attention. The psychoanalytical orientated psychiatrist in the first half of the last century followed the opinion that certain characteristic features and psychological factors might be important for the development of the disease, as depression, suppressing aggressive tendencies and problems to express emotions etc. (Sands, 1942). Furthermore, Parkinson's patients were claimed for punctuality and cleanness with trends towards perfectionism, conservatism and rigid moral standards. Peculiar features of the premorbid personality of Parkinson's patients were described by Toedes and Lees (1985) and in a detailed form by Poewe et al. (1985, 1990) and Gerstenbrand and Karamat (1999). As main sign of a Parkinson's personality inflexibility, moral rigidity and pedantic behaviour are registered. In their studies, the Innsbruck group

used a special test program including interviews with patients and their relatives, personality inventory (Giessen-Test) Adult Intelligence Scale (Wechsler Test) and for assessment of premorbid characters, a semi-standardised biographical interview with patients and their relatives, last but not the least a blinded graphomotor examination was analysed using samples from years ago. The personality structure was found as obsessive/compulsive behaviour (anancasticity), Parkinson's patients are pedantic, introverted, apprehensive, irresolute, undecided, wavering, hesitant, sceptical, full of tension and self reproaching. As a special feature Parkinson's patients are workaholics, teetotaler and mostly non-smokers with adhedonic traits. In the newer world history, some political leaders are known to suffer of Parkinson's disease at least Generalissimo Franco, Mao Tse Tung, Brezhnev and Adolf Hitler. Because of many existing documents, it was possible to study the premorbid and morbid personality of Hitler (Gerstenbrand and Karamat, 1999). All the previous announced traits could be documented in his personality, Hitler was a workaholic, he had difficulties in relationship with woman, he was an urgeon for ceremonial ritual procedures at political meetings and sport events, organising the 'Reichsparteitag' in the style of Richard Wagner's operas, the Meistersinger of Nürnberg and Tannhäuser. A special characteristic of Hitler was the failure to social and moral values and laws, constructing pseudo-ethical norm. Hitler had the obsession to have been elected by fate to keep safe Germany and Europe. Similar features as in Hitler's personality can be found in other leading persons suffering of Parkinsonian disease. Studies with Parkinson's patients of different ethnical groups and religious communities show interest parallels. The knowledge of a special personality of Parkinson's patients the anancastic personality with pedantic traits can be helpful in the management of the treatment program. Using the three column medicaments, physiotherapy and psychological guidance the knowledge of the special features in Parkinson personality can be helpful as basic strategy. Important for patients is the fact that Parkinson's patients generally are not suffering of dementia and be bothered by depression.

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### Basic mechanisms of nmda-receptor antagonism

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From the description of the direct and indirect loop system – basal ganglia, sensory motor cortex and motor thalamus – it is evident that glutamate mediates excitatory transmission at crucial points of the circuit. Recent evidence even further enhances the role of glutamate in the functional organisation. The distribution of ionotropic glutamate receptors within the basal ganglia, the dopamine–glutamate interaction and Parkinson's disease related changes in the functional organization of the basal ganglia will be focused on. The role of glutamate mediated toxicity and possible therapeutic interventions will be high lightened from the preclinical point of view.

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### Acetylcholinesterase inhibitors in Parkinson's disease with dementia: A clinical and brain perfusional study

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Background: Recent data indicating that the development of dementia is associated with higher mortality risk in PD, independently

of the motor impairment, can suggest that therapeutic approaches targeting dementia may improve life expectancy in patients with PD. There is substantial evidence that cholinergic deficits may significantly contribute to cognitive impairment and dementia in PD. A few recent studies suggested that acetylcholinesterase inhibitors (ChEIs) could improve cognitive and behavioural symptoms in dementia associated with PD, without worsening parkinsonism. Aims of the present study were to assess the clinical effects of rivastigmine and to investigate by regional cerebral blood flow (rCBF) SPECT the functional changes associated with the positive pharmacological response in patients with PD and dementia (PDD). Materials and methods: Seventeen PDD patients were treated for 6 months with ChEIs (10 with rivastigmine 6–12 mg, 7 with donepezil 5–10 mg, after individual dose optimization) as add-on to their regular anti-PD drugs that were unchanged during the study period except for three patients. The severity of the cognitive deficit was measured in all patients by Mini-Mental State Examination (MMSE), Global Deterioration Scale (GDS), and ADAS-cog performed at baseline and at the end of 6-month period. Motor function was evaluated by means of Unified Parkinson's Disease Rating Scale (UPDRS) at baseline and endpoint. Statistical analysis was performed by Student's paired *t*-test, and ANOVA with repeated measures. rCBF SPECT study was performed with <sup>99m</sup>Tc-ethyl cysteinate dimer (Neurolite<sup>®</sup>, Bristol-Myers Squibb) at baseline and at the completion of the study. Results: A clear-cut cognitive improvement was reported in PDD patients after 6-month treatment with ChEIs. The total score on the ADAS-cog significantly improved ( $p < 0.01$ ). The total MMSE score showed slight and non-significant improvement at 6 months compared with baseline. However, a significant improvement from baseline in the MMSE subscores of attention at 6 months 8 ( $p < 0.01$ ) was observed, with a deterioration at the drug withdrawal. No difference in motor performance as evaluated by UPDRS was reported. SPECT studies analyzed by Statistical Parametric Mapping (SPM 99) showed a significant ( $p < 0.01$ ) increase of rCBF in several clusters within the right cingulate, frontal and parieto-temporal regions bilaterally after rivastigmine with respect to baseline. No decrease of rCBF in any brain structures was reported in the follow-up SPECT study with respect to baseline. No difference in the pattern of changes of regional cortical perfusion was observed between PDD patients treated with rivastigmine and those treated with donepezil. Conclusions: The chronic treatment with ChEIs produced in PDD a striking improvement in cognitive mainly pre-frontal functions without worsening of parkinsonian features. Such findings could confirm the pivotal role played by the cholinergic system in dementia associated with PD. The increase of frontal perfusion after rivastigmine treatment might suggest that the clinical improvement is associated with a sort of re-afferentation in the caudate-cortical connecting systems.

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### Levodopa acute challenge test in a group of patients with diffuse Lewy body disease compared with a group of patients with Parkinson's disease

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Background: Few data about dopaminergic responsiveness of parkinsonian symptoms in Diffuse Lewy Body Disease (DLBD) are available. The aim of this study was to evaluate the differences in acute dopaminergic response to levodopa in a group of patients with diagnosis of probable DLBD compared with a group of Parkinson's disease (PD) patients. Materials and Methods: Twenty patients meeting the criteria for probable DLBD (McKeith et al., 1996) and 30 patients meeting the Gelb's criteria (1999) for probable PD were enrolled. DLBD patients and

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**Special Issue**

**DEMENTIA IN PARKINSON'S DISEASE**

International Symposium  
Salzburg, Austria, 24–27 October 2004

*Guest Editors*

Amos D. Korczyn  
Donald Calne  
Eric C. Wolters

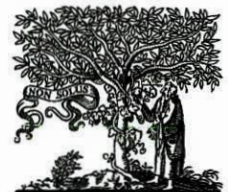


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### Premorbid and Morbid Personality in Parkinson's Disease Clinical Features

F. Gerstenbrand, W. Struhal  
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Mental Dysfunctions in Parkinson's Disease  
October 24-27, 2004  
Salzburg,

### Symptoms of Parkinson's Disease

30 %      Loss of Dopamine      70

<u>Preliminary sympt.</u>	<u>Early sympt.</u>	<u>Full stage</u>
Memory dysfunction	Depression, fear	Rigidity
Mood disorder	Vegetative disorder	Tremor
Performance brake	Vigilance disturbance	Akinesia
	Posture abnormality	Bradyphrenia
Sense of smell dysfunction	hypokinesia	Disturbance in postural reflexes
	Pain in vertebral spine, headaches	Disturbance of cognitive performance
		Disturbance of autonomic NS

Parkinson, 1817, Shaking palsy:

"The senses and intellects being uninjured"

Growing awareness to mental changes like depression and intellectual impairment as part of Parkinson's disease, since 1966

- Pollok and Hornabrook, 1966: Dementia
- Warburton, 1967: Depression symptoms
- Mindham, 1970: Psychiatric symptoms
- Celsia and Wanamaker 1972: Psychiatric disturbances
- Mayeux et al., 1981: Depression, intellectual impairment

### Psychological factors in premorbid personality of PD

Sands, 1942

- premorbid habit:
  - externally calm, introverted
  - suppressing aggressive tendencies
  - hardly expressing their emotions
  - "Masked personality"

### Depth Psychological Findings

Cohen-Booth, 1935; Mitscherlich, 1960; Korten and Ketterings, 1972:

- Readily subdue their own personal desires under social standards
- Strive for order
- Punctuality and cleanness
- Exhibit trends towards perfectionism
- Conservatism
- Rigid moral standards

## Parkinson's Disease and Smoking

Bauman et al., 1979; Martilla and Rinne, 1980; Godwin-Austen et al., 1982)

Non-smokers, higher risk for PD:

- less adventurous, outgoing or decisive, more shy and unhappy

Smokers, lower risk for PD

- Impulsive, arousal seeking, danger-loving, risk-takers and belligerent against authority

## Premorbid Personality of Parkinson Patients Innsbruck Group I

Poewe et al., 1983:

Examination with Giessen-Test (GT)

- Measurement of personality traits by self and foreign assessment, 40 items in 6 standard scales for the features social resonance, dominance, control, basic mood, previousness, social potency (Beckmann and Richter 1972)

Results: Marked trends to over control, depressiveness, positive social resonance and social impotency

Tendency towards perfect fulfillment of task, towards order and punctuality while expecting the same from the persons of their surroundings.

## Premorbid Personality of Parkinson Patients Innsbruck Group II

Poewe et al., 1990

used: mini-mental state (MMS) examination, Wechsler Adult Intelligence Scale (WAIS), intelligence quotient, VIQ plus subtests, Geriatric Depression Scale (GDS), Cattell's 16 PF semi-standardized biographical interview

• Results:

– MMS, WAIS, VIQ, GDS

- Introverted
- depressed
- pedantic
- rigid
- loners
- teetotaler

– 16 PF

- more socially alert
- apprehensive
- self-reproaching
- tensed
- driven
- restless
- skeptical and cautious in their actual personality

## Premorbid Personality of Parkinson Patients Innsbruck Group II

Poewe et al., 1990

### PREMORBID PERSONALITY IN PD

Evaluation of semistandardized interviews into premorbid behavior and personality

Study groups	Depressed/ introverted	Percent of experimentees scoring on item					
		Workaholic	Pedantic	Rigid	Loner	Nonsmoker	Teetotaler
Controls (N = 17)	17.5% (11/24)	55.5% (41/70)	29.5% (24/35)	14.5% (12/17)	17.5% (11/24)	49.5% (41/58)	29.5% (24/35)
PD (N = 38)	49%* (48/50)	71.5% (50/85)	75% (74/75)	50% (42/58)	47.5% (45/50)	66.5% (61/72)	28% (27/29)

\* p < 0.05 (PD vs controls)

Percentages given as means of two rating with individual ratings in brackets  
PD, Parkinson's disease

## PD in Leading Personality on the example of Adolf Hitler I

Gerstenbrand, Karamat, 1999

Hitler suffered from PD of equivalence type, severe tremor (left side), akinesia, rigidity

- First symptoms 1939: hypokinesia left arm
- Constantly increased after 1941
- Full symptoms 1944 after assassination attempt
- Severe PD in January 1945
  - Diagnosed by Prof. M. De Crinis, Neurologist, highest ranked SS physician
- Decision for treatment with special mixture with the knowledge of H. Himmler
- Hitler refused treatment afraid to be poisoned

## PD in Leading Personality on the example of Adolf Hitler II

Urfahr den 10. 11. 09<sup>1911</sup>

Handwritten text in old German script, showing excessive rigidity and restrained motions.

Hitler's handwriting, age of 20 years. Excessive rigidity, restrained motions, lack of flow and rhythm (old angular German handwriting)

### PD in Leading Personality on the example of Adolf Hitler III



Copy of a painting 19<sup>th</sup> century by A. Hitler, Michaelerplatz, Vienna photo-like, without feeling of motion

### PD in Leading Personality on the example of Adolf Hitler IV



Sketch for a stage design "Lohengrin" by A. Hitler, rigid structures

### PD in Leading Personality on the example of Adolf Hitler V

Analysis of premorbid and morbid personality  
(physician examinations, various documentation,  
handwriting and painting analysis)

F. Gerstenbrand, E.  
Karamat, 1999

- |   |                         |   |
|---|-------------------------|---|
| • Pedantic                                  | • Sceptical             | • No tendency toward addictiveness      |
| • Anancastic                                | • Tension, restlessness | • Difficult relationship with women     |
| • Introverted                               | • Teetotaler            | • Urge for ceremonial ritual procedures |
| • Apprehensive                              | • Non-smoker            |   |
| • Irresolute, undecided, wavering, hesitant | • Ahedonic              |   |
| • Self-reproaching                          | • Workaholic            | Obsessed by the idea to save Germany    |

### Premorbid and morbid traits in Parkinsonian patients

Clinical features, test results, semistandardized interviews, graphomotor analyses

#### Clinical features

- Anancastic
- Pedantic
- Introverted
- Apprehensive
- Irresolute
- Undecided
- Wavering
- Hestiant
- Self-reproaching
- Sceptical

#### Clinical features

- Inner tension
- Restlessness

#### Social attitudes

- Ahedonic
- No tendency towards addictiveness
- Difficult relationship with other sex
- Loner
- Non-smoker
- Teetotaler
- Workaholic