

SYLLABUS

Marrakesh, Morocco, November 12-17, 2011

XXth WORLD CONGRESS OF NEUROLOGY



SOCIÉTÉ MAROCAINE
DE NEUROLOGIE

WCN Education Program

Monday, 14 November, 2011

14:45-18:15

**HOW TO TREAT PARKINSON'S DISEASE: A PRACTICAL COURSE FOR OPTIMAL
TREATMENT OF OUR PARKINSONIAN PATIENTS**

Chairperson: **Erik Ch. Wolters**, *The Netherlands*

14:45 **EARLY (PREMOTOR) DIAGNOSIS AND TREATMENT OF PRE-MOTOR
SYMPTOMS IN PD**
Eduardo Tolosa, *Spain*

15:15 **DISCUSSION**

15:30 **TREATMENT OF MOTOR PARKINSONISM, WITH AN ACCENT ON THE
TREATMENT OF TREMOR**
Günther Deuschl, *Germany*

16:00 **DISCUSSION**

16:15 *Coffee Break*

16:45 **TREATMENT IN THE LATER STAGES OF PD**
Erik Ch. Wolters, *The Netherlands*

17:15 **DISCUSSION**

17:30 **VIRTUAL CLINIC: INTERACTIVE DISCUSSION ABOUT TREATMENT OF
SOME VIDEO-CASES**
Erik Ch. Wolters, *The Netherlands*,
Eduardo Tolosa, *Spain*
Günther Deuschl, *Germany*

PARKINSON'S DISEASE

END-STAGE CDS SOLUTIONS delivery systems

Erik Ch. Wolters
VU University Medical Center
Amsterdam

WFH
NOVEMBER 2011
MARRAKECH

TAKE HOME MESSAGES

1. THE RECOGNITION OF PATIENTS, SUITABLE FOR INFUSION THERAPIES
2. KNOWLEDGE ABOUT THE SYMPTOMATIC EFFECTS OF CHANGING FROM PERORAL TO PUMP THERAPY IN ADVANCED PD PATIENTS
3. KNOWLEDGE ABOUT THE POSSIBLE SIDE-EFFECTS AND TECHNICAL CHALLENGES WITH PUMP TREATMENTS IN PARKINSON'S DISEASE

AS OF NOW,
TREATMENT IN PARKINSON'S DISEASE
COMPRISES MAINLY
THE SYMPTOMATIC TREATMENT OF

PARKINSONISM

supplementation of cerebral dopamine	L-dopa / carbidopa plus COMT/MAO-inhibitors
substitution of cerebral dopamine	dopamine agonists

the efficacy of levodopa is limited by its short serum half-life:
 L-dopa: about 60 minutes
 L-dopa + DDI: about 90 min

as PD progresses and striatal dopamine storage capacity reduces, oral L-dopa related fluctuations in serum levodopa lead to pulsatile dopamine receptor stimulation, which might lead to motor fluctuations, dyskinesias and puning

DRUGS	SUBSTANCE-RELATED COMPLICATIONS	TREATMENT-RELATED COMPLICATIONS
L-dopa/carbidopa plus COMT/MAO inhibitors	nausea orthostatic hypotension dopamine dependency syndrome	impulse control disorders gambling, hypersexuality, compulsive shopping, binge eating
dopamine agonists	nausea orthostatic hypotension ergotaminic effects or E.D.S. delusions hallucinations	impulse control disorders

DOPAMINOMIMETIC - INDUCED DYSKINESIA

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 L-dopa: about 60 minutes
 L-dopa + DDI: about 90 min

as PD progresses and striatal dopamine storage capacity reduces, oral L-dopa related fluctuations in serum levodopa lead to pulsatile dopamine receptor stimulation

Intermittent, but not continuous levodopa treatment induces dyskinesias in MPTP-lesioned monkeys* and/or 6-OHDA lesioned rats**

Di Monte DA, et al. *Mov Disord* 2000;15:459-66
 Blanchet PJ, et al. *Adv Neurol* 2001;86:337-44
 Marin C, et al. *Mov Disord* 2006;21:646-53

Juncos JL, et al. *Ann Neurol* 1999;25:473-478
 Marin C, et al. *Mov Disord* 2006;21:646-53

... and the same was seen in apomorphine treated monkeys

Intermittent levodopa treatment induces dyskinesias in MPTP-lesioned monkeys* and/or 6-OHDA lesioned rats**

Continuous levodopa treatment does not induce dyskinesias in MPTP-lesioned monkeys* and/or 6-OHDA lesioned rats**

excessive pulsatile dopamine receptor stimulation
in the long run
is supposed to induce downstream changes in the gene
and protein synthesis with behavioral sensitization,
causing hypersensitivity of the
dopaminergic receptors

in the dorsal motor striatal circuit
this will cause
dyskinesia

excessive pulsatile dopamine receptor stimulation
in the long run
is supposed to induce downstream changes
in the gene and protein synthesis
with behavioral sensitization,
causing hypersensitivity of the
dopaminergic receptors

in the ventral limbic striatal circuit
this will cause
punding

PUNDING
punding behaviour
is a kind of compulsive hobbyism:
an intense fascination for common objects
with repetitive, obsessive, meaningless actions
such as cleaning, collecting, dismantling,
sorting and/or repairing of those objects,
often in combination with severe hyperkinesia

relief by performing, but not obsessiveness,
closely resembles
obsessive-compulsive disorders

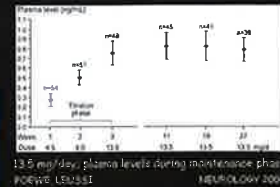
Dyskinesia and punding may be
prevented and/or reversed by
**continuous dopaminergic
stimulation (CDS)**
focusing on a more sustained,
physiologic stimulation of striatal
dopaminergic receptors

continuous dopaminergic stimulation

- Levodopa plus COMT/MAO-inhibitors
- Oral dopamine agonists with very long T1/2
- Continuous transdermal dopamine agonists
- Continuous subcutaneous dopamine agonists
- Continuous levodopa intestinal infusion
- Continuous HF-DBS-STN

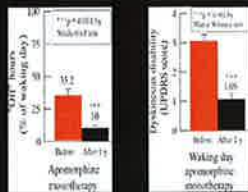
(COMPENSATING FOR THE STRIATAL DOPAMINE DEFICIENCY BY CONTINUOUSLY PROVIDING THE SUBSTRATUM OVERACTIVITY)

DOPAMINE AGONIST PATCHES



ROTIKITINE/LISURIDE PATCHES MAY INDUCE STABLE PLASMA LEVELS WITH REDUCED 'OFF' TIME, BUT AS OF YET THERE IS NO INFORMATION ABOUT THEIR PROPENSITY TO INDUCE or REDUCE DYSKINESIA

APOMORPHINE



APOMORPHINE and LISURIDE S.C. (versus levodopa monotherapy) MAY REDUCE 'OFF' TIME and DYSKINESIA



DBS-STN

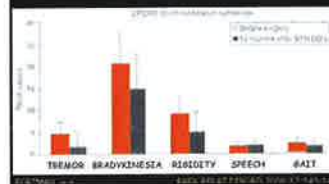
Ali Benabid



in PD patients, STN-DBS may result in

- persistently improved motor behaviour
- reduced motor fluctuations and dyskinesias
- reduced dopaminomimetic medication
- transient increase quality of life

FARINA et al. JCLIN NEUROL 2006; 46: 595-600
MAY 2006; 24(11): 1111-1117

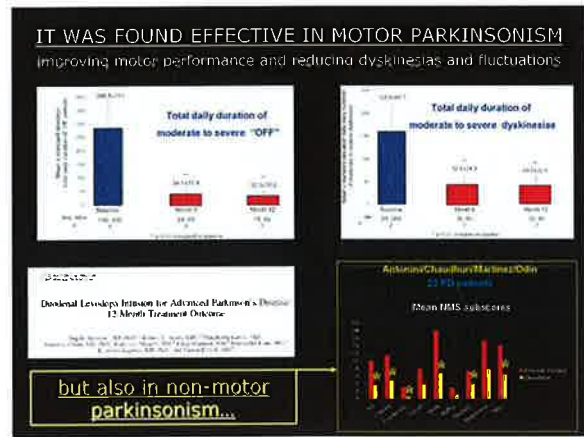
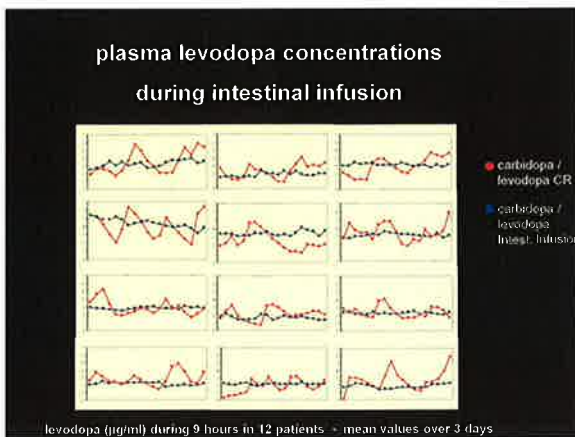


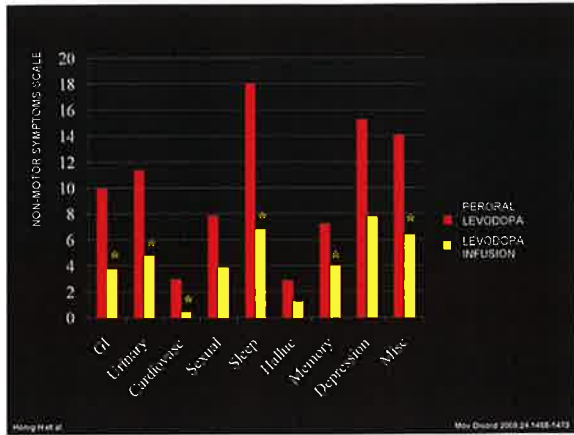


in order to obtain continuous dopamine receptor stimulation, also intraduodenal infusion of the levodopa/carbidopa enteral gel is efficient, safe and clinically superior to individually optimized combinations of conventional medications in PD patients with motor fluctuations.

intraduodenal infusion of levodopa offers an important alternative in treating patients with advanced Parkinson disease.

D. Nyholm et al. NEUROLOGY 2009;64:2114-221





known risks due to PEG surgery
hemorrhage, infection, peritonitis, ileus, inadvertent removal

known risks due to the stoma
hemorrhages, infection, peritonitis, pain, stomal leakage
local infections around the stoma are treated conservatively with a disinfectant; treatment with antibiotics is rarely needed

known risks due to the intestinal tube
dislocation of the intestinal tube sometimes via the stomach. Dislocation. Flakes by the PERCUTANEOUS system leads to reappearance of motor fluctuations
occlusion*, kinks or knots** of the intestinal tube lead to high-pressure signals from the pump.
* Dislocations are prevented by flushing the tube with tap water. ** Kinking, occluding, or tube displacement may need re-adjustment of the tubing.
Should complete failure of the intestinal tube or pump occur, the patient must be treated with intravenous levodopa until the problem is resolved.

known risks due to duodopa treatment
Levodopa-related complications such as somnolence, and dyskinesia may occur, though, but can be treated by adaptation of the dosage.

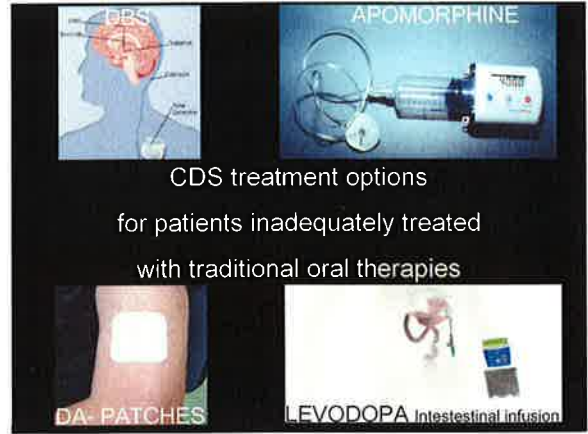
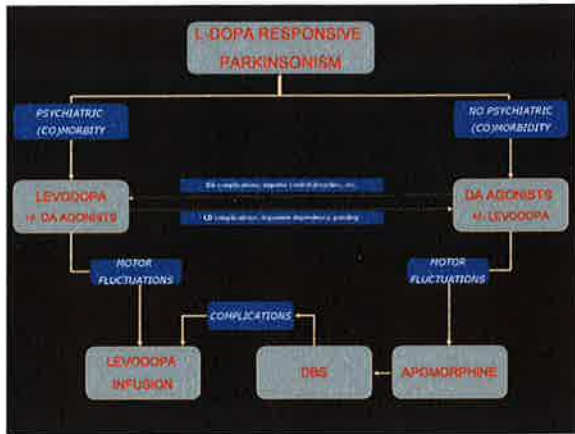
end-stage solutions are necessary in debilitating

motor-fluctuations
AKINESIA, DYSTONIA and DYSKINESIA

non-motor fluctuations
SWALLOWING DISORDERS
SLEEP DISORDERS
ORTHOSTATIC HYPOTENSION
APATHY & DYSPHORIA, ANXIETY & PANICK ATTACKS
DEPRESSION and PSYCHOSIS

drug-related complications
DOPAMINE DEPENDENCY SYNDROME
IMPULSE CONTROL DISORDERS

Apomorphine	DBS	Levodopa infusion
All ages motor & non-motor response fluctuations	Younger patients motor response fluctuations	All ages motor & non-motor response fluctuations
SOMETIMES + LEVODOPA	OFTEN + LEVODOPA	NO NEED FOR POLYPHARMACY
CONTRA-INDICATIONS +IMPULSE CONTROL DISORDERS +PRE-EXISTING/CONCOMITANT PSYCHOSIS	CONTRA-INDICATIONS +IMPULSE CONTROL DISORDERS +PRE-EXISTING/CONCOMITANT DEPRESSION, DEMENTIA, PSYCHOSIS	CONTRA-INDICATIONS +DOPAMINE DEPENDENCY SYNDROME
	surgical complications	surgical complications
apomorphine-related complications	stimulation-related complications	levodopa-related complications (?)



- ## TAKE HOME MESSAGES
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