Reduced sympathetically induced heart rate variability during sleep in Parkinson's disease.

A case-control polysomnography-based study.

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The authors declare no conflict of interest.

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Plan

1. Background
2. Objectives
3. Methods
4. Results
5. Conclusions

Background:

- Pathonanatomical data and MIBG-SPECT

  postganglionic noradrenergic cardioselective denervation in PD patients

- linked with ?
  - missing BP overshooting in Valsalva manoeuvre
  - fatigue, shortness of breath?

(Iwanaga K, 1999; Druschky A, 2000; Mitsui J, 2006; Rascol O, 2009; Goldstein DS, 2003 and 2010)

Background:

- Heart rate variability (HRV) in PD

  In wakefulness: reduced variability in head-up tilt test

  In sleep : reduced (« blunted ») variability

  but controversial results

  no subanalysis in terms of sleep stages

- HRV in idiopathic REM sleep behavior disorder

  Reduced sympathetic influence on HRV during REM sleep

(Ferini-Strambi, 1996; Haapaniemi, 2001; Puursiainen, 2002; Devos, 2003; Kallio, 2004; Lanfranchi 2007)

Objectives:

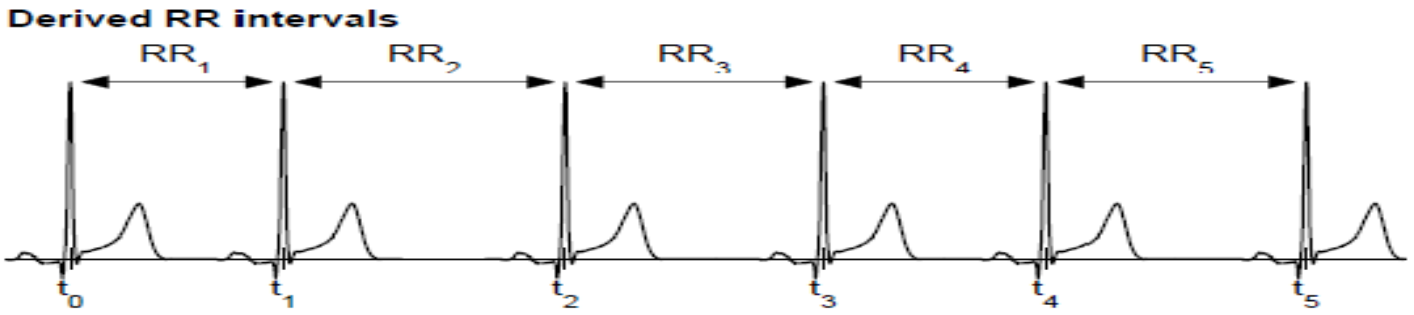
- To study HRV during nocturnal sleep in PD.
- To subanalyze effect in REM versus NREM sleep.
- We hypothesized that PD patients would show a reduction of sympathetic influence during REM and NREM.

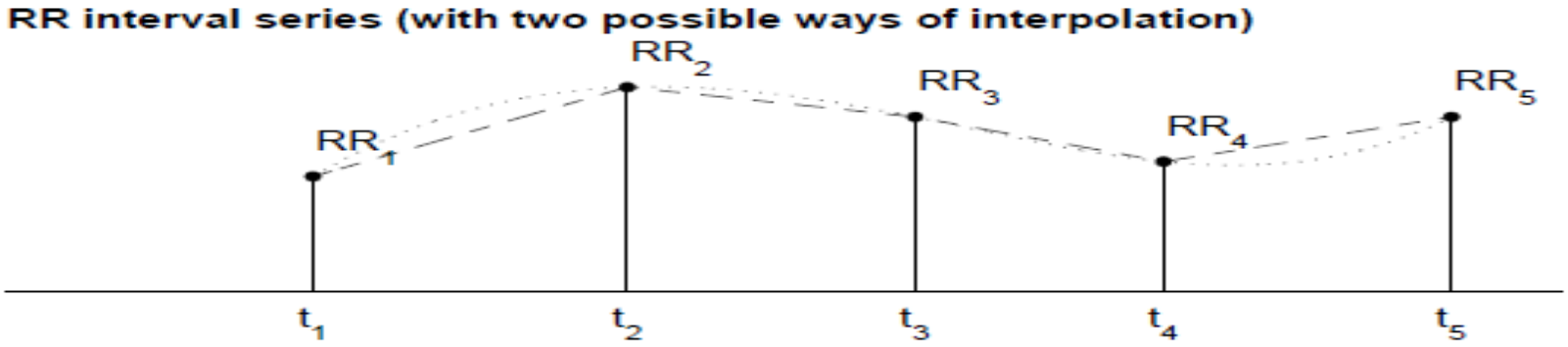
METHODS :

- Subjects : 35 PD patients and 35 gender-, age- and AHI (Apnea Hypopnea Index)-matched controls

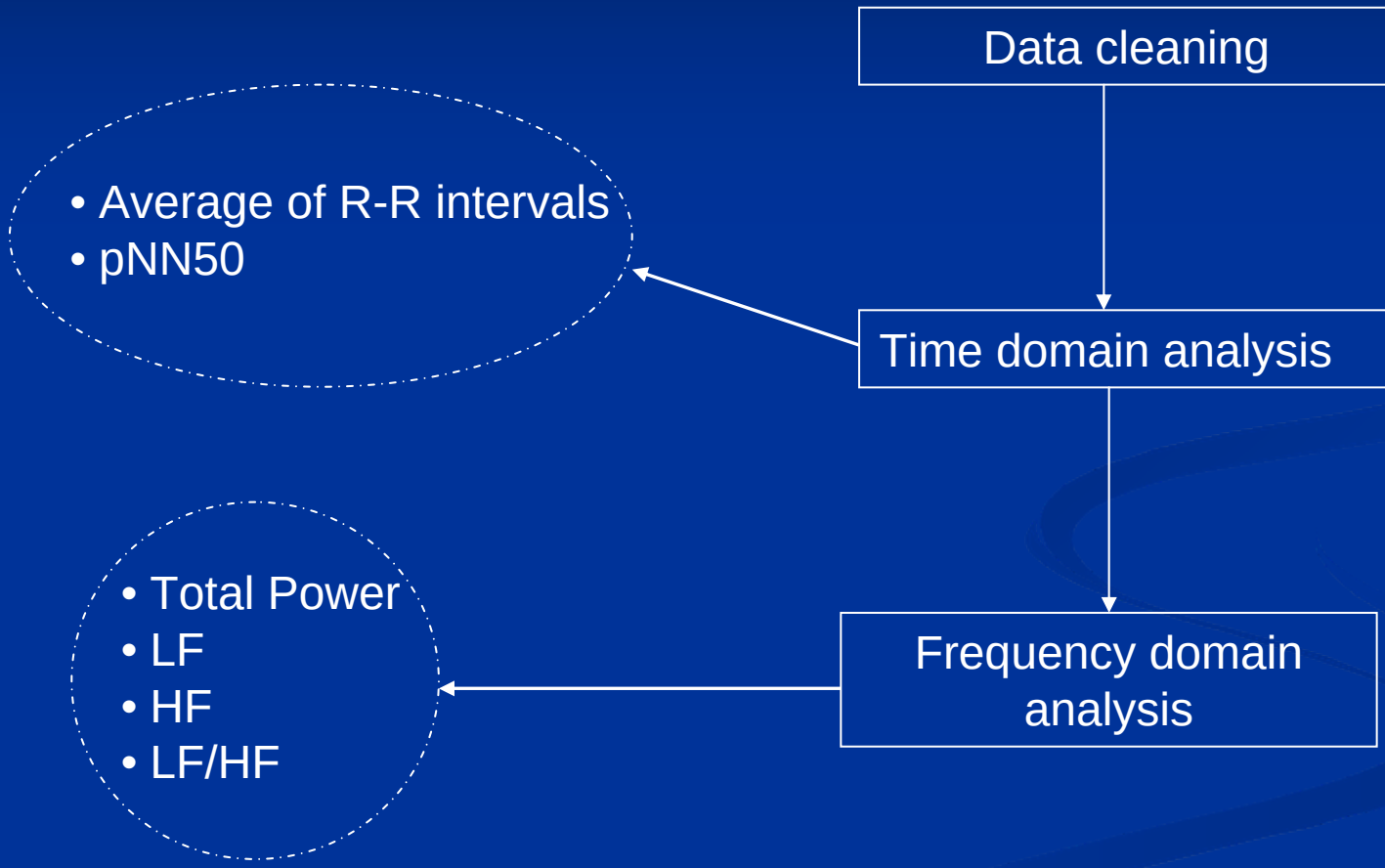
- Data Collection and analysis : One-night polysomnography (PSG) was used to assess R-R variability during NREM and REM sleep

What are R-R intervals ?

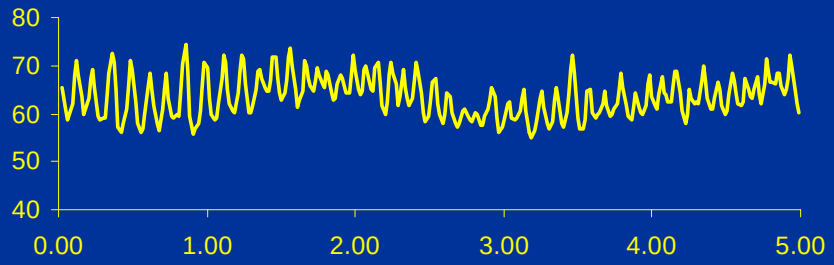


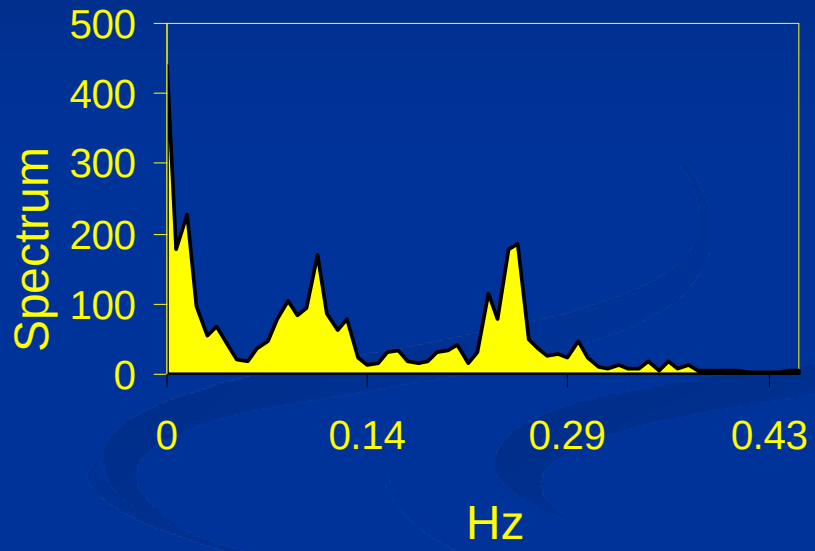


The differents steps of the analysis



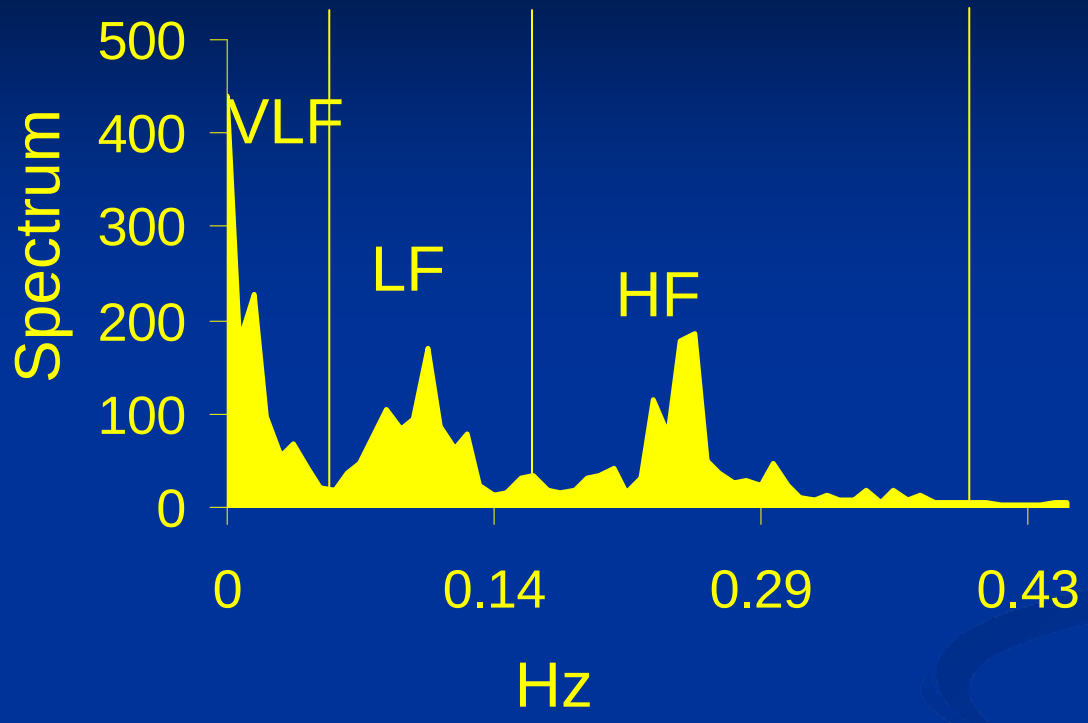
Frequency domain analysis





Fast Fourrier Transformation algorithm

Frequency domain analysis



VLF : Very Low Frequency : 0.003-0.04 Hz

LF : Low frequency, mainly sympathetic influences : 0.04-0.15 Hz.

HF : High frequency, mainly parasympathetic influences : 0.15-0.40 Hz

Results : demographic characteristics

Demographic Characteristics in PD patients and Controls

Demographic Characteristics	PD patients (N=35)	Controls (N=35)	P Value
Age, years	65.5 ± 8.9	64.8 ± 8.5	0.58
Gender, male	80% (28/35)	80% (28/35)	1

Data are presented as means ± SD

Results : sleep characteristics

Sleep Characteristics in PD patients and Controls

Sleep characteristics	PD patients (N=35)	Controls (N=35)	P Value
Sleep latency, min	52.1 ± 68.1	39.0 ± 41.7	0.88
Total sleep time, min	317.5 ± 94.6	326.1 ± 115.8	0.21
Sleep efficiency, %	72.4 ± 14.5	74.34 ± 19.98	0.21
Stage 1 - 2, %	44.6 ± 16.4	50.2 ± 13.7	0.21
Stage 3 - 4 , %	15.6 ± 12.4	12.7 ± 9.8	0.4
NREM, %	59.3 ± 17.4	62. 3 ± 12.4	0.75
REM sleep, %	8.7 ± 6.7	9.4 ± 5.2	0.3

Data are presented as means ± SD

Results : Respiratory measures

Respiratory measures and Periodic leg movement index in PD patients and Controls

Respiratory measures	PD patients (N=35)	Controls (N=35)	P Value
Microarousal index, no./h	11.3 ± 13.8	14.3 ± 16.3	0.3
Apnea-hypopnea index, no./h	9.4 ± 13.7	14.9 ± 15.8	0.12
Mean oxygen value (%)	92.9 ± 1.6	91.9 ± 2.7	0.07
Periodic leg movement index			
Periodic leg movement index, no./h	17.5 ± 34.0	8.5 ±16.9	0.45

Data are presented as means ± SD

no/h : Number per hours.

Results : Characteristics of PD patients

Characteristics of PD patients	
Disease duration, years	6.6 ± 4.6
Dosage of levodopa, mg	497.5 ± 292.1
Data are presented as means ± SD	
Distribution of the Hoehn-Yahr Stages	
Stage 1	8.7 % (N=3)
Stage 2	51.4% (N=18)
Stage 3	34.3% (N=12)
Stage 4	5.7% (N=2)

Results : Time domain analysis of HRV

Variable	PD patients		Controls		P Value ANOVA
	NREM (N = 35)	REM (N = 28)	NREM (N = 35)	REM (N = 34)	
R-R intervals, ms	935.9 ± 151.9	950.4 ± 147.3	960.5 ± 136	953.5 ± 130.7	Stage : P = NS Group : P = NS Interaction : P = NS
pNN50, %	17.7 ± 20.9	15.8 ± 18.9	17 ± 17.9	15.4 ± 16.7	Stage : P = NS Group : P = NS Interaction : P = NS

Data are presented as mean ± SD.

NS : No Significant.

No significant differences with time-domain variables

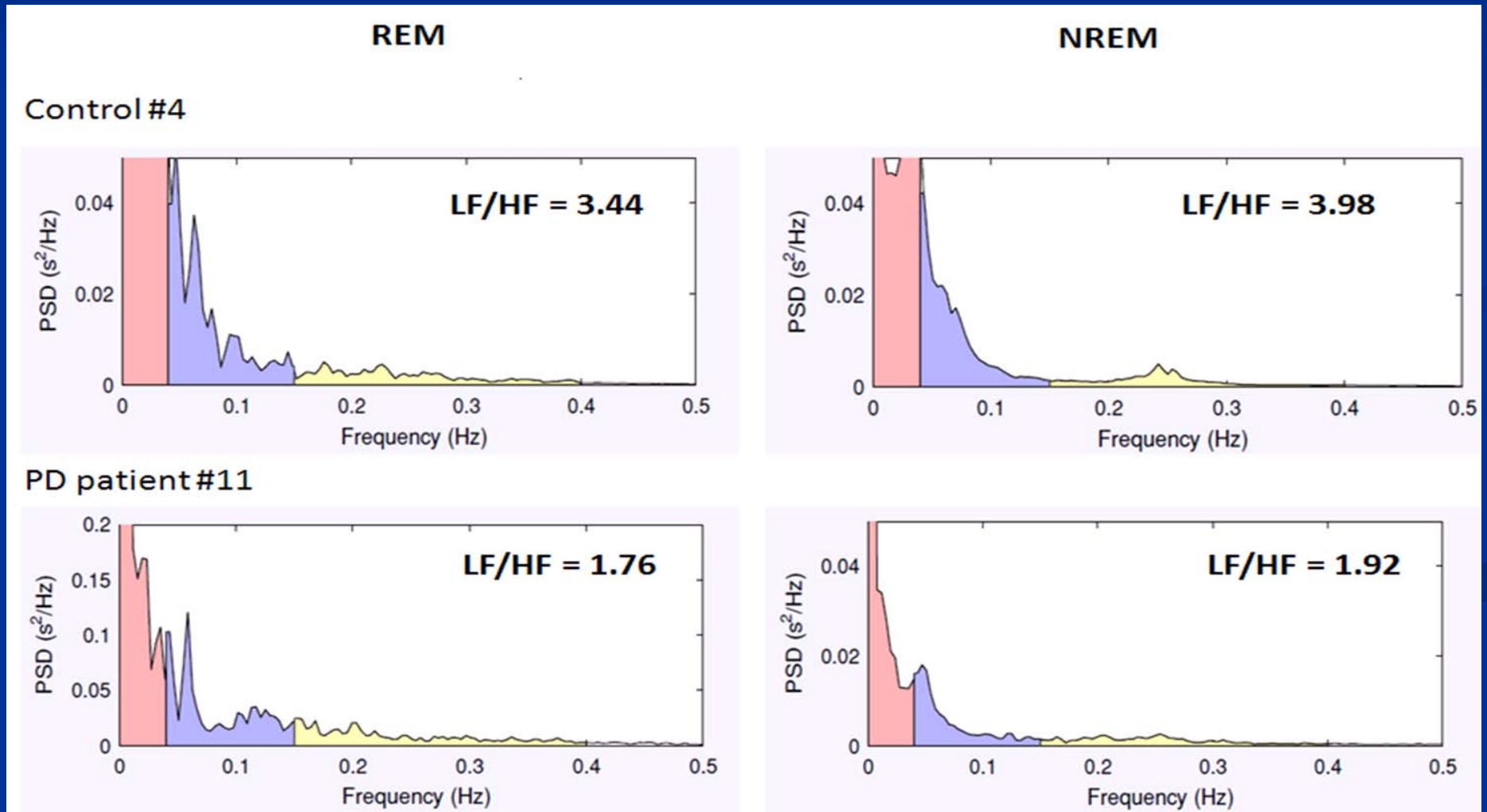
Results : Frequency domain analysis of HRV

Variable	PD patients		Controls		P Value ANOVA
	NREM (N = 35)	REM (N = 28)	NREM (N = 35)	REM (N = 34)	
LF, n.u	57.6±16.7	60.4±17.4	63.9±12.1	67.7±12.9	Stage : P = NS **Group : P = 0.0065** Interaction : P = NS
HF, n.u	42.5±16.7	39.6±17.4	36.1±12.1	32.3±12.9	Stage : P = NS **Group : P = 0.0065** Interaction : P = NS
LF/HF	1.67±0.9	2.04±1.3	2.36±2.5	2.96±2.6	Stage : P = NS **Group : P = 0.0187** Interaction : P = NS

Data are presented as mean ± SD.
NS : No Significant.

Significant differences with frequency-domain variables

Example of spectrum during NREM and REM for a control and a patient



Conclusions

- In comparison to controls, PD patients show reduced sympathetic influence on HRV in *both* NREM and REM sleep stages.
- Thus the relative parasympathetic influence is more important in PD patients than in controls.
- Thus ratio sympathetic/parasympathetic influence is lower in PD patients than in controls.

Conclusions

- Extending similar findings in iRBD :
  - iRBD : reduction of sympathetic influence only in REM.
  - IPD : Reduction of sympathetic influence in both REM and NREM

- Clinical relevance: unknown
  - disease-induced sympathetic "brake" ?
  - limited nocturnal cardioprotection in PD patients ?

(Lanfranchi PA, Fradette L, Gagnon JF, Colombo R, Montplaisir J. Cardiac Autonomic Regulation During Sleep in Idiopathic REM Sleep Behavior Disorder. Sleep 2007; 30:1019-25)

Limitations & strengths

- Limitations
  - Retrospective study
  - PD patients tested while on dopaminergic medications
  - PD patients in different disease stages
  - Asymmetrical gender distribution

- Strengths
  - Controls matched for respiratory events
  - Careful exclusion of RR-outliers
  - Comparison REM vs. NREM

Thank you