노년기 수면장애의 신경생리학적 지표

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Contents

- Age-related sleep changes
- Sleep disorders commonly seen in the elderly

(Insomnia)

- Sleep Apnea Syndrome
- Restless Legs Syndrome (RLS) and
  Periodic Limb Movements during Sleep (PLMS)
- REM Sleep Behavior Disorder (RBD)

Age-related sleep changes

Introduction

- Age-related sleep changes

Box 1: Typical sleep changes with aging

- Decreased total nocturnal sleep time
- Delayed onset of sleep
- Advanced circadian phase: early to bed, early to rise
- Reduced slow-wave sleep
- Reduced rapid-eye-movement (REM) sleep
- Reduced threshold for arousal from sleep
- Fragmented sleep with multiple arousals
- Daytime napping

(Wolkove, CMAJ 2007:176:1299-304)

J. Sleep Res. (2003) **12**, 87–93

Actigraphy suggests age-related differences in napping and nocturnal sleep

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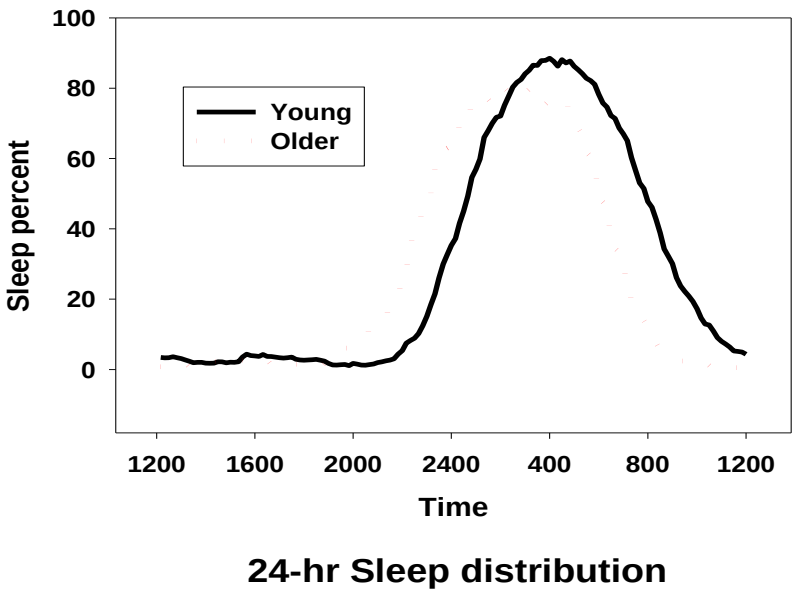
SUMMARY The aim of this study was to contrast the time distribution of out-of-bed napping in young and older adults through recordings of wrist activity, and to evaluate the correlates of napping with nocturnal sleep. Seventy-three young adults between 18 and 32 years and 60 older adults between 60 and 75 years of age participated in the study. Subjects were selected for good general health and had few sleep complaints. They wore wrist-activity monitors and kept daily sleep logs for 1 week. Automatic sleep scoring was edited by the authors, supplemented by sleep logs and illumination data as well as activity data. Napping episodes were modestly increased in older adults, but there was no difference in the daily duration of napping. Older adults napped more in the evening (especially within 2 h before bedtime), whereas young adults napped more in the afternoon. The older adults with evening naps ($n = 31$) showed earlier nocturnal wake-up times and decreased nocturnal sleep duration compared with the older adults without evening naps ($n = 29$). There was no difference in nocturnal sleep between young adults with afternoon naps ($n = 32$) and without afternoon naps ($n = 41$). In determining the effects of napping on nocturnal sleep, timing of napping and age are important. Maintaining alertness during the evening (e.g. by bright light exposure or moderate exercise) would be a possible approach to delay wake-up times in older adults.

KEYWORDS aging, circadian, naps, sleep, wrist activity

Table 1 Nocturnal sleep parameters of young and older adults

Sleep parameters	*Young (n = 73)*	*Older (n = 60)*	*P-value*
Bedtime	00:17 ± 1:11	22:39 ± 1:20	<0.001
Wake-up time	08:11 ± 1:23	06:35 ± 1:04	<0.001
Sleep-onset time	00:24 ± 1:11	22:50 ± 1:20	<0.001
Sleep-offset time	08:10 ± 1:23	06:30 ± 1:05	<0.001
TIB (min)	474.5 ± 54.5	475.9 ± 64.3	0.894
SL (min)	7.4 ± 2.9	10.6 ± 5.6	<0.001
SPT (min)	465.5 ± 55.4	460.2 ± 62.9	0.600
TST (min)	420.8 ± 48.2	366.1 ± 53.2	<0.001
SE (%)	88.8 ± 3.9	77.4 ± 9.4	<0.001
WASO (min)	44.7 ± 19.8	94.1 ± 54.3	<0.001

Values are mean ± SD; TIB, time in bed; SL, sleep latency; SPT, sleep period time; TST, total sleep time; SE, sleep efficiency; WASO, wake-up time after sleep onset.



24-hr Sleep distribution

(Yoon, J Sleep Res 2003:12:87-93)

Circadian Rhythms in Aging (1)

1) Age-dependent impairment in phase shifting: Shift work adaptation↓
2) Flattening of the diurnal sleep-wake rhythm amplitude: ↑napping
3) Phase advance: more larklike

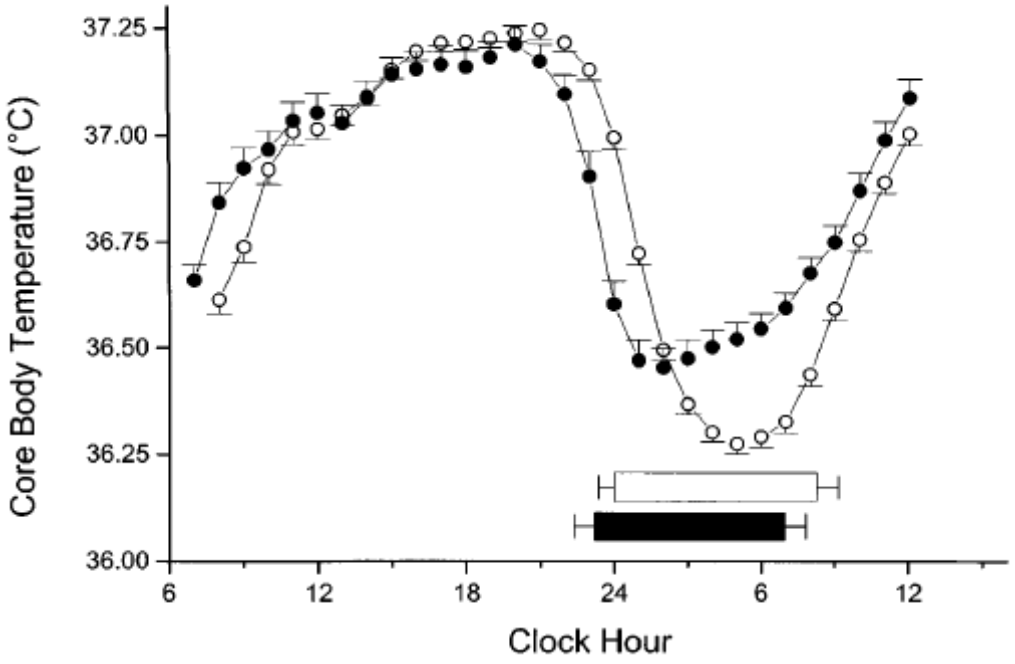


Fig. 3. Core body temperature waveforms averaged with respect to time of day for young and older subjects. ●, Older subjects (n = 43); ○, young subjects (n = 97); solid bar, usual sleep episode of older subjects (mean ± 1 SD); open bar, usual sleep episode of young subjects (mean ± 1 SD). Shown are data from scheduled *day 3*, the

(Duffy, Am J Physiol 1998:275:1478-87)

Age-Related Changes of Circadian Rhythms and Sleep-Wake Cycles

In-Young Yoon, MD, PhD, Daniel F. Kripke, MD,* Jeffrey A. Elliott, PhD,* Shawn D. Youngstedt, PhD,* Katharine M. Rex, BA,* and Richard L. Hauger, MD†*

OBJECTIVES: To compare relationships between the sleep-wake cycle and endogenous circadian rhythms in young and older adults and to examine correlates between evening naps and circadian rhythms in older adults.

DESIGN: For 1 week of home recording, subjects wore wrist-activity monitors and kept daily sleep logs. After the home monitoring, subjects entered the laboratory on a 90-minute sleep-wake schedule and were monitored on this schedule for at least 30 hours.

SETTING: Community living and laboratory.

PARTICIPANTS: Sixty-seven young adults, aged 18 to 32, and 56 older adults, aged 60 to 75, who were healthy and had few sleep complaints.

MEASUREMENTS: Times of nocturnal sleep, out-of-bed napping, and illumination were obtained at home. Sleep propensity and oral body temperature (OBT) were measured in the laboratory, along with circadian rhythms of cortisol and 6-sulfatoxymelatonin (aMT6s, assayed from urine samples collected every 90 minutes).

RESULTS: Home sleep times and illumination acrophases (fitted peak times) were advanced in older adults. The phase angles (time intervals) between onset of aMT6s and sleep onset were not changed in older adults, but sleep offset was more advanced than acrophase and offset of aMT6s with aging. Acrophases of cortisol and sleep propensity were advanced in older adults to the same extent as sleep times, but OBT was less advanced than sleep times. Older adults who took evening naps showed more advanced sleep offset and circadian rhythms of aMT6s, but there were no differences in the phase angles of sleep onset and circadian rhythms of aMT6s and cortisol compared with older adults who did not take evening naps.

CONCLUSION: Measuring different circadian markers suggested different phase relationships between the sleep-wake cycle and endogenous circadian rhythms in aging. Early awakening in older adults cannot be explained simply by a relative phase advance of the circadian system. Evening naps and advanced illumination may play a role in the advance of the circadian system in aging. J Am Geriatr Soc 51:1085–1091, 2003.

Key words: sleep-wake; circadian; aging; melatonin; naps

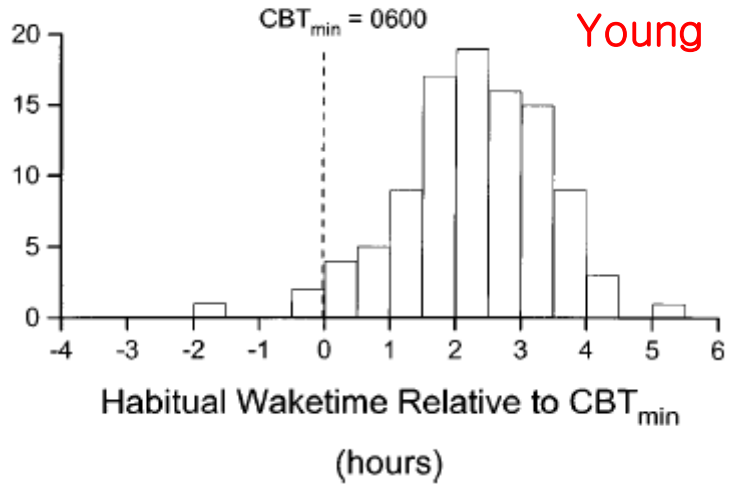
Older people often go to bed early at night and wake up early in the morning.[1,2] The advance of sleep time in older people has been explored in reference to endogenous circadian rhythms. Although it is generally accepted that older people show a phase advance of circadian rhythms compared with young people,[3,4] some studies have reported no phase advance of core body temperature (CBT)[5] or melatonin acrophase[6] in older people. There has also been some controversy about changes of phase relationships between sleep time and circadian rhythms in older people. In one study,[7] the interval between the CBT fitted minimum and awakening time was not different between young and older subjects. The interval was 85 minutes for the young group and 95 minutes for the older group. A similar result was replicated in another study, with the awakening time being

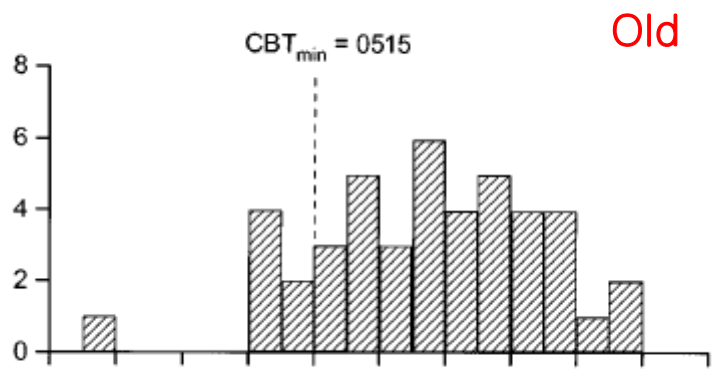
Circadian Rhythms in Aging (2)

Table 1. Parameters of Nocturnal Sleep at Home and Circadian Rhythms of 6-Sulphatoxymelatonin (aMT6s) and Cortisol in the Laboratory of Young and Older Adults

Parameter	Young (n = 67)	Older (n = 56)	*P*-value
	Mean ± Standard Deviation		
Sleep onset time	00:23 ± 1:12	22:51 ± 1:19	<.001
Sleep offset time	08:11 ± 1:22	06:32 ± 1:06	<.001
Total sleep time, minutes	421.7 ± 48.3	367.1 ± 51.6	<.001
Wake time after sleep onset, minutes	45.08 ± 20.29	94.67 ± 54.43	<.001
aMT6s onset	23:10 ± 1:41	22:01 ± 2:14	.002
aMT6s acrophase	03:39 ± 1:30	03:02 ± 1:40	.004
aMT6s offset	8:29 ± 2:04	8:04 ± 1:45	.245

(Yoon, JAGS 2003:51:1085-91)





(Duffy, Am J Physiol 1998:275:1478-87)

Circadian Rhythms in Aging (3)

- Typical sleep period is more advanced than circadian markers in the elderly

1) The earlier bedtimes and wakeup times in the elderly
   : Changes in the circadian timing system is not the only answer.
2) A weakening of homeostatic processes in the regulation of sleep and waking
   : Decreased ability to consolidate sleep in the elderly
   : Earlier exposure to light in the morning and evening nap
   : Earlier wakeup times

Sleep Apnea Syndrome

Prevalence

Table 1. Sample Characteristics by Sleep-Disordered Breathing Severity*

Characteristic	No. of Participants	Apnea-Hypopnea Index		
		<5	5-14	≥15
Total sample	5615	53	29	18
Sex				
Male	2648	42	33	25
Female	2967	63	26	11
Age, y				
39-49	519	70	19	10
50-59	1648	60	24	16
60-69	1668	49	32	19
70-79	1425	46	33	21
80-99	355	44	36	20

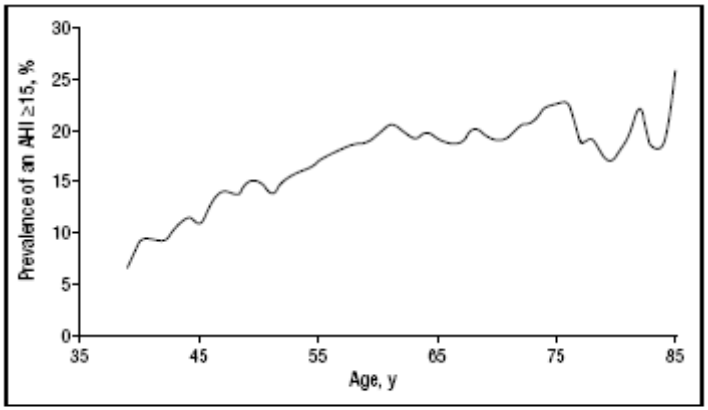


Figure 1. Smoothed plot (5-year moving average) of the prevalence of an apnea-hypopnea index (AHI) of 15 or greater by age.

(Young, Arch Intern Med 2002:162:893-900)

c.f.) Vitoria-Gasteiz, Spain Cohort
: 71-100 years, men: AHI≥ 5, 81% / AHI≥ 15, 57%
women: AHI≥ 5, 80% / AHI≥ 15, 49%

Mechanisms for the increasing prevalence

1. Upper airway (UA) collapsibility ↑
   : UA resistance ↑, pharyngeal wall fat deposit ↑
   muscular endurance ↓

2. Sleep fragmentation ↑ and Slow wave sleep ↓
   → respiratory instability characterized by periodic breathing and central apneas

3. Ventilatory control instability

4. Not receiving HRT in women
   : The role of sex hormones in UA muscle activity, UA resistance
   and ventilatory control

→ An amplification of well-established causes of SAS

(Launois, Sleep Med Rev 2007:11:87-97)

AGE AND RESPIRATORY DISTURBANCE

Polysomnographic Respiratory Abnormalities in Asymptomatic Individuals

Milena K. Pavlova, MD; Jeanne F. Duffy, MBA, PhD; Steven A. Shea, PhD

(Pavlova and Duffy, Sleep 2008:31:241-248)

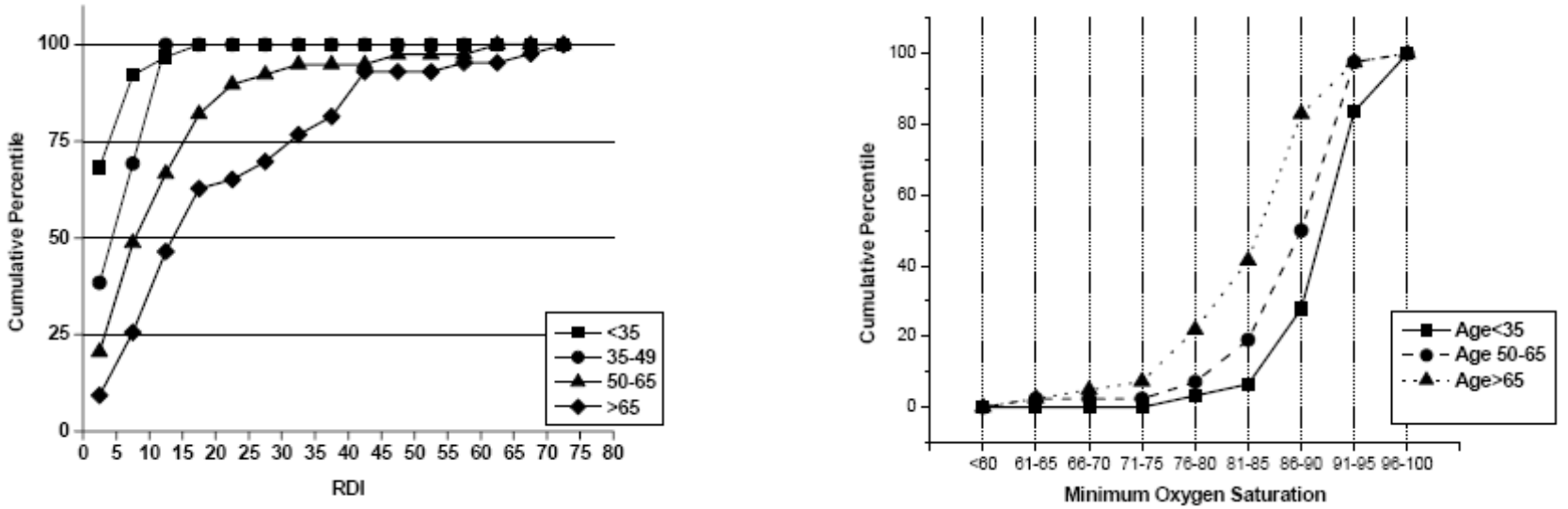


Figure 2—Cumulative relative frequency of respiratory disturbance index (RDI: events per hour of sleep; upper plot) and minimum arterial oxyhemoglobin saturation recorded overnight (%: lower plot) according to age group. More than 95% of the subjects younger than 50 had an RDI < 12.5, whereas fewer than 50% of the subjects older than 65 years had RDI < 12.5. The increasing RDI with age was associated with concomitant lower minimum arterial oxyhemoglobin saturation with age (1 age group was omitted from the arterial oxyhemoglobin saturation plot due to missing or insufficient data).

CV Disease and SAS (1)

1. Weaker or no association between CV risk factors and SAS in the populations ≥ 65 years than the ones < 65 years

1) Relation of sleep-disordered breathing to cardiovascular disease risk factors: the Sleep Heart Health Study. *Newman AB. Am J Epidemiol. 2001:154:50-9.* - *only in women*

2) Age-dependent associations between sleep-disordered breathing and hypertension : the Sleep Heart Health Study. *Haas DC, Circulation. 2005:111:614-621.* - *no association in OSA pts ages over 60 years*

2. The relationship between CV disease and SAS is maintained with aging.

1) Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study.*Nieto FJ, JAMA. 2000: 283:1829-36.*

2) Sleep-disordered breathing and cardiovascular disease: cross-sectional results of the Sleep Heart Health Study. *Shahar E. Am J Respir Crit Care Med. 2001:163:19-25.*

CV Disease and SAS (2)

Eur Respir J 2009; 33: 797–803
DOI: 10.1183/09031936.00023208

Association between C-reactive protein and unrecognised sleep-disordered breathing in the elderly

F. Roche*,#, J-M. Gaspoz*,#, V. Pichot*,¶, M. Picard-Kossovsky#, D. Maudoux*, A. Garcin*, S. Celle*,¶, E. Sforza* and J.C. Barthélémy*,¶ on behalf of the PROOF and SYNAPSE Study Groups

TABLE 3 Spearman correlation coefficients relating log C-reactive protein (CRP) with nocturnal parameters

	Log CRP	AHI	ODI	AAI
AHI				
Coefficient	0.060	1		
p-value	0.09			
ODI				
Coefficient	0.121	0.803		
p-value	0.006	<0.0001		
AAI				
Coefficient	0.037	0.799	0.652	1
p-value	0.301	<0.0001	<0.0001	
S_{p,O_2} <90% time %				
Coefficient	0.078	0.162	0.295	0.074
p-value	0.027	<0.0001	<0.0001	0.036
Minimal S_{p,O_2}				
Coefficient	-0.082	-0.408	-0.571	-0.291
p-value	0.020	<0.0001	<0.0001	<0.0001
Sleep duration				
Coefficient	-0.013	-0.103	-0.023	-0.131
p-value	0.704	0.003	0.519	0.001

AHI: apnoea/hypopnoea index; ODI: oxygen desaturation index; AAI: autonomic arousals index; S_{p,O_2}: arterial oxygen saturation measured by pulse oximetry; AAI: autonomic respiratory-related arousal index.

CV Disease and SAS (3)

Sleep Breath (2009) 13:11–17
DOI 10.1007/s11325-008-0210-x

ORIGINAL ARTICLE

Endothelial dysfunction and inflammatory reactions of elderly and middle-aged men with obstructive sleep apnea syndrome

Seockhoon Chung · In-Young Yoon · Yoon-Kyung Shin · Chul Hee Lee · Jeong-Whun Kim · Hee Jeong Ahn

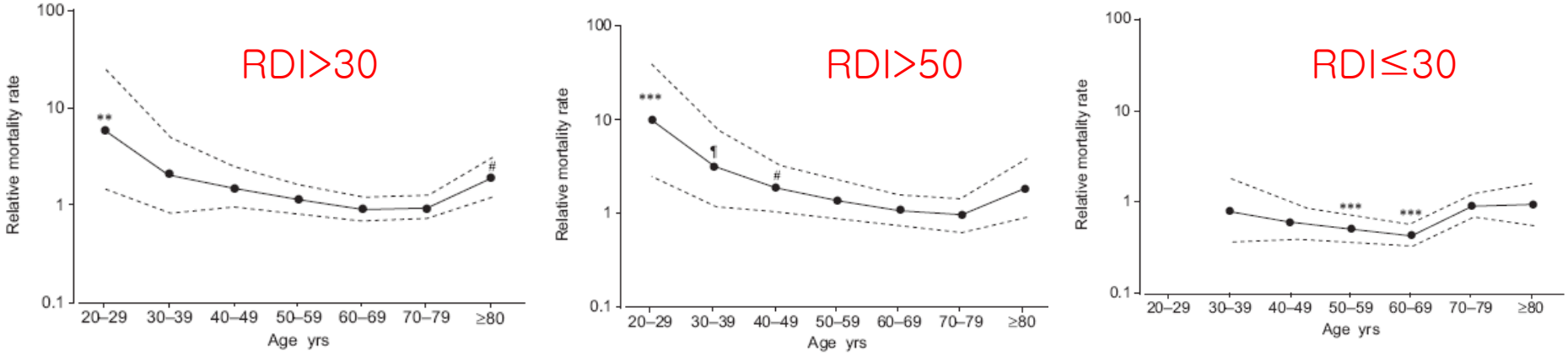
Table 3 Stepwise multiple linear regression model of FMD and Log CRP in middle-aged and elderly OSAS patients

Group	Dependent variable	Included parameters	Beta	Adjusted R^2	p value
Middle-aged	FMD	Lowest O_2 saturation	0.25	6%	<0.01
	Log CRP	BMI	0.22	11%	<0.01
		Waist-to-hip ratio	0.21		
Elderly	FMD	No variable	–	–	–
	Log CRP	AHI	0.46	19%	<0.01

OSAS Obstructive sleep apnea syndrome, *FMD* flow-mediated dilatation, *CRP* C-reactive protein, *BMI* body mass index, *ODI* oxygen desaturation index, *AHI* apnea hypopnea index

Mortality and SAS (4)

- Declining all-cause mortality rates with age



(Lavie, Eur Respir J 2005:25:514-520)

1. Marked CV response in young severe OSA → Early mortality
   → Only patients resistant to SAS seen among elderly patients

2. Pre-conditioning effect due to repeated intermittent hypoxia
   → Promoting some degree of cardiovascular protection

Cognitive Impairment and SAS (1)

Sleep-Disordered Breathing and Cognitive Impairment in Elderly Japanese-American Men

Daniel J Foley, MS[1]; Kamal Masaki, MD[2,3]; Lon White, MD, MPH[2,3]; Emma K. Larkin, MHS[4]; Andrew Monjan, PHD, MPH[5]; Susan Redline, MD, MPH[4]

(SLEEP 2003:26:596–599)

Table 2—Sociodemographics, selected risk factors, and medical conditions by severity of sleep-disordered breathing: HAASSA 1999-2000

Characteristics	Sleep-disordered Breathing[1] Total (N=718)	AHI<5 (N=204)	AHI=5-29 (N=376)	AHI ≥30 (N =132)
Age 85 yrs and older	27.2%	30.4%	27.1%	25.0%
Married	77.1	76.0	74.7	83.3
High school education	57.3	54.9	58.0	57.6
Body mass index ≥30	3.6	3.9	2.1	6.8*
Neck size >16 inches	16.1	12.8	16.0	22.0
Habitual Snoring	20.9	13.7	20.7	31.1**
Daytime drowsiness	20.2	16.7	19.4	30.3**
IADL/ADL difficulty	25.4	24.5	24.7	29.6
Depressed mood (CESD-11>8)	9.5	9.8	8.8	12.9
Poor cognition (CASI<74)	12.0	15.7	11.2	18.2
History of:				
Stroke	12.6	11.8	12.5	14.4
CHD	21.4	23.0	19.7	23.5
Hypertension	62.9	59.3	62.2	71.2
Diabetes	25.9	24.5	26.1	28.0

Table 3—Mean cognitive functioning scores[1] by severity of sleep-disordered breathing: HAASSA 1999-2000

AHI	CASI	MMSE	Short-term Memory	Attention	Concentration
Range	0-100	0-30	0-12	0-8	0-10
<5 (absent)	83.3	24.1	7.9	6.4	7.7
5-14 (mild)	83.7	24.2	8.0	6.4	7.7
15-29 (moderate)	83.5	24.1	8.0	6.4	7.7
30+ (severe)	83.6	24.2	8.0	6.4	7.7

[1] Mean score is adjusted for age; HAASSA, Honolulu-Asia Aging Study of Sleep Apnea; CASI, Cognitive Abilities Screening Instrument; MMSE, Mini-Mental State Examination; AHI, apnea-hypopnea index

Cogni

SAS (2)

ELDERLY WITH SLE

Cognitive Funct
Population: the

Healthy Elderly

Emilia Sforza, MD, PhD*[1]; Fréd
Sébastien Celle, PhD[1]; Delphine

Beauchet, MD, PhD[3];
MD, PhD[1]

):33:515–521)

Table 3—Scores of cognitive function tests (mean ± SD) of participants according to apnea-hypopnea index (AHI)

	AHI < 15 (n = 382)	AHI 15-30 (n = 278)	AHI > 30 (n = 167)	*P
Subjective cognitive difficulties	29.1 ± 1.9	29.2 ± 1.9	29.1 ± 2.0	ns
MMSE (score)	28.4 ± 1.7	28.7 ± 1.4	28.6 ± 1.2	ns
FCSR				
Total Immediate recall	15.4 ± 0.9	15.4 ± 0.8	15.2 ± 1.1	ns
Total Delayed recall	15.6 ± 0.9	15.6 ± 0.8	15.2 ± 1.3	0.02
Free Delayed recall	12.2 ± 2.2	12.1 ± 2.3	11.7 ± 2.8	0.04
Recognition score	15.9 ± 0.4	15.9 ± 0.4	15.8 ± 0.6	0.06
Visual memory	12.5 ± 1.6	12.4 ± 1.8	12.4 ± 1.8	ns
DST				
Digit span forward	5.5 ± 1.0	5.5 ± 1.1	5.4 ± 1.1	ns
Digit span backward	4.2 ± 1.0	4.2 ± 0.9	4.2 ± 1.0	ns
Baddeley dual task				
Dual task decrement	93.5 ± 10.1	93.0 ± 10.5	92.9 ± 12.2	0.08
Trail Making				
Trail Making Test A (speed)	47.5 ± 15.8	46.5 ± 15.4	47.5 ± 15.4	ns
Trail Making Test A (errors)	0.10 ± 0.3	0.10 ± 0.4	0.13 ± 0.4	ns
Trail Making Test B (speed)	103.5 ± 48.8	104.3 ± 50.6	103.2 ± 48.5	ns
Trail Making Test B (errors)	0.45 ± 0.9	0.47 ± 0.7	0.46 ± 0.9	ns
Semantic memory				
Verbal fluency Phonemic	19.3 ± 6.5	19.2 ± 6.4	19.5 ± 7.2	ns
Verbal fluency Semantic	29.5 ± 7.8	30.0 ± 8.3	30.6 ± 8.5	ns
Stroops				
Word (score)	98.1 ± 13.7	97.9 ± 13.9	96.5 ± 15.2	ns
Color (score)	70.7 ± 10.7	70.6 ± 11.2	68.1 ± 11.5	0.03
Color word (score)	49.3 ± 7.7	49.2 ± 8.3	49.0 ± 8.6	ns
WAIS Similarities test	16.9 ± 5.5	16.9 ± 5.5	17.3 ± 5.5	ns

FCSR, Free and cued selective reminding test; DSST, digit symbol substitution test.
*One-way Anova

Cognitive Impairment and SAS (3)

Minimal Cognitive Impairment in the elderly with SAS (in SNUBH)

	Without SAS AHI<15 (n=23)	With SAS 5≤AHI<30 (n=21)	With SAS AHI≥30 (n=21)	*p*
MMSE	26.2±2.6	27.2±1.8	26.1±3.0	.266
Verbal Fluency (semantic)	16.1±3.8	16.7±5.8	16.3±4.4	.917
BNT	12.2±1.8	12.6±1.6	11.4±4.4	.157
WLM _immediate recall	19.3±3.6	19.3±3.2	17.7±3.9	.229
WLRT _delayed recall	**7.1±1.6**	**7.2±1.5**	**6.0±1.2**	**.016**
WLRcT _recognition	9.1±1.4	9.4±1.4	9.3±1.0	.719
CPT	10.0±1.5	10.2±1.1	9.8±1.1	.539
Visual memory (CR)	7.3±2.6	7.3±3.4	6.8±3.0	.831
TMT_A_error	.39±.65	.43±.68	.43±.81	.980
TMT A time	**58.6±20.4**	**48.9±24.9**	**68.2±33.8**	**.072**
TMT B error	1.1±1.4	1.2±1.8	2.1±1.7	.111
TMT B time	175.7±77.1	144.3±85.2	175.4±79.4	.352

SAS, Sleep apnea syndrome; MMSE, Mini-Mental State Examination; BNT, Boston naming test; WLM, word list memory-immediate test; WLRT, word list-delayed free recall test; WLRcT, word list-recognition test; CPT, constructional performance; CR, Constructional recall; TMT, trail making test;

Daytime sleepiness and SAS (1)

- Is sleepiness increased with aging ?

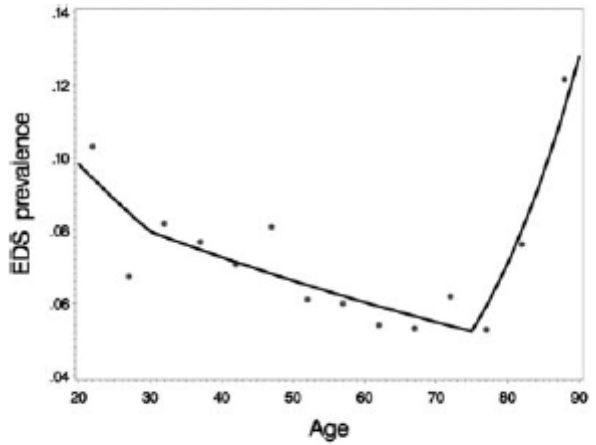


FIG. 1. Age-specific prevalence of EDS.

(Bixler, J Clin Endocrinol Metab 2005:90:4510-15)

Table 4. Prevalence(%) of sleep problems by age and sex.

	Male							Female						
	20-29	30-39	40-49	50-59	60-69	70+	total	20-29	30-39	40-49	50-59	60-69	70+	total
Difficulty initiating sleep	17.4	14.8	13.1	12.5	13.4	14.8	14.2	21.0	18.1	13.8	21.4	23.6	21.8	20.0
Difficulty maintaining sleep	9.5	14.8	16.2	18.6	23.0	29.0	18.1	17.0	21.7	19.5	24.2	26.8	30.7	23.4
Early morning awakening	9.6	16.1	26.0	34.7	40.3	35.2	26.9	11.1	12.3	15.8	22.4	30.1	31.6	20.6
Loss of deep sleep	29.4	30.8	27.5	18.7	13.0	11.0	22.1	33.7	34.8	29.3	23.4	16.3	11.3	24.8
Interruption of sleep by snoring or dyspnea	1.5	3.3	3.3	3.1	2.5	1.8	2.6	0.8	1.0	1.5	2.2	1.7	1.5	1.5
Disagreeable sensations in legs	1.7	2.7	2.7	2.0	2.6	3.2	2.4	3.1	2.8	2.9	3.5	3.7	4.2	3.4
Excessive daytime sleepiness	4.6	3.8	3.5	2.1	1.8	0.9	2.8	4.0	2.8	3.0	1.9	0.9	0.7	2.2
n	2241	2262	2397	2710	2252	1737	13599	2400	2434	2488	2914	2424	2455	15115

(Kaneita, J Epidemiol 2005:15:1-8)

Daytime sleepiness and SAS (2)

Risk Factors for Excessive Sleepiness in Older Adults

Allan I. Pack, MB, ChB, PhD,[1,2] David F. Dinges, PhD,[1,3] Philip R. Gehrman, PhD,[1] Bethany Staley, RPSGT,[1] Frances M. Pack, RN,[1] and Greg Maislin, MS, MA[1,2]

(Ann Neurol 2006:59:893–904)

Table 4. Final Multivariable Model and Sensitivity Analysis for Final Multivariable Model

	Final Multivariable Model[a]		Sensitivity Analysis for the Final Multivariable Model[b]
Variables	OR (95% CI)	*p*	OR (95% CI)
Apnea–hypopnea index (OR for 20-events/hr increase)	1.4 (1.1–1.9)	0.01	1.4 (1.0–1.9)
PSQI self-report of overall sleep quality (OR for one-point increase)	2.3 (1.6–3.6)	<0.0001	1.8 (1.1–3.0)
% Time in REM sleep (OR for 6.8% increase)	1.4 (1.1–1.9)	0.01	1.4 (1.0–2.0)
Pain or physical discomfort ≥3 times/week	5.9 (2.2–19.0)	0.001	19.2 (3.3–370.2)
Any wheezing or whistling from chest at night	3.2 (1.4–8.0)	0.001	5.1 (1.6–18.7)
US Pharmacopoeia more/less common vs rare/none	1.9 (1.1–3.3)	0.02	1.5 (0.8–3.1)
Male sex	1.9 (1.0–3.5)	<0.05	3.7 (1.6–9.0)
>7 alcoholic beverages per week	0.42 (0.20–0.86)	0.02	0.28 (0.10–0.72)

Daytime sleepiness and SAS (3)

Sleep disordered breathing in an elderly community-living population: Relationship to cardiac function, insomnia symptoms and daytime sleepiness

Peter Johansson [a,b,*], Urban Alehagen [a,b], Eva Svanborg [c,d], Ulf Dahlström [a,b], Anders Broström [c,e]

(Sleep Med 2009:10:1005–1011)

Table 1
Characteristics of the population and subjective sleep complaints across the severity of SDB.

Characteristics	AHI					
	<5 No SDB (*n* = 148, 45%)	⩾5 Mild SDB (*n* = 107, 32%)	⩾15 Moderate SDB (*n* = 53, 16%)	⩾30 Severe SDB (*n* = 23, 7%)	p^1	p^2
Male, % (*n*)	43 (64)	53 (57)	55 (29)	61 (14)	0.2	**0.035**
Age, mean (SD)	78.6 (3.5)	78.1 (2.9)	78.7 (3.2)	78.5 (3)	0.48	0.77
SBP, mean (SD)	148 (18)	149 (19)	148 (23)	146 (17)	0.91	0.64
DBP, mean (SD)	74 (9)	75 (9)	75 (9)	76 (9)	0.81	0.36
BMI, mean (SD)	26.7 (3.6)	28.2 (5)	27.4 (4.3)	29.9 (4.3)	**0.001**	**0.02**
Comorbidities						
Diabetes, % (*n*)	22 (32)	22 (23)	32 (17)	22 (5)	0.43	0.35
HT, % (*n*)	71 (105)	72 (77)	81 (43)	70 (16)	0.52	0.4
IHD, % (*n*)	21 (31)	27 (29)	36 (19)	26 (6)	0.2	0.06
RD, % (*n*)	18 (27)	16 (17)	11 (6)	17 (4)	0.7	0.36
TIA/Stroke, % (*n*)	5 (8)	8 (9)	15 (8)	17 (4)	0.08	**0.02**
Medication						
ACEI/ARB, % (*n*)	21 (31)	34 (36)	32 (17)	26 (6)	0.12	0.06
B-blockers, % (*n*)	27 (40)	43 (46)	57 (30)	44 (10)	**0.001**	**<0.01**
Digoxin, % (*n*)	4 (6)	7 (8)	6 (3)	4 (1)	0.69	0.52
Diuretics, % (*n*)	32 (48)	35 (37)	38 (20)	48 (11)	0.52	0.51
Hypnotics, % (*n*)	15 (23)	13 (14)	13 (7)	22 (5)	0.73	0.97
Insomnia symptoms						
DIS, % (*n*)	36 (53)	38 (41)	51 (27)	52 (12)	0.15	**0.04**
DMS, % (*n*)	65 (96)	63 (67)	66 (35)	61 (14)	0.95	0.84
NRS, % (*n*)	36 (54)	41 (44)	49 (26)	52 (12)	0.27	0.06
EMA, % (*n*)	43 (63)	36 (38)	38 (20)	44 (10)	0.68	0.5
Excessive daytime sleepiness						
ESS, mean (SD)	6.5 (3.8)	6.6 (3.8)	6.8 (3.5)	6.7 (4.1)	0.81	0.57
ESS ⩾ 10, % (*n*)	18 (27)	21 (22)	24 (13)	22 (5)	0.8	0.36

Daytime sleepiness and SAS (4)

Effects of Age on the Clinical Features of Men with Obstructive Sleep Apnea Syndrome

Seockhoon Chung[a] In-Young Yoon[b] Chul Hee Lee[c] Jeong-Whun Kim[c]

(Respiration 2009:78:23–29)

Table 5. Results of subjective assessment scales and polysomnographic findings related with sleep structures

	Young (n = 254)	Middle-aged (n = 373)	Elderly (n = 130)	p value
Total sleep time, min[a–c]	370.9 ± 61.3	354.7 ± 56.2	333.3 ± 57.3	<0.01
Sleep efficiency, %[a–c]	86.9 ± 9.3	83.4 ± 10.5	76.3 ± 11.6	<0.01
Wake time during sleep period, min[a–c]	48.6 ± 45.3	61.4 ± 43.0	87.3 ± 50.9	<0.01
Wakes, n[a, b]	9.5 ± 6.5	12.9 ± 15.4	15.8 ± 23.5	<0.01
Sleep latency, min	15.9 ± 41.9	12.9 ± 26.5	19.7 ± 30.2	0.12
Stage 1, %	14.7 ± 8.2	16.3 ± 9.0	16.9 ± 10.4	0.04
Stage 2, %[b, c]	52.5 ± 10.7	51.6 ± 11.0	47.0 ± 14.8	<0.01
Stage 3 and 4, %[a, b]	6.3 ± 5.8	2.7 ± 4.1	1.9 ± 5.3	<0.01
REM sleep, %	15.4 ± 5.8	14.7 ± 6.3	13.7 ± 7.4	0.06
Respiratory arousal index	16.2 ± 19.4	16.2 ± 19.1	14.2 ± 18.2	0.56
PSQI[b, c]	7.4 ± 3.3	8.0 ± 4.4	10.0 ± 5.1	<0.01
Patients with PSQI > 5, n[1]	167/239 (69.9%)	227/345 (65.8%)	81/106 (76.4%)	0.11
ESS[b, c]	10.8 ± 4.7	10.6 ± 5.4	7.8 ± 5.0	<0.01
Patients with ESS > 10, n[1, b, c]	126/246 (51.2%)	175/366 (47.8%)	36/114 (31.6%)	<0.01

[a] $p < 0.05$, young versus middle-aged; [b] $p < 0.05$, young versus elderly; [c] $p < 0.05$, middle-aged versus elderly.
[1] Estimated in patients who responded to each scale.

Restless Legs Syndrome (RLS)

Diagnostic Criteria

Essential diagnostic criteria for RLS

1	An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs (Sometimes the urge to move is present without the uncomfortable sensations and sometimes the arms or other body parts are involved in addition to the legs)
2	The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting
3	The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues
4	The urge to move or unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night (When symptoms are very severe, the worsening at night may not be noticeable but must have been previously present)

IRLSSG, 1995
→ NIH revision, 2003

(Allen, Sleep Med 2003;4:101-119)

하지 불안 증후군의 진단기준(필수항목)

1. 다리를 움직이고 싶은 강한 충동을 느낀다. 이러한 충동은 다리에 불편한 혹은 불쾌한 감각과 동반되어 나타나는 경우가 흔하다.

2. 움직이고 싶은 충동 혹은 불쾌한 감각이 눕거나 앉아있는 동안, 즉 휴식 중이나 가만히 있는 동안에 발생하거나 악화된다.

3. 움직이고 싶은 충동 혹은 불쾌한 감각이 걷거나 다리를 뻗는 등의 움직임에 의해 부분적으로 혹은 완전히 해소되며, 최소한 움직이는 동안에는 이러한 증상의 해소가 지속된다.

4. 움직이고 싶은 충동 혹은 불쾌한 감각이 낮보다 저녁 혹은 밤에 더 심하거나 저녁 혹은 밤에만 발생한다.

Psychiatry and Clinical Neurosciences (2005), **59**, 350–353

Short Communication

Prevalence of restless legs syndrome and associated factors in the K : The Korean Health and Ge

12.1%

Epidemiology of Rest ean Adults

Yong Won Cho, MD, PhD[1,6]; Won Chul Shi , PhD[4,6]; Ju Han Kim, MD, PhD[5,6]; Richard P. Allen, PhD[7]; Christopher J. Earley, MBBCh, PhD[7]

SLEEP 2008;31(2):219-223.

7.5%

Restless Legs Syndron f Korean Adults: Prevalence, Impact on Quality of Lif -IV Psychiatric Disorders

Seong-Jin Cho, MD, PhD[1]; Jin Pyo Hong, MD PhD[4]; Sung Man Chang, MD, PhD[5]; Maeng Je Cho, MD, PhD[3]; Hochang B. Lee,

SLEEP 2009;32(8):1069-1076.

0.9%

J. Sleep Res. (2010) 19, 87– stless legs syndrome

doi: 10.1111/j.1365-2869.2009.0073

Prevalence, con f restless legs syndrome in th – results from the Korean Longitudinal Study on Health and Aging

KI WOONG KIM[1,2], IN-YOUNG YOON[1,2], SEOCKHOON CHUNG[1], YOON-KYUNG SHIN[3], SEOK BUM LEE[1], EUN AE CHOI[4], JOON HYUCK PARK[1] and JONG-MIN KIM[5]

[1]Department of Neuropsychiatry, Seoul National University Bundang Hospital, Gyeonggi-do, [2]Department of Psychiatry, Seoul National

8.4% in the elderly

Pathophysiology (1)

* Central dopamine system dysfunction

1) Therapeutic effects of L-dopa and dopamine agonists
2) Akathisia – caused by dopamine receptor-blocking agents
3) Imaging studies – mixed results

* Brain Iron Deficiency

* Genetics – familial aggregation of RLS

* Opiate system dysfunction

Korean Longitudinal Study on Health and Aging (KLoSHA)

	RLS (N=59)	Non-RLS (N=655)	Significance
Hemoglobin (g/dL)	13.7 ± 1.2	13.9 ± 1.4	0.3
Iron (μg/dL)	105.7 ± 37.8	102.7 ± 36.0	0.55
Ferritin (ng/ml)	119.4 ± 106.0	114.6 ± 121.1	0.77
Ferritin (< 50ng/ml, %)	18.6	22.1	0.36
Transferrin (mg/dL)	236.7 ± 39.9	238.2 ± 44.1	0.8
TIBC (μg/dL)	326.6 ± 51.0	332.0 ± 52.3	0.45

Studies using SPECT or PET

- Nigrostriatal dopamine system

Presynaptic transporter

1) No difference between RLS patient and normal controls (SPECT)
2) Reduction in RLS patients (PET)

Postsynaptic receptor

1) No difference (SPECT)
2) Lower D2 receptor binding (PET and SPECT)

- Striatal and extrastriatal postsynaptic system

Cervenka, Brain 2006;129 (Part 8): 2017-2028

D2-Rc availability ↑ in RLS

: Higher Rc density (due to upregulation) or hypoactive DA transmission

Objectives

- To investigate striatal presynaptic DA transporters (DAT) and D2 receptors in elderly patients with RLS

- To find the correlation between DA dysfunction and RLS severity in the RLS patients

Subjects

- Thirteen drug-naïve elderly patients with RLS and 12 healthy controls

- Diagnosis of RLS
  : Face to face interview, four diagnostic criteria by NIH
  Severity of RLS – IRLSSG Severity Scale
  Depressive symptoms – Geriatric Depression Scale (GDS)

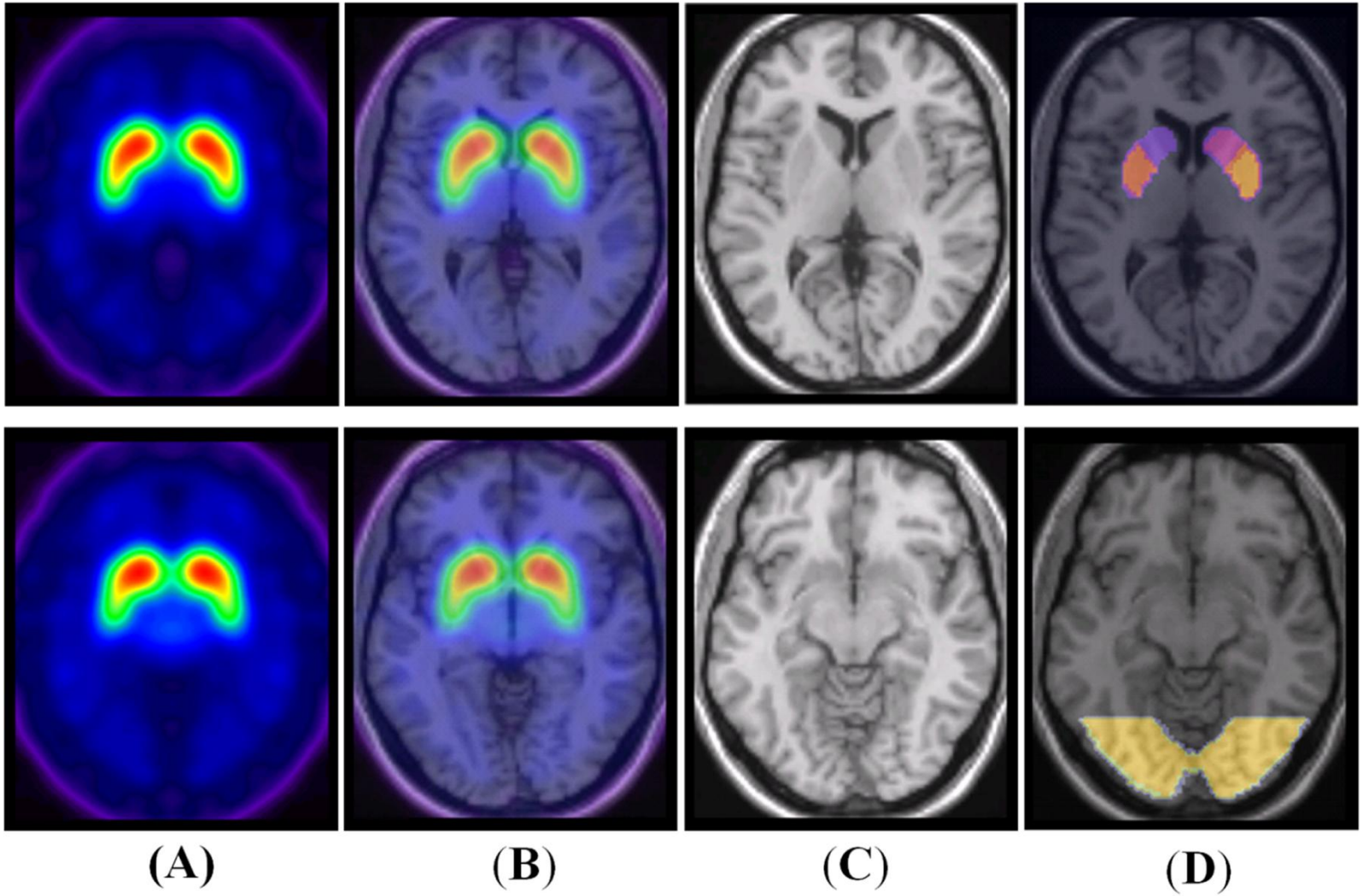
- Exclusion
  : Parkinson's disease, Major depressive disorder

SPECT Scans

- A triple-headed rotating γ-camera system equipped with low-energy, high resolution, parallel-hole collimators

- Data acquisition
  1) ^{123}I-βCIT SPECT
     : 20-22 hours after injection of 167-185 MBq of ^{123}I-βCIT
     (16:30 – 18:30)
  2) ^{123}I-IBZM SPECT
     : 90 min after injection of 167-185 MBq of ^{123}I-IBZM
     (19:00 – 21:00)
  3) At least 1 week apart between two SPECTs

- ROI for entire striatum, caudate and putamen
  : Manually defined on the SPECT template superimposed on standard MRI



^{123}I-βCIT template superimposed onto the standard MRI (A,B,C).
ROIs were manually drawn on the [123I] β-CIT after overlapping with standard brain MRI, and striatal ROI was divided into the caudate and putamen (D).

Subjects characteristics

	Control (N=12)	RLS (N=13)	*P* Value
Age, yr	71.8±6.2	81.1±8.7	< 0.01
Sex M/F	8/4	4/9	0.11
RLS severity		17.0±4.4 (range: 9-26)	
GDS	7.3±4.7	7.3±4.2	0.97

DAT and D2 Rc density

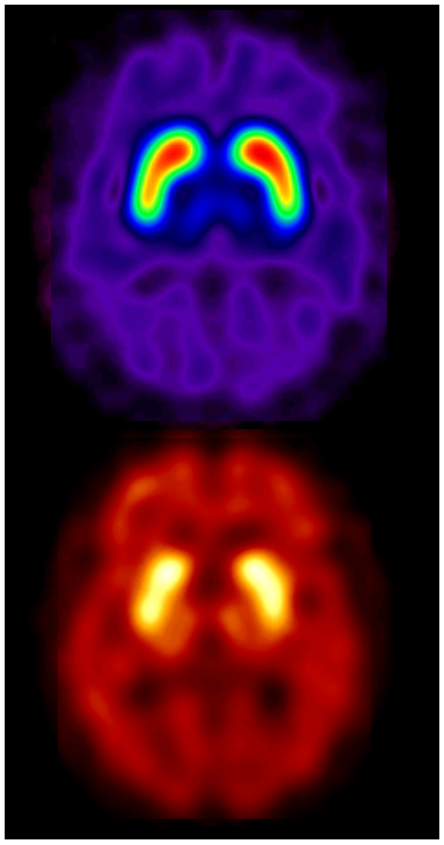
	^{123}I-βCIT			^{123}I-IBZM		
	Control	RLS	*P* Value	Control	RLS	*P* Value
Caudate	7.3±1.1	8.4±1.3	0.037	0.73±0.24	0.82±0.15	0.325
Ant. putamen	7.8±1.1	8.8±1.4	0.079	0.98±0.22	1.03±0.21	0.572
Post. putamen	6.5±1.0	7.2±1.1	0.041	0.88±0.20	0.93±0.20	0.533
Striatum	7.2±1.1	8.1±1.2	0.046	0.85±0.21	0.91±0.18	0.448

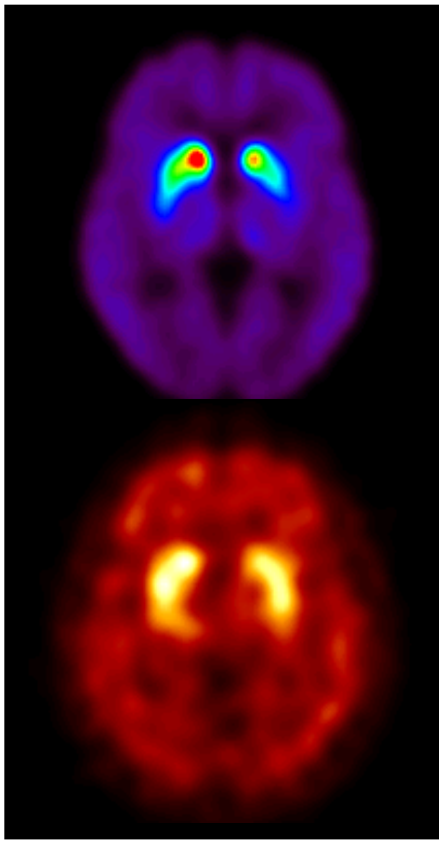
ANCOVA, covariate - age

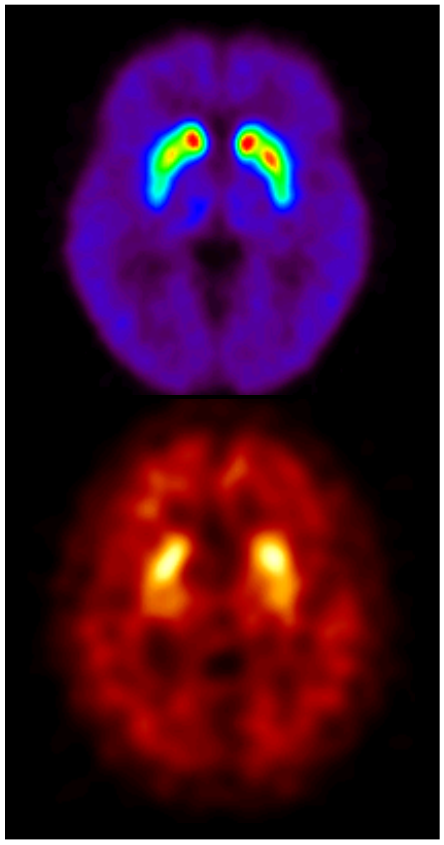
Correlational analysis

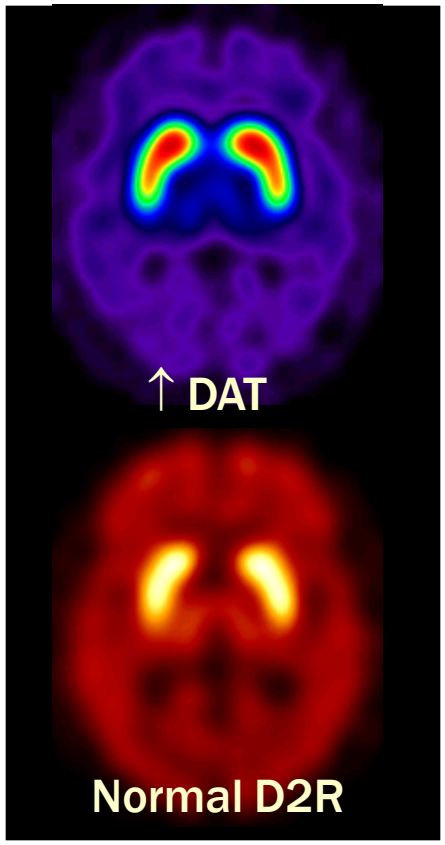
	^{123}I-βCIT		^{123}I-IBZM	
	RLS severity	*P* Value	RLS severity	*P* Value
Caudate	-0.366	0.268	0.386	0.241
Ant. putamen	-0.304	0.364	0.431	0.186
Post. putamen	-0.354	0.285	0.229	0.499
Striatum	-0.346	0.297	0.362	0.273

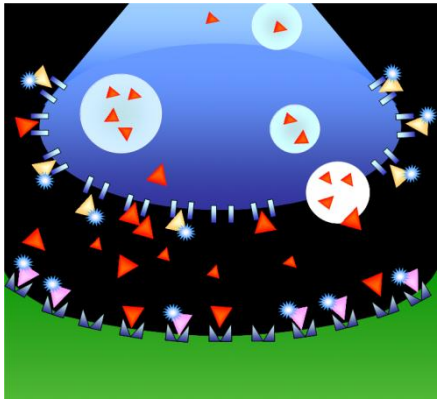
Partial correlation, control variables – age and GDS

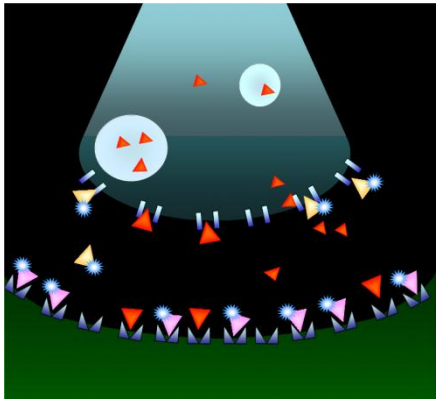


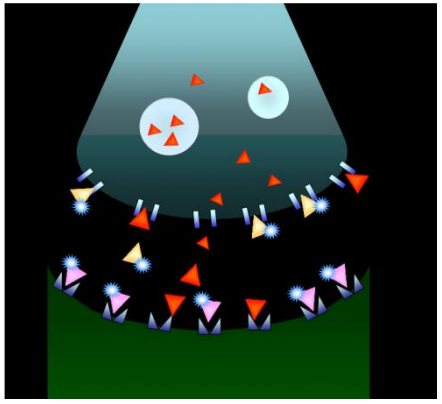


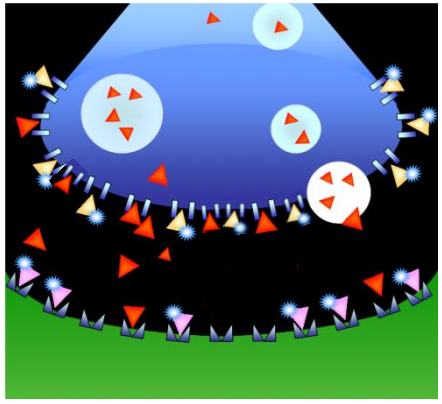












Normal

PD

MSA

RLS

Conclusion

- Nigrostriatal dopamine system in RLS
  : Presynaptic transporter ↑, postsynaptic receptor ↔

1) A novel finding

2) Suggesting functional change of DA system in RLS
   in comparison to structural change of DA system in PD

3) Differences between PD and RLS
   i) No progression of RLS to PD
   ii) Fluctuating clinical course
   iii) Circadian variation of symptoms
   iv) RLS - More prevalent in female

REM sleep behavior disorder (RBD)

Diagnostic Criteria

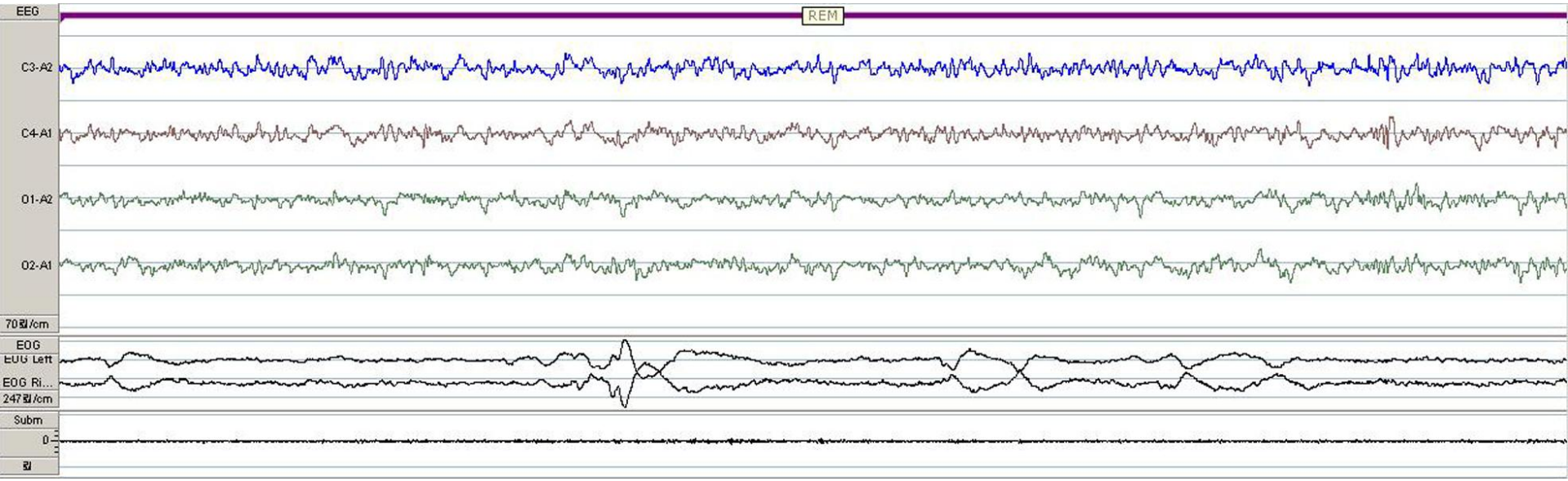
- REM Sleep Behavior Disorder (ICSD-2, 2005)

A) Presence of REM sleep without atonia (**RSWA**)
: the EMG finding of excessive amounts of sustained or intermittent elevation of submental EMG tone
: excessive phasic submental or limb EMG twitching

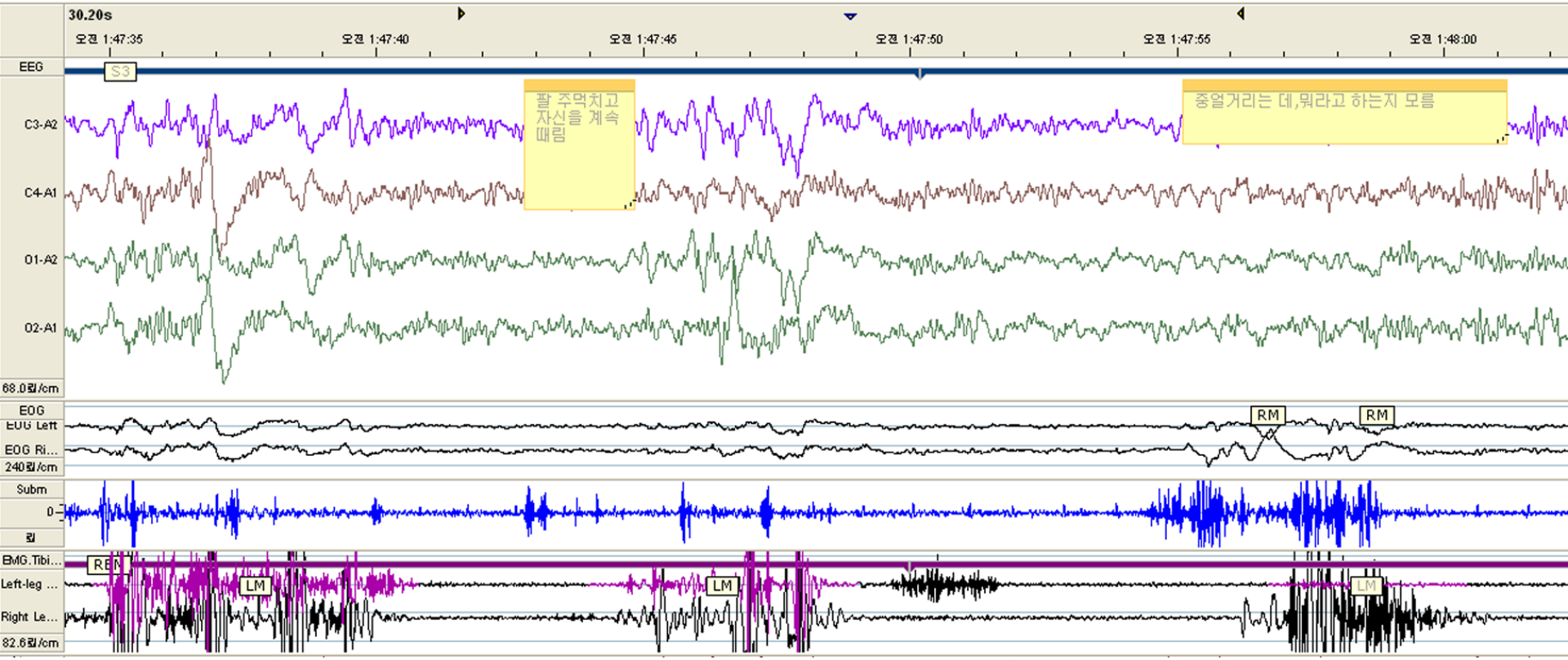
B) At least one of the following
i) Sleep related injurious or disruptive behaviors by history
ii) Abnormal REM sleep behaviors during NPSG

C) No EEG epileptiform activity during REM sleep
D) No other causes

Normal REM sleep



PSG of RBD



1. Excessive limb EMG twitching
2. Vigorous and violent behavior

European Journal of Neurology 2010, **17:** 487–492 doi:10.1111/j.1468-1331.2009.02854.x

The implication of nigrostriatal dopaminergic degeneration in the pathogenesis of REM sleep behavior disorder

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Keywords:
dopamine transporter, FP-CIT SPECT, REM sleep behavior disorder

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Accepted 2 October 2009

Background and purpose: The pathogenesis of rapid eye movement (REM) sleep behavior disorder (RBD) is not clear despite its frequent association with Parkinson's disease (PD). We investigated whether the nigrostriatal dopaminergic system is involved in the development of idiopathic RBD.

Methods: Fourteen patients with RBD, 14 patients with PD and 12 normal controls were included in the study. The diagnosis of RBD was confirmed on polysomnography. All the participants performed single-photon emission computed tomography imaging 3 h after injection of [^{123}I]FP-CIT. During REM sleep of the RBD patients, each 30-s epoch was rated as 'tonic' when there was at least 50% of tonically maintained chin electromyography (EMG) activity in the epoch. Phasic EMG activities were calculated as the percentage of 3-s mini-epoch containing phasic EMG events (leg and chin, separately).

Results: The RBD patients showed a trend of lower binding in the striatum than the normal controls ($P = 0.07$), and the significance was revealed in the putamen ($P = 0.02$). However, in 11 individual cases of the 14 RBD patients, the dopamine transporter (DAT) densities in the putamen still remained within the normal range. In the RBD patients, there was no correlation between EMG activities and DAT densities.

Conclusions: Nigrostriatal dopaminergic degeneration could be a part of the pathogenesis of RBD, but not essential for the development of RBD. The lack of correlation between RBD severity and DAT densities suggests that another pathogenic process not related to nigrostriatal dopaminergic transmission may be implicated in RBD.

Introduction (1)

- High association between RBD and synucleinopathy neurodegenerative disease

1) Presence of RBD
   : 33-60% of Parkinson's disease (PD)
   50-80% of dementia with Lewy bodies (DLB)
   80-95% of multiple system atrophy (MSA)

2) Development of degenerative disorders among RBD patients
   : Nearly 40% of RBD → PD
   : 45-50% of RBD → PD and DLB

→ The involvement of DA system in the pathogenesis of RBD

Introduction (2)

- Findings against major role of DA system in RBD

1) Clonazepam
: Highly effective in the treatment of RBD
: Mechanism of action
- partly through serotonergic activity with no influence on the dopaminergic system (Mahowald and Schenk, 2005)

2) Pramipexole
: D2-D3 dopamine receptor agonist
: Little effect of RBD-related symptoms in PD
(Kumru et al, Sleep, 2008)

→ Reevaluation of DA system in the pathogenesis of RBD

Objectives

- To find whether the nigrostriatal dopaminergic system is involved in the pathogenesis of RBD by measuring presynaptic DA transporter (DAT) density using FP-CIT SPECT

- To investigate the relationship between the PSG RBD scores and dopaminergic integrity in RBD

Subjects

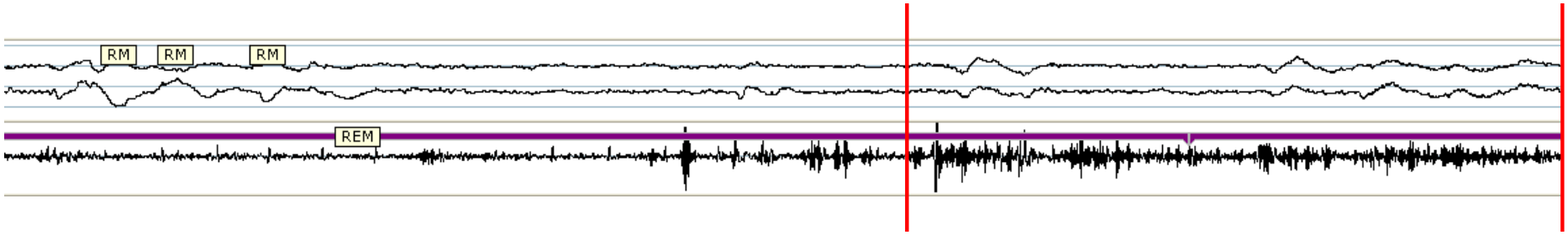
- 14 patients with RBD (66.6±4.5 yrs, M:F = 11:3)
  14 patients with Parkinson's disease
  (67.0±4.1 yrs, M:F = 11:3)
  12 healthy elderly control (63.3±5.7 yrs, M:F = 8:4)

- RBD patients – NPSG
  All the patients - [123I]-FP-CIT SPECT

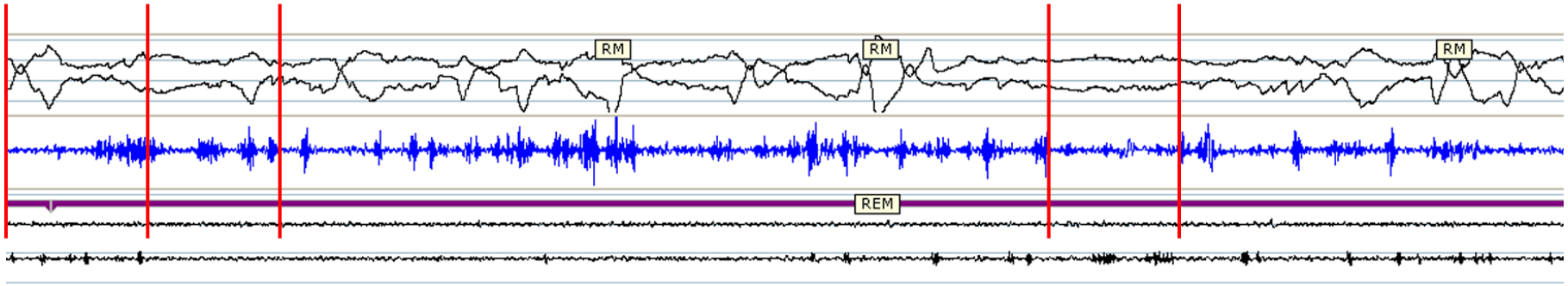
Polysomnography

- Analysis of muscle activity during REM (Lapierre et al., Neurology, 1992)

'Tonic' epoch: at least 50% of tonically maintained chin EMG



Phasic %: % of 3 sec mini-epochs with EMG bursts (chin and leg)



Results (1)

Table 2 [^{123}I]FP-CIT uptake of the patients with rapid eye movement sleep behavior disorder (RBD), Parkinson's disease (PD) and healthy controls

	Controls (n = 12)	RBD (n = 14)	PD (n = 14)	F-value	Significance (P-value)[a]
Caudate	4.38 ± 0.93	3.73 ± 1.16	2.67 ± 0.77	10.49	0.22, 0.016**, 0.001***
Putamen	3.61 ± 0.64	2.82 ± 0.92	1.63 ± 0.51	25.39	0.02*, < 0.001**, < 0.001***
Entire striatum	3.97 ± 0.76	3.24 ± 1.02	2.11 ± 0.61	17.24	0.073, 0.002**, < 0.001***
C/P ratio	1.20 ± 0.09	1.33 ± 0.15	1.65 ± 0.22	27.44	0.153, < 0.001**, < 0.001***

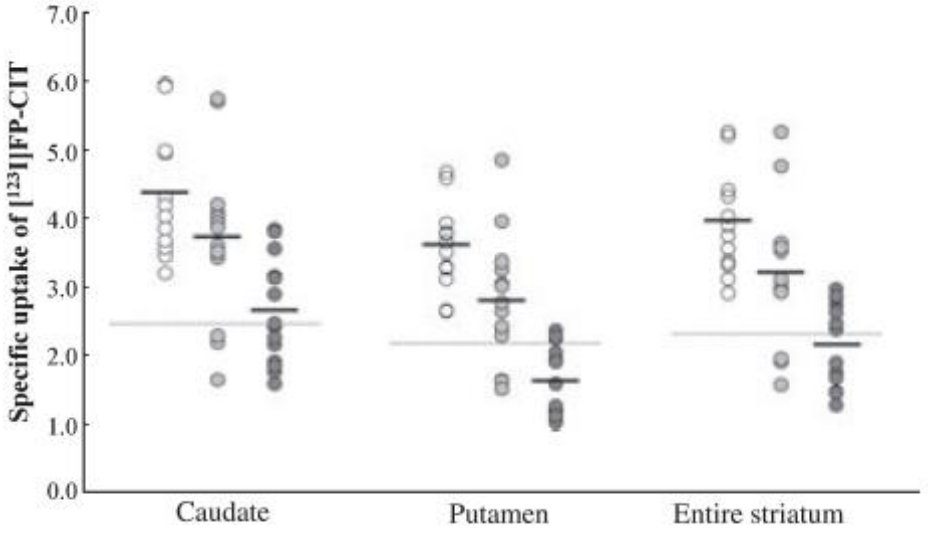
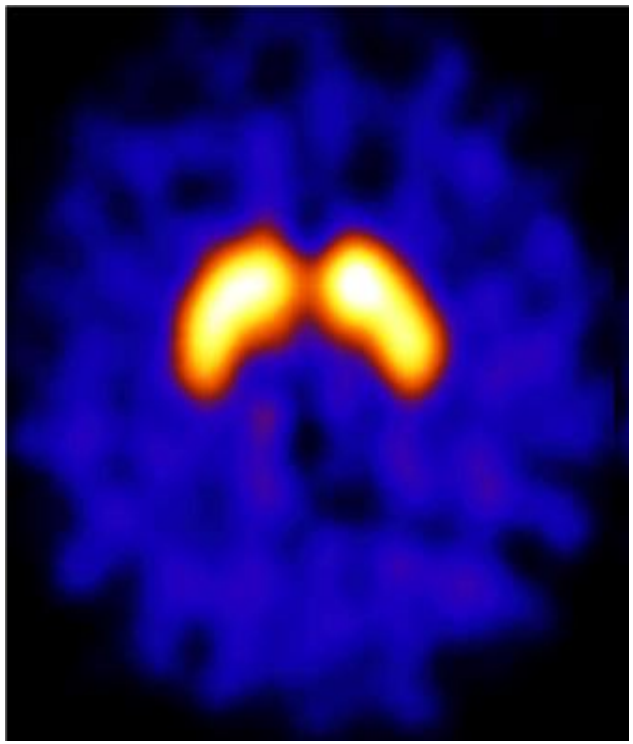
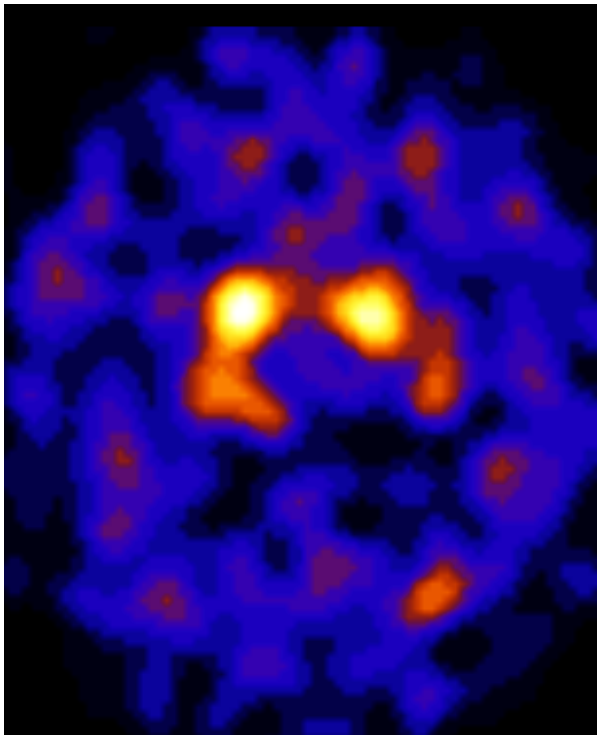


Figure 2 Striatal dopamine transporter density (○ controls, ◎ RBD, ● PD).

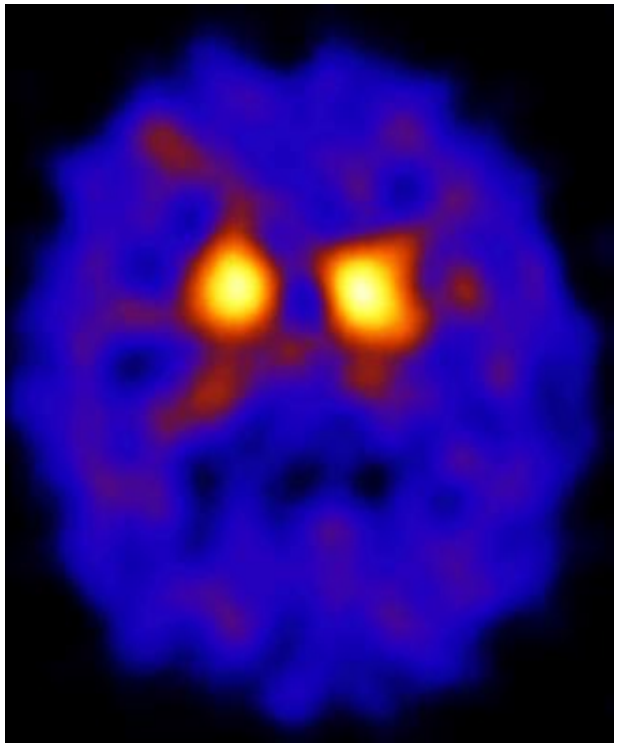
[123I]-FP-CIT SPECT



Healthy Control



RBD



IPD

Results (2)

Table 3 Correlation coefficients between DAT density and polysomnographic EMG activities

	Tonic chin (%)	Phasic chin (%)	Phasic leg (%)
Caudate	0.102	0.167	–0.300
Putamen	–0.030	0.189	–0.112
Striatum	0.039	0.180	–0.212

Tonic chin (%) denotes percent of 30-s epoch of rapid eye movement sleep having at least 50% tonically maintained chin EMG activity in the epoch; phasic chin (%) and leg (%) were calculated as the percentage of 3-s mini-epoch containing phasic EMG events in the leg and chin, respectively; DAT, dopamine transporter; EMG, electromyography; $P < 0.05$.

Conclusion

- DAT ↓ in the putamen of RBD patients, However

1) Most RBD patients; slightly reduced DAT densities, spanning the low normal ranges
2) No rostrocaudal gradient in reduction of DAT density in RBD patients

- No correlation between DAT density and PSG EMG

1) PSG EMG activities during REM sleep
; representing the severity of RBD
→ No correlation between DAT density in the striatum and clinical severity of RBD

➔ Questioning the major role of nigrostriatal dopaminergic pathway in RBD

Conclusions

- Early bed times and wake-up times in the elderly could not be solely explained by advanced circadian rhythms. Weakened homeostatic processes and evening nap might be another factors for the change.
- SAS-related complications such as increased mortality, CV disease, daytime sleepiness and cognitive impairments might be attenuated with aging.
- DA system changes in RLS might be functional unlike structural DA system changes in PD
- Nigrostriatal dopaminergic degeneration could be a part of the pathogenesis of RBD, but not essential for the development of RBD