Oral Presentation
August 10, 2015 at 14:10-14:40

Short sleep duration, sleep disorders, and traffic accidents

Yuichi Inoue

Tokyo Medical University
Neuropsychiatric Research Institute, Tokyo, Japan

Conflict of Interest Disclosures
– Authors/Presenters

☐ The authors do not have any potential conflicts of interest to disclose,

OR

☑ The authors wish to disclose the following potential conflicts of interest related to content in this lecture:

Type of Potential Conflict	Details of Potential Conflict
Grant/Research Support	-
Consultant	-
Speakers' Bureaus	Otsuka Pharmaceutical Co., Ltd, Astellas Pharma Inc, Eisai Co., Ltd.,Philips Respironics GK, Takeda Pharmaceutical Company Limited, Alfresa Pharma Corporation, MSD K.K.
Financial support	-
Other	HISAMITSU PHARMACEUTICAL Co., Inc.（Investigational Device/Drug）

Driving risk and sleep problems

- ***Drowsiness and falling asleep at the wheel are identified as one of main causes of traffic accidents including fatal crashes.***

- ***Falling asleep at the wheel associated with sleep restriction or nocturnal driving has been known to be incriminated in 20% of traffic accidents.***

JSC

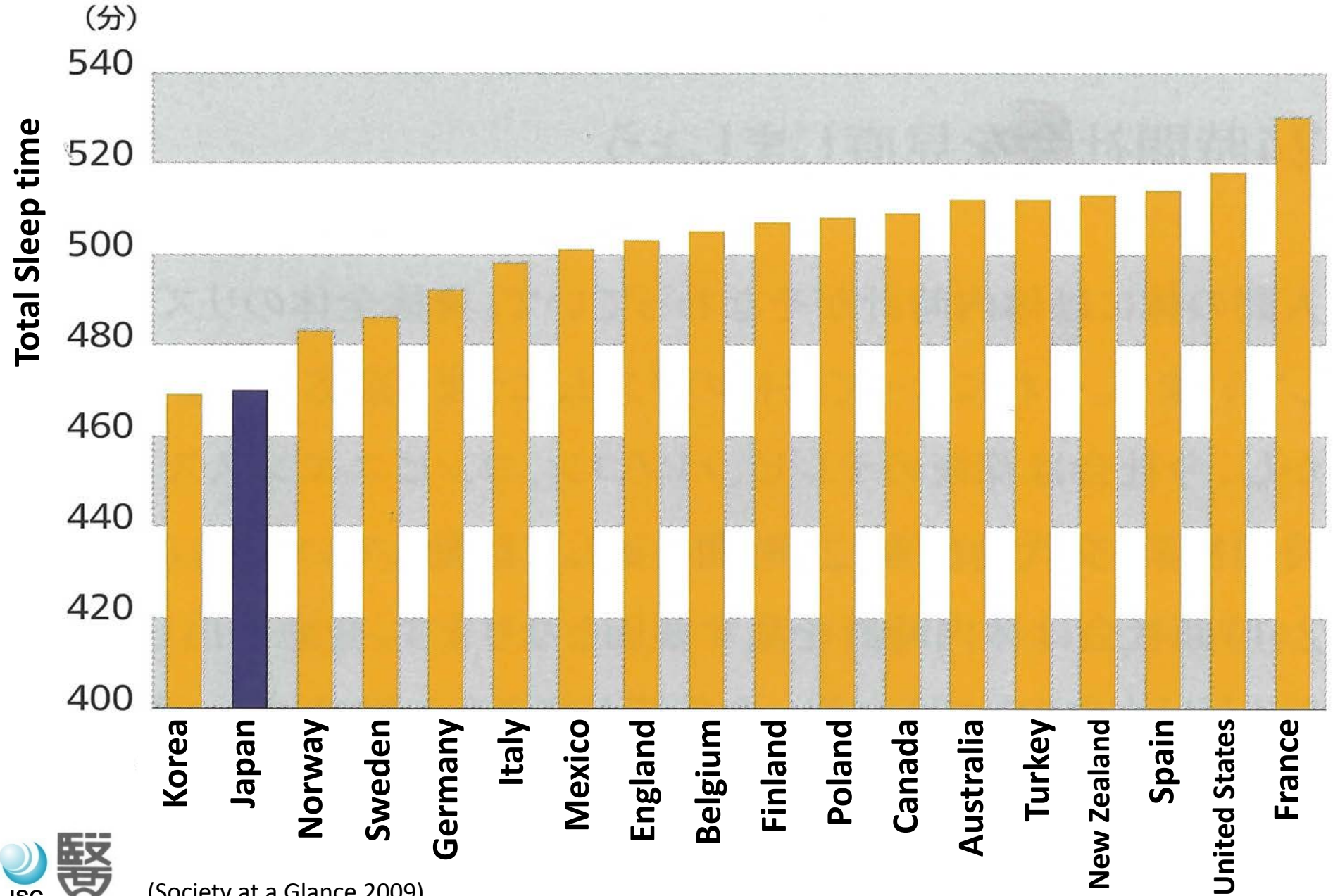
The rate of the population having excessive daytime sleepiness (EDS) is estimated at about 10 to 15% in industrialized countries.

Main causes of sleepiness and its related accidents

- ***Sleep insufficiency (acute and chronic)***
- ***Circadian rhythm problems（including shift work)***
- ***Chronic sleep disprders (OSAS, CNS hypersomnias)***
- ***Effect of drug and substance use***

JSC

Average sleep length in populations of 18 countries



(Society at a Glance 2009)

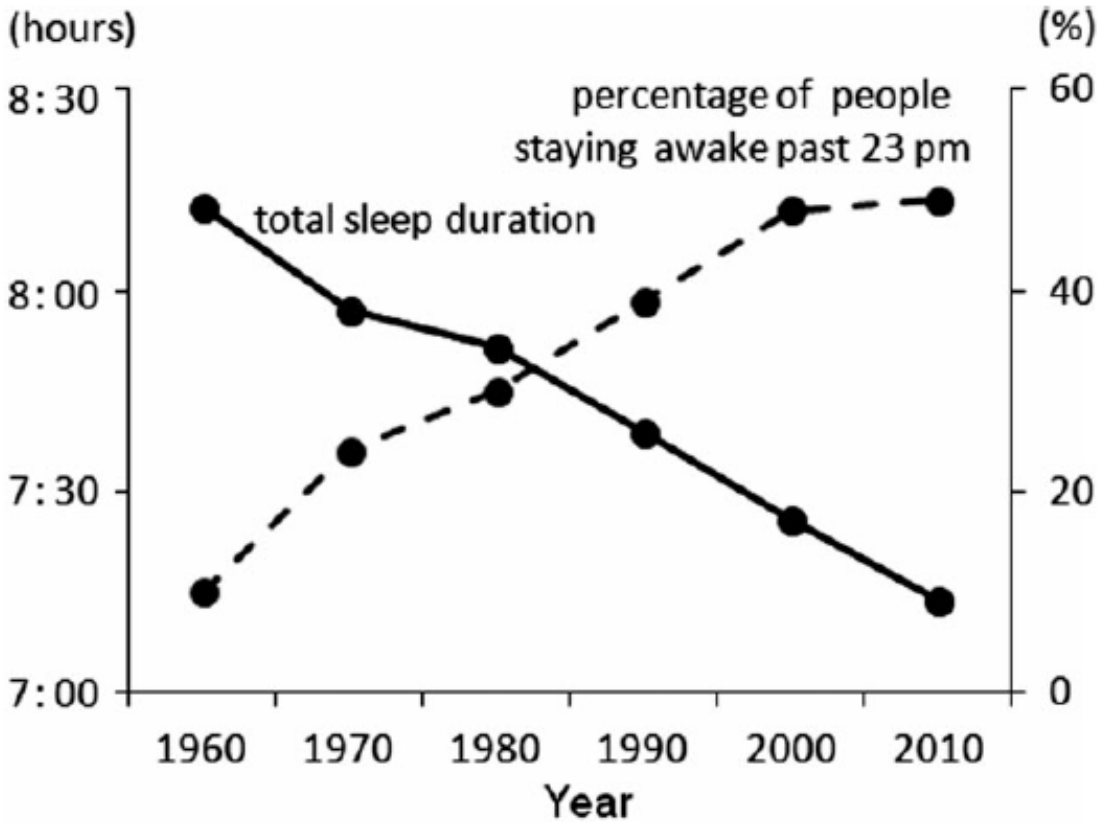
Top 10 night owl nations in bed after 12pm (ACNielsen 2004)

1.Portugal	75%
2.Taiwan	69%
3.Korea	68%
4.Hong Kong	66%
5.Spain	65%

6. Japan	60%
7. Singapore	54%
8. Malaysia	54%
9. Thailand	43%
10.Italy	39%

Seven of the world's 10 biggest night owl nations hail from Asia Pacific!

JSC



Changes in Japanese sleep duration and percentage of people staying awake past 11:00 PM.

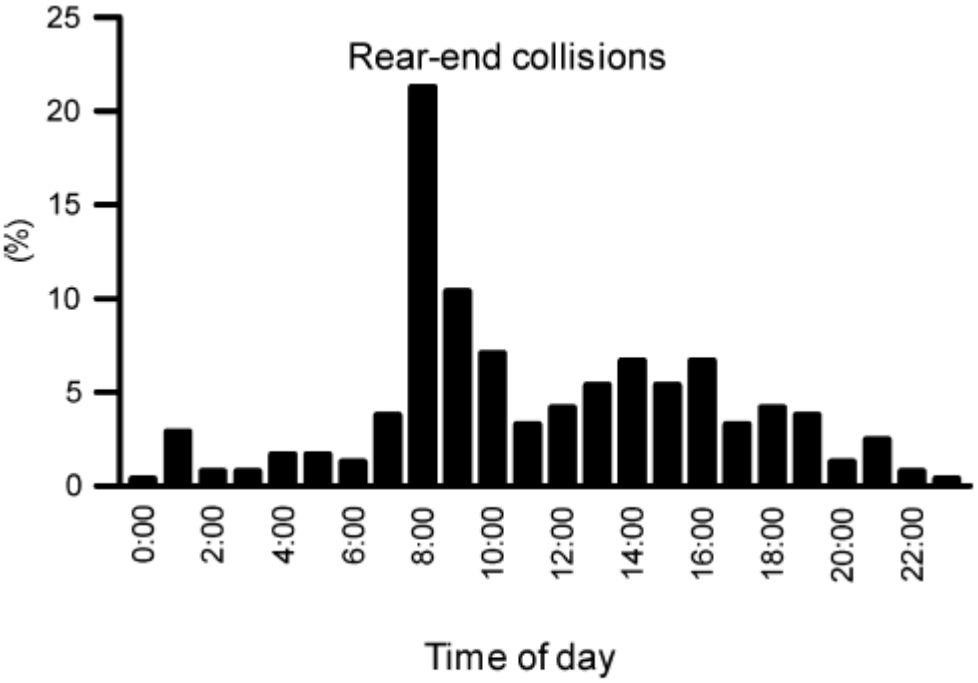
This figure shows the percentage of Japanese people who stay awake past 11:00 PM on weekdays and the average subjective total sleep time from 1960 to 2010. In 1960, 90% of the population were already asleep at 11:00 PM and typically slept for over 8 h. However, sleeping times gradually fell over the surveyed period. In 2010, half of the population remained awake past 11:00 PM with an average sleeping time of 7 h and 14 min.

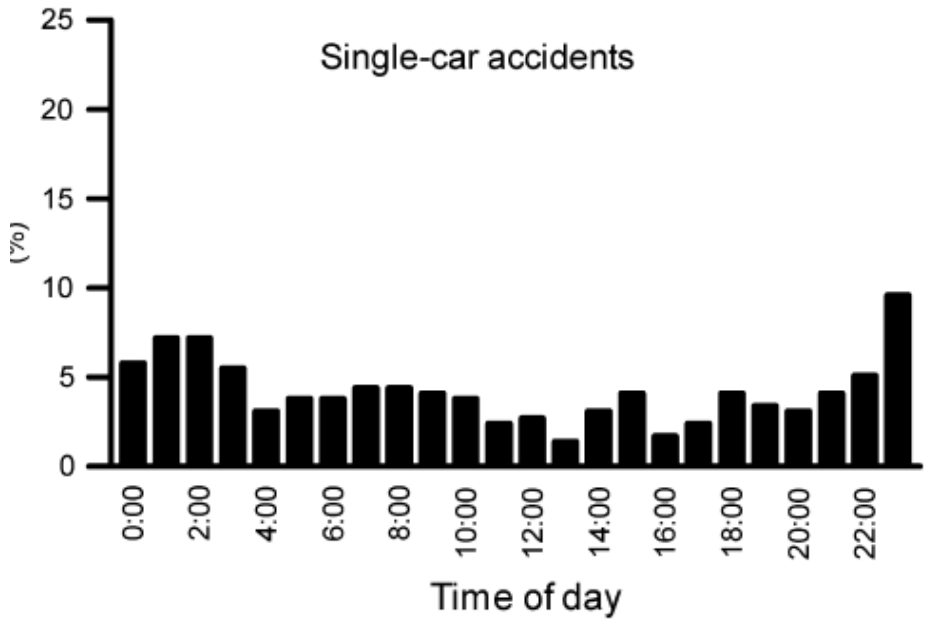
(Inoue Y et al. Sleep Biol Rhythms. 2014; 12(2): 96–105.)

Condition of driving and sleep disorders in Japan (especially in Tokyo area)

- ***Lots of traffic jams and resultant large number of rear end collisions***
- ***The rate of persons who are engagement in shift work reaches 20% of the population***
- ***Clearly shorter length of nocturnal sleep compared with rural area***
- ***Similar rate of obstructive sleep apnea syndrome with Western countries (although obesity is less frequent)***

JSC





Time distributions of rear-end collisions and single-car accidents

Large percentage of both rear end collisions and single car accidents are strongly related with drowsy driving, but diurnal distribution is different between these two types of accidents.

Abe T, Inoue Y et al. *J Sleep Res.* (2010)

JSC

Result of multiple logistic regression analyses on the associated factors for the presence of single-car accident

	Total	*Single-car accident*		*Univariate model*		*Multivariate model*	
Predictor	*n*	*n*	*%*	*Odds ratio (95% CI)*	*P*-value	*Adjusted odds ratio (95% CI)*	*P*-value
Gender							
Female	453	62	13.7	1.00 (ref)		1.00 (ref)	
Male	1079	231	21.4	1.72 (1.27–2.33)	<0.01	1.14 (0.72–1.80)	0.59
Age (years)							
≤25	649	176	27.1	2.44 (1.88–3.16)	<0.01	1.94 (1.29–2.91)	<0.01
>25	883	117	13.3	1.00 (ref)		1.00 (ref)	
BMI (kg m^{-2})							
<25	1237	241	19.5	1.00 (ref)			
≥25	295	52	17.6	0.88 (0.64–1.23)	0.47		
Sleep duration of prior night (h)							
<6	90	30	33.3	3.45 (2.14–5.55)	<0.01	2.45 (1.38–4.35)	<0.01
≥6	987	125	12.7	1.00 (ref)		1.00 (ref)	
Length of time driving (min)*	1289	218	16.9	1.05 (1.03–1.08)	<0.01	1.04 (1.00–1.07)	<0.05
Time zone of occurrence							
Nap zone (13–16)	227	25	11.0	0.95 (0.60–1.50)	0.82	1.15 (0.60–2.20)	0.67
Nighttime zone(21–06)	284	150	52.8	8.57 (6.33–11.58)	<0.01	8.84 (5.65–13.81)	<0.01
Other zone (06–13, 16–21)	1021	118	11.6	1.00 (ref)		1.00 (ref)	

*Odds ratios of the length of time driving correspond with increment for each step of 10-min.
BMI, Body Mass Index; CI: confidence interval; ref: reference category.

Younger age, sleep loss, longer driving elapsed times and night driving are associated with the occurrence of single car accident.

Abe T, Inoue Y et al. *J Sleep Res.* (2010)

Result of multiple logistic regression analyses on the associated factors for the presence of rear-end collisions

	Total	*Rear-end collision*		*Univariate model*		*Multivariate model*	
Predictor	*n*	*n*	*%*	*Odds ratio (95% CI)*	*P*-value	*Adjusted odds ratio (95% CI)*	*P*-value
Gender							
Female	449	58	12.9	1.00 (ref)		1.00 (ref)	
Male	1030	182	17.7	1.45 (1.05–1.99)	<0.05	1.28 (0.89–1.84)	0.19
Age (years)							
≤25	570	97	17.0	1.10 (0.83–1.46)	0.51		
>25	909	143	15.7	1.00 (ref)			
BMI (kg m^{-2})							
<25	1193	197	16.5	1.00 (ref)			
≥25	286	43	15.0	0.90 (0.63–1.28)	0.54		
Sleep duration of prior night (h)							
<6	87	27	31.0	2.39 (1.48–3.89)	<0.01	2.20 (1.31–3.70)	<0.01
≥6	1024	162	15.8	1.00 (ref)		1.00 (ref)	
Length of time driving (min)*	1281	210	16.4	1.05 (1.03–1.08)	<0.01	1.05 (1.02–1.07)	<0.01
Time zone of occurrence							
Nap zone (13–16)	244	42	17.2	1.11 (0.77–1.61)	0.58		
Nighttime zone(21–06)	163	29	17.8	1.16 (0.75–1.78)	0.51		
Other zone (06–13, 16–21)	1072	169	15.8	1.00 (ref)			

*Odds ratios of the length of time driving correspond with increment for each step of 10-min.
BMI, Body Mass Index; CI: confidence interval; ref: reference category.

Sleep loss and longer driving elapsed time was associated with the occurrence of rear end collisions.

Abe T, Inoue Y et al. *J Sleep Res.* (2010)

JSC

The frequencies of falling asleep and feeling sleepiness while driving (in previous one year) among general drivers in Tokyo metropolitan area

	Percentage (N)
Experience of falling asleep while driving (N=3250)	
None	88.6 % (2880)
One time	5.5 % (180)
Two times	2.0 % (64)
Three times or more	3.9 % (126)
Experience of feeling sleepiness while driving (N=4033)	
Never	32.4 % (1308)
Occasionally	45.4 % (1832)
Often	19.4 % (784)
Usually	2.7 % (109)

11.4%

77.5%

Abe T, Inoue Y et al. *Sleep Biol Rhythms.* (2011)

JSC

Multivariate logistic regression results for associated factors for MVCs caused by falling asleep among sleep related variables adjusted for demographic variables among general drivers.

Predictor	Multivariate model†† Adjusted odds ratio (95% CI)	p
Self-reported sleep duration on weekdays (hr)		
<6	8.02 (1.08–59.60)	<0.05
6 – <7	6.28 (0.83–47.43)	0.07
7 – <8	1.00 (ref)	
8 – <9	3.62 (0.22–58.89)	0.37
≥9††	–	–
Loud snoring or apnea		
No	1.00 (ref)	
Yes	2.07 (1.12–3.82)	<0.05
Frequency of sleepiness while driving		
Never	1.00 (ref)	
Occasionally	12.98 (1.72–97.68)	<0.05
Often	38.33 (5.13–286.23)	<0.01
Usually	35.59 (3.56–355.77)	<0.01

Abe T, Inoue Y et al. *Sleep Biol Rhythms* (2011)

JSC

Diagnoses of the 1243 patients with excessive daytime sleepiness (ESS≧11)

Diagnosis	*n*	%
Obstructive sleep apnea syndrome	431	34.7
Idiopathic hypersomnia (IHS w/o LST)	136	10.9
Narcolepsy (with or w/o CA)	109	8.8
Behaviorally induced insufficient sleep syndrome (BIISS)	88	7.1
Circadian rhythm sleep disorders	76	6.1
Sleep disorders associated with mental disorders	54	4.3
Periodic limb movement disorder or restless legs syndrome	33	2.7
Insomnia	30	2.4
Parasomnias	14	1.1
Long sleeper	12	1.0
Recurrent hypersomnia	3	0.2
More than two diseases causative for daytime sleepiness	69	5.6
(of which ISS + other hypersomnia)	25	2.0
Undiagnosed	188	15.1

61.5%

The data was collected from consecutive patients who visited Outpatient clinic of our sleep disorder center in 2005 and 2006

Komada Y, Inoue Y et al. *Sleep Med.* (2008)

JSC

Diagnoses of 1243 patients with excessive daytime sleepiness

Diagnosis	*n*	%
Obstructive sleep apnea syndrome	431	34.7
Idiopathic hypersomnia	136	10.9
Narcolepsy	109	8.8
Insufficient sleep syndrome	88	7.1
Circadian rhythm sleep disorders	76	6.1
Sleep disorders associated with mental disorders	54	4.3
Periodic limb movement disorder or restless legs syndrome	33	2.7
Insomnia	30	2.4
Parasomnias	14	1.1
Long sleeper	12	1.0
Recurrent hypersomnia	3	0.2
More than two diseases causative for daytime sleepiness	69	5.6
ISS + other hypersomnia	25	2.0
Undiagnosed†	188	15.1

†Patients who did not have a confirmed diagnosis due to interruption of diagnostic examination or treatment, or patients in whom two clinicians did not completely agree on the final diagnosis. ISS, insufficient sleep syndrome.

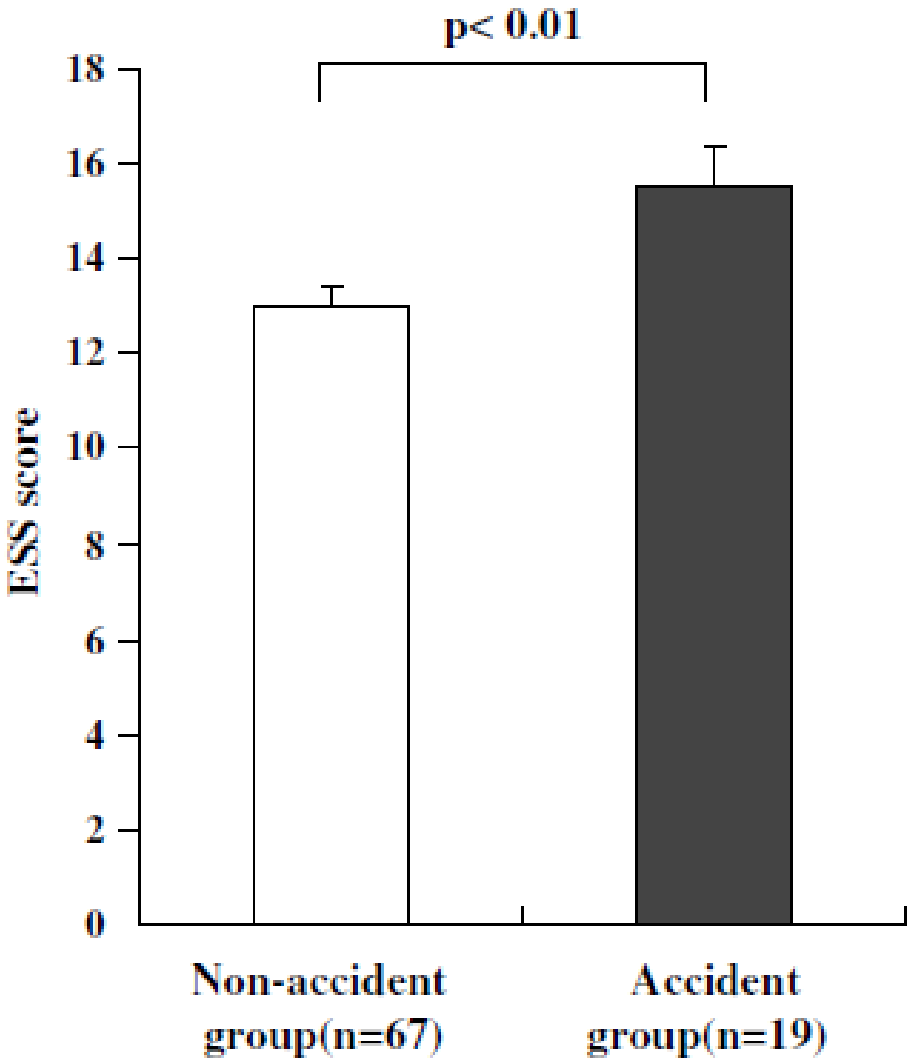
(Inoue Y et al. Sleep Biol Rhythms. 2014; 12(2): 96–105.)

Comparison of descriptive variables among the five groups with major hypersomnias

	Mean age of initial visit		Mean age of symptoms		ESS score of the initial visit		BMI		Sleep length of weekday	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
insufficient sleep syndrome	30.2	7.3	28.6	7.5	13.6	3.4	22.2	2.8	5.5	0.8
Sleep apnea syndrome	45.1	12.1***	–	–	12.5	3.6**	27.4	4.9***	6.1	1.0***
Idiopathic hypersomnia	31.4	9.0	19.2	7.3***	14.3	3.0	21.8	3.1	6.3	1.1***
Narcolepsy	31.0	13.3	17.2	7.5***	15.7	3.0***	23.4	4.1*	6.4	1.3***
Circadian rhythm sleep disorders	27.7	8.1	18.9	6.4***	12.4	3.7*	21.9	3.8	7.8	2.3***

Results with post-hoc test (compared with ISS). ****P < 0.0001; **P < 0.01, *P < 0.05. We excluded obstructive sleep apnea syndrome from* the analysis of mean age of symptoms because the data for people with this syndrome in the population are unknown. BMI, body mass index; ESS, Epworth Sleepiness Scale; ISS, insufficient sleep syndrome.

(Inoue Y et al. Sleep Biol Rhythms. 2014; 12(2): 96–105.)



The comparison of ESS scores between the accident group and the non-accident group in BIISS population.

Komada Y, Inoue Y et al. *Sleep Med.* (2008)

JSC

Driving risk and Insufficient sleep syndrome (ISS)

- ***Undoubtedly, ISS is one of the main cause of elevated daytime sleepiness, but most of persons with ISS do not aware of their sleep insufficiency and resultant EDS).***
- ***Result of our clinical based study showed that***

  -BIISS was highly prevalent among young (less than 35 years of age) males

  -The rate of vehicular accident became high in persons with severe sleepiness.

Komada Y, Inoue Y, sleep Med (2008)

JSC

Shift work and drowsy driving/crashes

The Diagnoses of Sleep Disorders According to the *ICSD 2nd* Among the Subject occupational Drivers With Subjective EDS (ESS＞10)

	N	%
SWD	48	32.7
OSAS	30	20.4
Behaviorally induced insufficient sleep syndrome	12	8.2
Delayed sleep phase disorder	11	7.5
Insomnia	10	6.8
Idiopathic hypersomnia without long sleep time	7	4.8
Periodic limb movements disorder	5	3.4
Other	3	2.0
Error in answering questionnaire	6	4.1
Lost to follow-up	15	10.2
Total	147	100.0

SWD was the most frequent cause of EDS among the subway and bus drivers in metropolitan area!

Asaoka S, Inoue Y et al. *J Occup Environ Med.* (2010)

JSC

The Comparison of Descriptive Variables Among the Three Groups

	Control (C)	SWD (S)	OSAS (O)	χ^2 or z	P	Results of Post Hoc Test
N	2816	48	116	—	—	—
Bus drivers (%)	76.2*	83.3	85.3†	6.41	<0.05	—
ESS	4.14 (2.53)	13.08 (1.90)	7.48 (4.49)	208.14	<0.001	C < O < S
Age	44.48 (9.92)	40.13 (5.78)	46.16 (8.68)	13.10	<0.01	S < C, O
SBP (mm Hg)	126.7 (13.3)	124.3 (11.2)	139.22 (17.22)	62.07	<0.001	S, C < O
DBP (mm Hg)	77.6 (9.8)	77.3 (9.3)	86.85 (12.80)	66.25	<0.001	S, C < O
BMI (kg/m^2)	24.1 (3.2)	24.3 (3.2)	27.80 (3.47)	120.17	<0.001	C, S < O
PM-AHI (/h)	—	6.28 (3.22)	37.86 (21.29)	−10.04	<0.001	—
PSG-AHI (/h)	—	—	37.88 (19.83)	—	—	—
SOL on MSLT (min)	—	—	7.85 (5.86)	—	—	—

*The number of bus drivers is significantly smaller than the expected value.
†The number of bus drivers is significantly larger than the expected value.
Values are expressed as mean (standard deviation).

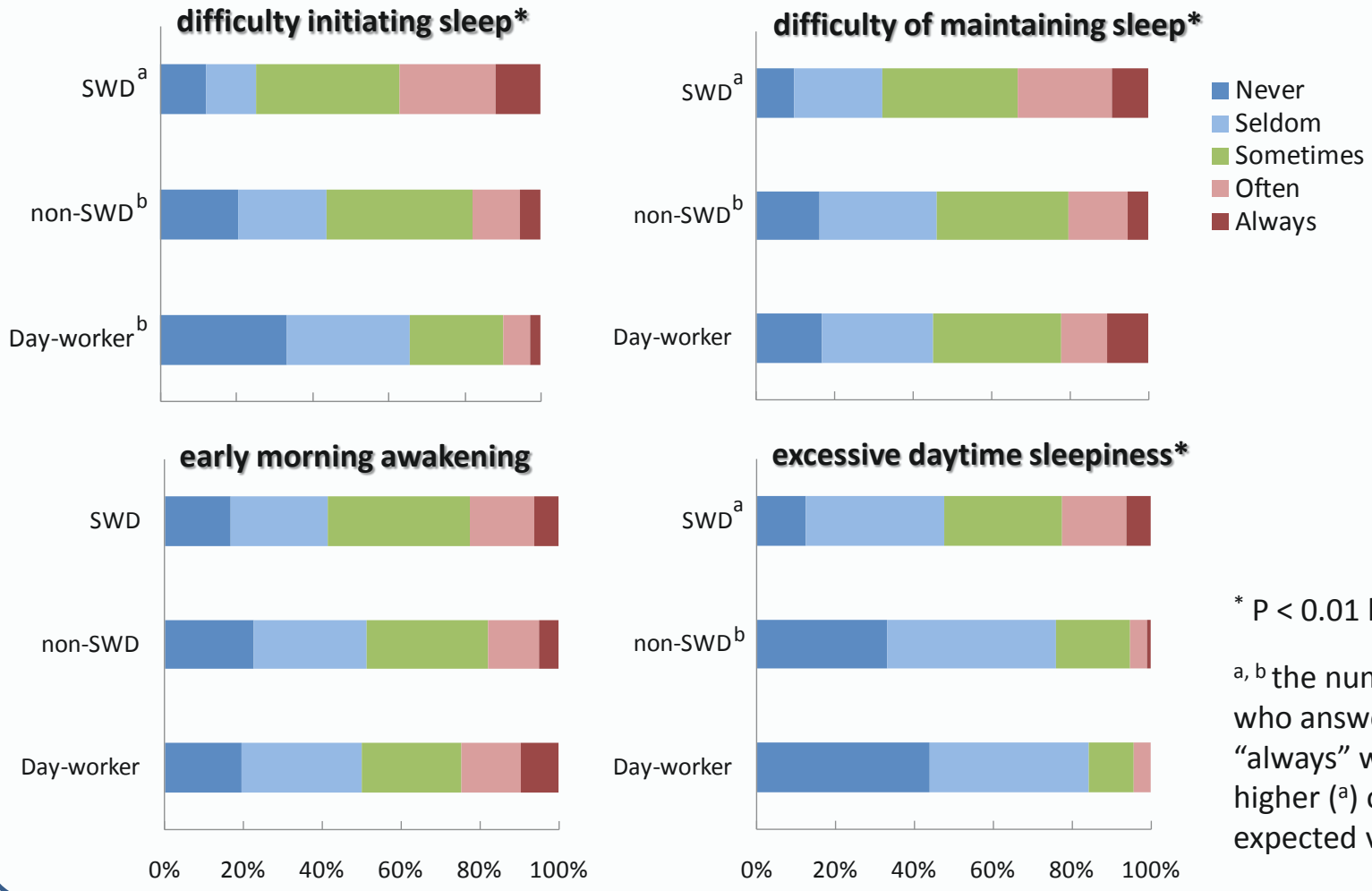
Obesity and hypertension were more frequent in OSAS drivers.However, Level of EDS was significantly higher in SWD drivers than those with OSAS（AHI＞15）.

Asaoka S, Inoue Y et al. *J Occup Environ Med.* (2010)

JSC

Prevalence of SWD among nurses working on two shift

- **The rate of SWD in this population was 24.4%.**



* $P < 0.01$ by chi-square test.

[a, b] the number of the nurses who answered "often" or "always" was significantly higher ([a]) or lower ([b]) than expected value.

Asaoka S, Komada Y, Inoue Y ; Jchronobiol (in press)

Comparisons of the score of daytime functioning among the three groups

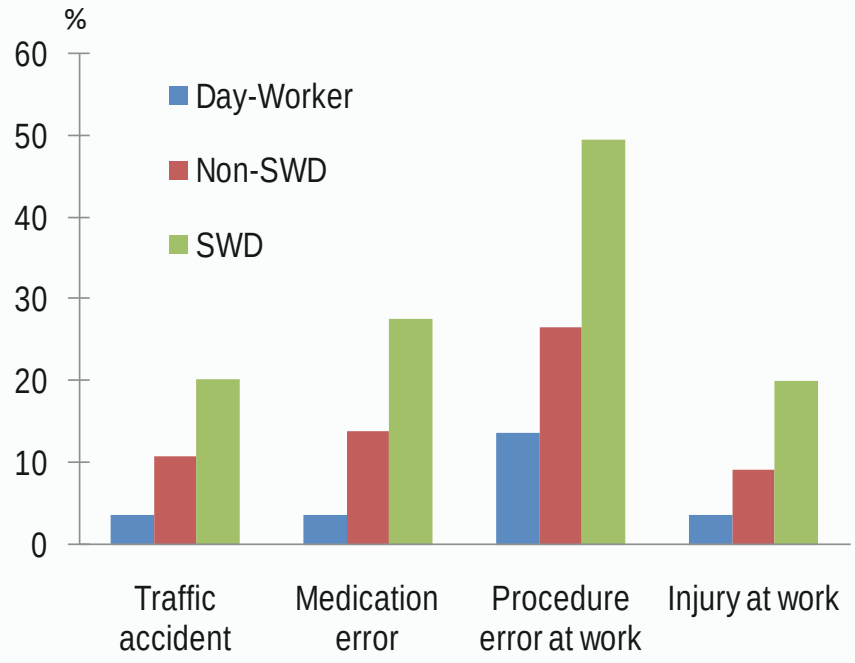
	Day-worker (Day)	Shift-worker without SWD (w/o SWD)	Shift-worker with SWD (SWD)	F value		Results of Post Hoc Test
PCS	48.80 (5.96)	49.12 (6.46)	46.98 (5.74)	10.37	*	SWD < Day, w/o SWD
MCS	46.84 (7.73)	45.78 (7.89)	41.86 (7.48)	25.70	*	SWD < Day, w/o SWD
CESD	13.32 (9.60)	15.67 (9.93)	20.70 (10.04)	28.86	*	Day, w/o SWD < SWD

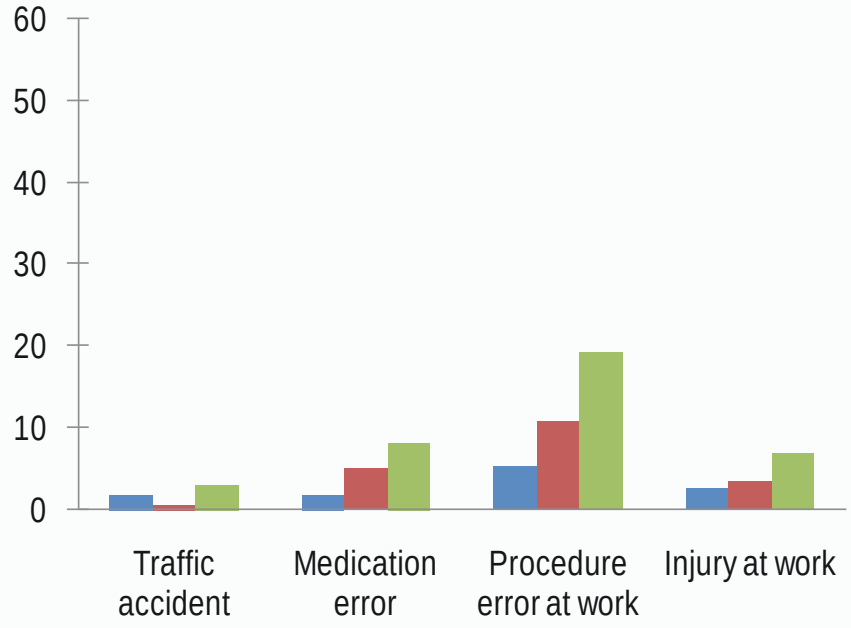
PCS: physical component score of SF-8. MCS: mental component score of SF-8.
CESD: Center for Epidemiological Studies Depression Scale.
Values are expressed as mean (standard deviation). * $p < 0.001$

Depression scale was higher and scores of MCS and PCS of SF-8 were lower in SWD affected shift work nurses.

Asaoka S, Komada Y, Inoue Y ; Jchronobiol (in press)

Rate of the number of the nurses who experienced near-miss (left) and accidents (right) during past one-year.





The rate of reported number of accidents and near miss were highest among SWD affected nurses.

JSC

Drowsy driving and OSAS

Univariate and multivariate logistic regression results of associated factors for motor vehicle accident (MVA) among OSAS drivers.

	Total	MVA		Univariate relative risk			Multivariate relative risk		
	n	*n*	%	(95% CI)[*1]		*p*	(95% CI)[*1]		*p*
Age									
< 47	305	39	12.8						
≥ 47	311	36	11.6			*ns*			*ns*
Usual sleep length									
< 7 hr	312	37	11.9						
≥ 7 hr	296	37	12.5			*ns*			*ns*
ESS score [*2]									
< 11	256	17	6.6						
≥ 11, < 16	228	28	12.3	1.97	(1.05 - 3.70)	*< 0.05*	1.87	(0.99 - 3.53)	*= 0.05*
≥ 16	132	30	22.7	4.14	(2.18 - 7.83)	*< 0.0001*	3.56	(1.85 - 6.84)	*< 0.001*
AHI [*3]									
< 40	297	24	8.1						
≥ 40	319	51	16.0	2.17	(1.30 - 3.62)	*< 0.05*	1.75	(1.03 - 2.98)	*< 0.05*

[*1] Relative risks approximated with odds ratios. CI denotes confidence intervals

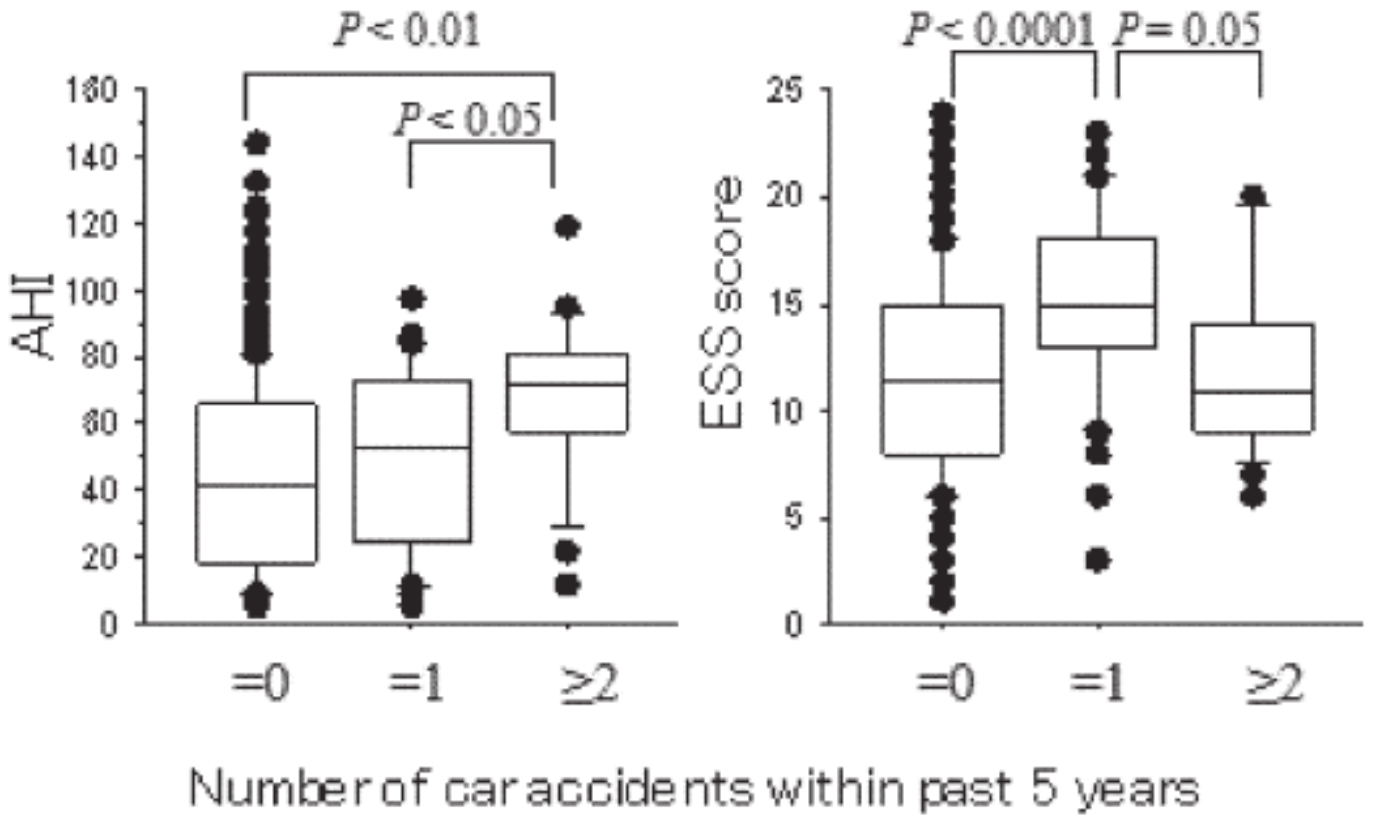
[*2] Epworth Sleepiness Scale before treatment

[*3] Apnea hypopnea index before treatment

AHI≧40/hr and ESS≧16 may be predictive of MVA in OSAS drivers.

Komada Y, Inoue Y et al. *Tohoku J Exp Med.* (2009)

JSC

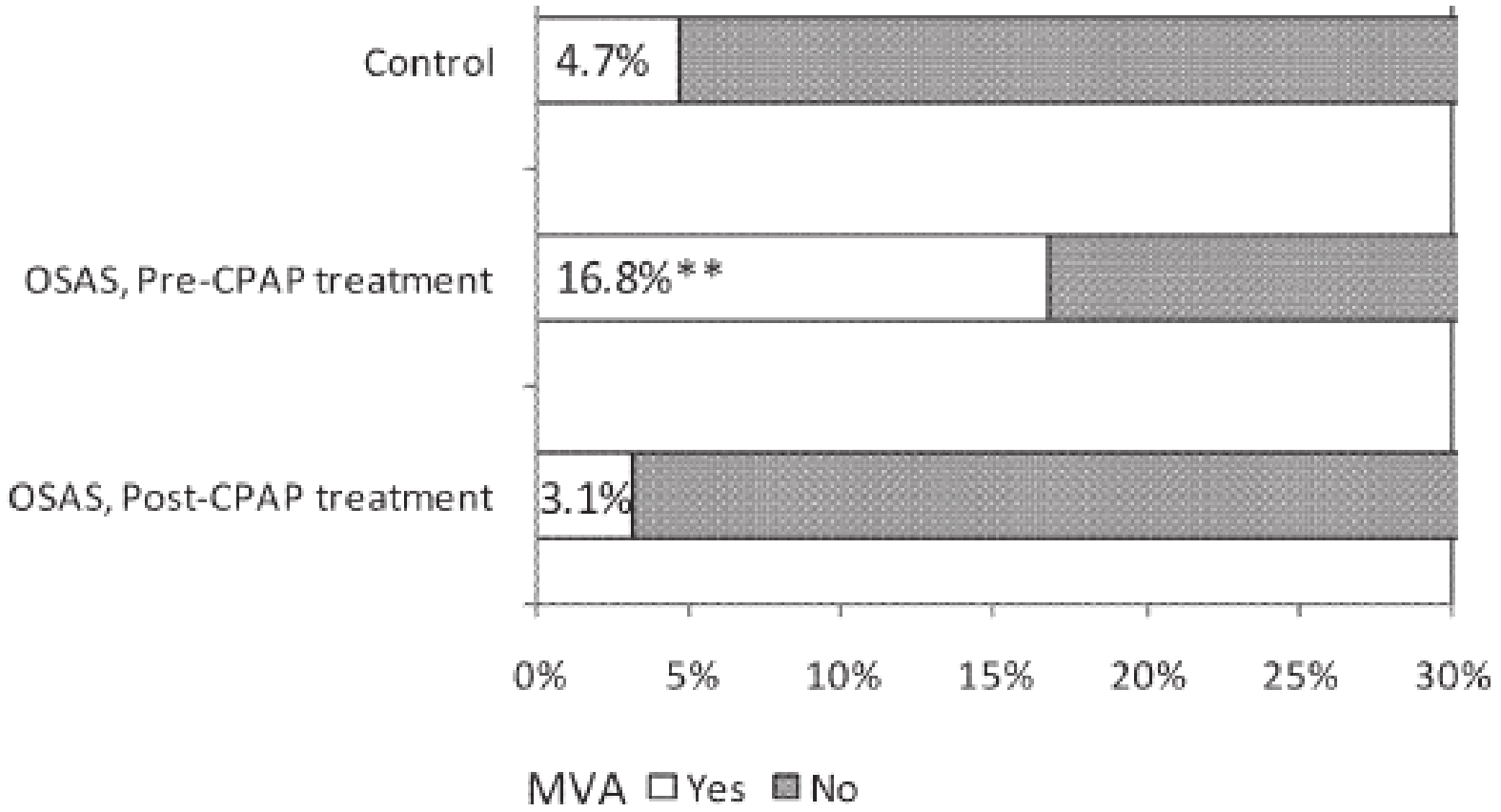


Comparison of AHI (left panel) and ESS score (right panel) between the group categorized by number of MVA.

Group with two times or more MVAs have higher AHI, but ESS score in this group is lower than the group with single MVA episode.

Komada Y, Inoue Y et al. *Tohoku J Exp Med.* (2009)

JSC



Comparison of the proportion of experiences of MVAs between control subjects and OSAS patients treated with CPAP treatment (pre and post data) .

Control group: n=600, OSAS patient group:n =291, MVA:motor vehicle accident, CPAP: continuous positive airway pressure, **p<0.01

Komada Y, Inoue Y et al. *Tohoku J Exp Med.* (2009)

JSC

Between-group (patients and healthy subjects) comparisons for the driving accident during the last 5 years.

	Driving accident during thelast 5 years									
	NoN = 622		YesN = 130		Model 0		Model 1		Model 2	
Variable	n	%	n	%	OR [95% CI]	p	OR [95% CI]	p	OR [95% CI]	p
Conditions										
Healthy subjects	404	64.95	66	50.77	1	0.006	1	0.002	1	0.07
Patients without treatment	81	13.02	28	21.54	2.12 [1.28;3.50]		2.21 [1.30;3.76]		2.62 [1.10;6.26]	
Patients with treatment	137	22.03	36	27.69	1.61 [1.03;2.52]		2.04 [1.26;3.30]		2.39 [1.06;5.36]	
Category of subjects and drug exposure										
Healthy subjects	404	65.37	66	50.77	1	0.0009	1	0.0007	1	0.04
Patients without treatment	81	13.11	28	21.54	2.12 [1.28;3.50]		2.20 [1.29;3.73]		2.43 [1.02;5.81]	
Patients with treatment for $\leq$ 5 years	71	11.49	27	20.77	2.33 [1.39;3.89]		2.68 [1.56;4.62]		2.90 [1.27;6.62]	
Patients with treatment for > 5 years	62	10.03	9	6.92	0.89 [0.42;1.87]		1.23 [0.56;2.69]		1.41 [0.49;4.06]	
Category of central disorders of hypersomnolence										
None	404	64.95	66	50.77	1	0.006	1	0.002	1	0.06
NT1	104	16.72	25	19.23	1.47 [0.89;2.45]		1.68 [0.97;2.91]		1.90 [0.77;4.65]	
NT2	58	9.32	24	18.46	2.53 [1.47;4.36]		2.82 [1.60;4.96]		3.14 [1.32;7.44]	
IH	56	9.00	15	11.54	1.64 [0.88;3.07]		2.04 [1.05;3.95]		2.31 [0.94;5.71]	

Model 0: Crude association; Model 1: Adjustment for gender, age, unmarried status, coffee intake, and energy drinks consumption; Model 2: Adjustment for all the covariates in model 1 plus ESS and naps.

- **No difference in the rate among disease categories**
- **Untreated patients and patients in the early stage of the treatment are at a hjgh risk of causing MVCs**

(Pizza F et al. PLoS One. 2015; 10(6): e0129386.)

Correlation Between the Descriptive Variables and the Involvement of Automobile Accidents or Near-Miss Incidents Among the CNS hypersomnia Patients

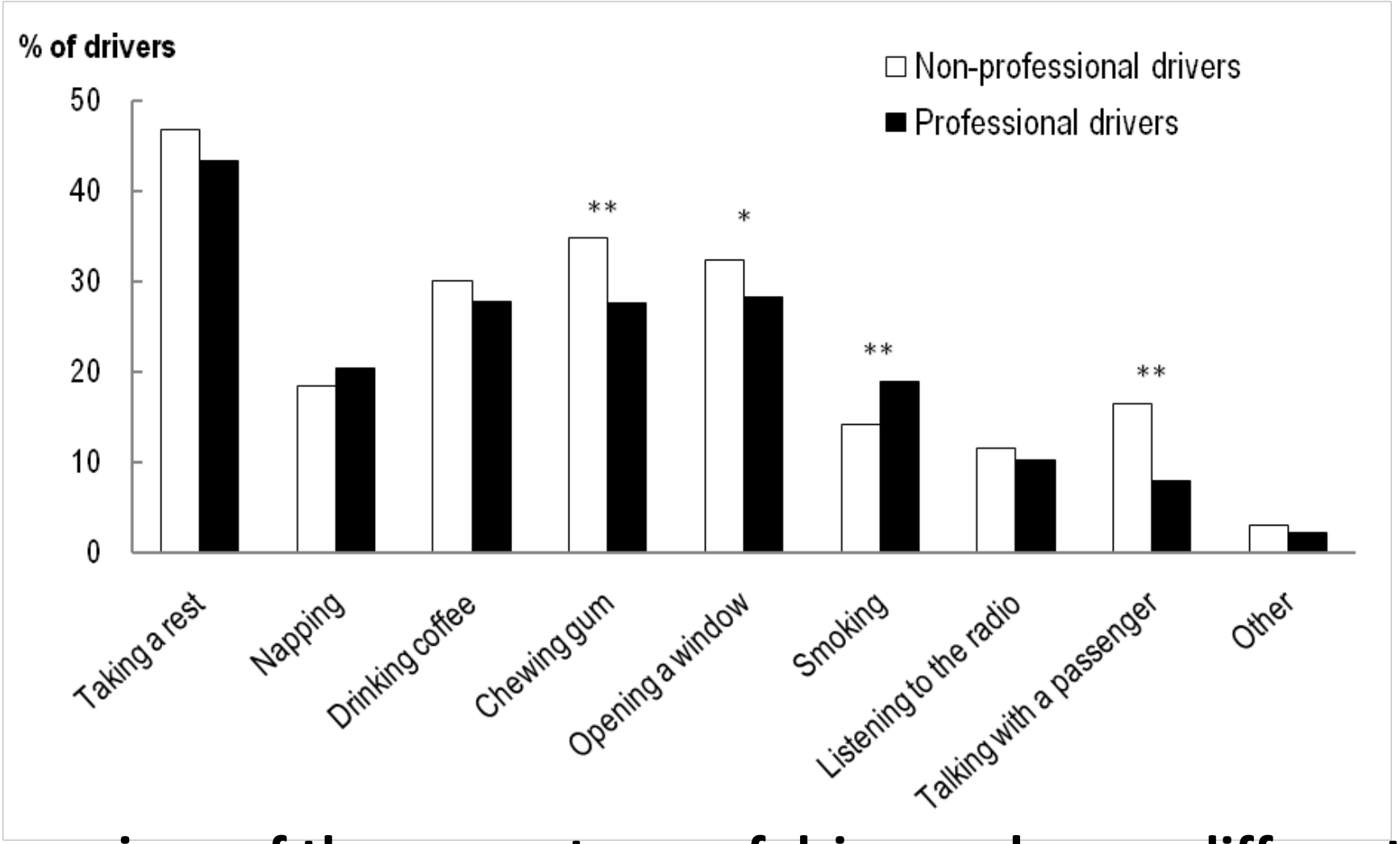
	Crude			Adjusted		
	OR	95%CI	p value	OR	95%CI	p value
gender						
male						
female	0.88	0.36-2.17	n.s.	0.64	0.22-1.90	n.s.
age						
for every increase of one year	1.03	0.97-1.08	n.s.	1.01	0.92-1.10	n.s.
disease duration						
for every increase of one year	1.04	0.98-1.10	n.s.	1.03	0.95-1.13	n.s.
diagnosis						
IHS without LST						
NA with CA	3.00	0.85-10.58	n.s.	1.74	0.40-7.57	n.s.
NA without CA	1.00	0.31-3.27	n.s.	1.00	0.27-3.69	n.s.
ESS score						
0 - 10						
11 - 15	4.25	0.76-23.81	n.s.	4.68	0.66-33.06	n.s.
16 -24	12.06	2.12-68.54	0.005	14.63	1.97-108.67	0.009

OR, odds ratio; 95% CI, 95% confidence interval. NA, narcolepsy; CA, cataplexy; IHS, idiopathic hypersomnia; LST, long sleep time; ESS, Epworth Sleepiness Scale. n = 80

The severity of daytime sleepiness in CNS hypersomnias is associated with experience of vehicular accidents.

Ozaki A, Inoue Y et al. *J Clin Sleep Med.* (2008)

JSC



Comparison of the percentages of drivers who use different countermeasures when they feel sleepy at the wheel.

** $p < 0.01$, * $p < 0.05$ (chi-square test) between professional and non-professional drivers.
Participants were allowed to choose multiple countermeasures.

Asaoka S, Ionue Y et al. *Sleep Med* (in press)

JSC

Factors associated with napping as a countermeasure among non-professional drivers

Predictor		Univariate Model N	Odds ratio (95% CI)	p	Multivariate Model (forward selection) N	Adjusted odds ratio (95% CI)	p
Gender	Female	768	1.00 (ref)		558	1.00 (ref)	
	Male	2403	1.70 (1.35 - 2.14)	< 0.001	1784	1.79 (1.38 - 2.33)	< 0.001
Shift-work	No	3019	1.00 (ref)		2117	1.00 (ref)	
	Yes	313	1.76 (1.35 - 2.30)	< 0.001	225	1.48 (1.09 - 2.01)	< 0.05
Current awareness of insufficient sleep	No	2126	1.00 (ref)		1490		
	Yes	943	1.48 (1.22 - 1.79)	< 0.001	665		n.s.
	Unknown	263	1.36 (0.99 - 1.87)	< 0.10	187		n.s.
Loud snoring and respiratory pauses during sleep	No	2651	1.00 (ref)				
	Yes	673	1.19 (0.96 - 1.46)	0.114			
Existence of diagnosed sleep disorders	No	3239	1.00 (ref)				
	Yes	61	1.42 (0.79 - 2.56)	0.244			
Experience of drowsy driving	No	2433	1.00 (ref)		2107		
	Yes	274	1.71 (1.30 - 2.24)	< 0.001	235		n.s.
Experience of traffic accidents caused by falling asleep	No	2584	1.00 (ref)		2314		
	Yes	32	2.03 (0.99 - 4.17)	< 0.10	28		n.s.
BMI (kg/m^2)	< 25	2552	1.00 (ref)		1858		
	≥ 25	675	1.32 (1.08 - 1.63)	< 0.01	484		n.s.
Annual driving distance (km)	≤ 5000	2050	1.00 (ref)		1449	1.00 (ref)	
	> 5000	1315	1.43 (1.20 - 1.71)	< 0.001	893	1.50 (1.23 - 1.83)	< 0.001
Usual nocturnal sleep duration on weeknights (hours)	7 - 8	518	1.00 (ref)		354		
	< 5	273	1.58 (1.09 - 2.28)	< 0.05	194		n.s.
	5 - 6	1119	1.51 (1.14 - 1.99)	< 0.01	795		n.s.
	6 - 7	1281	1.15 (0.87 - 1.52)	0.333	895		n.s.
	≥ 8	143	0.74 (0.42 - 1.29)	0.289	104		n.s.
Frequency of subjective sleepiness while driving	Never or occasionally	2697	1.00 (ref)		1890	1.00 (ref)	
	Sometimes or usually	621	1.33 (1.08 - 1.64)	< 0.01	452	1.33 (1.05 - 1.68)	< 0.05
ESS score	≤10	1673	1.00 (ref)				
	≥11	731	0.92 (0.75 - 1.13)	0.403			
Age (years)	> 25	2980	1.00 (ref)				
	≤ 25	352	1.22 (0.93 - 1.60)	0.155			
Period after acquisition of driving license (years)	3 - 20	1884	1.00 (ref)		1342	1.00 (ref)	
	>20	1481	0.67 (0.56 - 0.81)	< 0.001	1000	0.70 (0.58 - 0.86)	< 0.001

Male gender, shift worker, longer annual driving distance, frequent occurrence of subjective sleepiness and longer driving license acquisition period were significantly associated with taking naps while driving.

Asaoka S, Ionue Y et al.
Sleep Med (in press)

JSC

Factors associated with napping as a countermeasure among professional drivers

		Univariate Model						Multivariate Model (forward selection)					
Predictor		N	Odds ratio (95% CI)				p	N	Adjusted odds ratio (95% CI)				p
Gender	Female	50	1.00		(ref)			37	1.00		(ref)		
	Male	618	4.38	(1.34	-	14.29)	< 0.05	435	4.91	(1.47	-	16.36)	< 0.01
Shift-work	No	515	1.00		(ref)			339					
	Yes	193	1.72	(1.17	-	2.53)	< 0.01	133					n.s.
Current awareness of insufficient sleep	No	397	1.00		(ref)								
	Yes	246	0.88	(0.59	-	1.30)	0.514						
	Unknown	60	0.90	(0.46	-	1.78)	0.770						
Loud snoring and respiratory pauses during sleep	No	516	1.00		(ref)								
	Yes	185	1.11	(0.74	-	1.68)	0.602						
Existence of diagnosed sleep disorders	No	667	1.00		(ref)								
	Yes	18	1.10	(0.36	-	3.38)	0.874						
Experience of drowsy driving	No	438	1.00		(ref)								
	Yes	95	1.36	(0.84	-	2.20)	0.208						
Experience of traffic accidents caused by falling asleep	No	490	1.00		(ref)			455	1.00	(ref)			
	Yes	18	3.39	(1.31	-	8.77)	< 0.05	17	3.84	(1.41	-	10.47)	< 0.01
BMI (kg/m^2)	< 25	512	1.00		(ref)								
	≥ 25	181	1.04	(0.69	-	1.57)	0.854						
Annual driving distance (km)	≤ 5000	239	1.00		(ref)			145					
	> 5000	477	1.62	(1.07	-	2.44)	< 0.05	327					n.s.
Usual nocturnal sleep duration on weeknights (hours)	7 - 8	87	1.00		(ref)								
	< 5	78	1.14	(0.52	-	2.52)	0.741						
	5 - 6	251	1.41	(0.75	-	2.65)	0.285						
	6 - 7	253	1.33	(0.71	-	2.51)	0.372						
	≥ 8	38	0.56	(0.17	-	1.83)	0.341						
Frequency of subjective sleepiness while driving	Never or occasionally	481	1.00		(ref)								
	Sometimes or usually	219	1.23	(0.84	-	1.81)	0.286						
ESS score	≤ 10	309	1.00		(ref)								
	≥ 11	142	0.88	(0.57	-	1.37)	0.568						
Age (years)	> 25	658	1.00		(ref)								
	≤ 25	53	1.28	(0.67	-	2.47)	0.455						
Period after acquisition of driving license (years)	3 - 20	366	1.00		(ref)			258					
	> 20	350	0.58	(0.40	-	0.85)	< 0.01	214					n.s.

Only male gender and experience of sleepiness related accidents were associated with taking naps as a countermeasure.

Asaoka S, Ionue Y et al.
Sleep Med (in press)

JSC

To prevent drowsiness related vehicular accidents・・・・

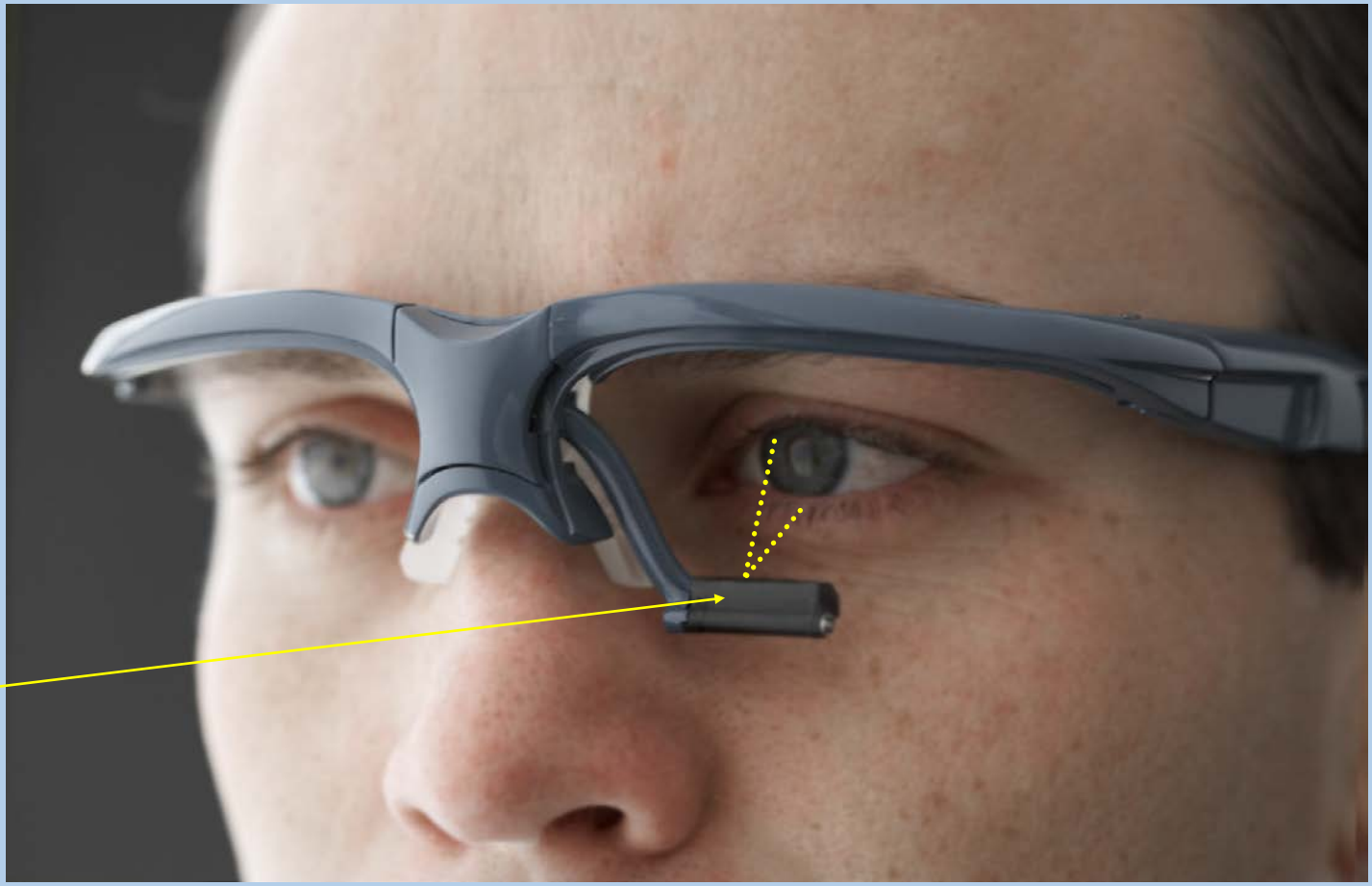
- We should raise the awareness of the impact of drowsiness related driving accidents and the significance of sleep problems including shift work and sleep insufficiency.

・ Work schedule for occupational drivers should be modified to provide them sufficient time to take a nap(or take a rest) for preventing the occurrence of drowsiness.

・Not all the patients with OSAS or CNS hypersomnias have the elevated risk of vehicular accidents. Identification of severely affected patients is important.

OPTALERT™

Method: The Optalert™ System of IR Oculography



Alert, 3 hours after waking, performing a psychomotor vigilance task

Drowsy, after 27 hours awake, performing a psychomotor vigilance task

Eye movement tracking system (EMR-9)

EMR-9

- eye movement
- pupil size
- PERCLOS

EOG

- blink (vertical EOG)
- slow eye movement(horizontal EOG)

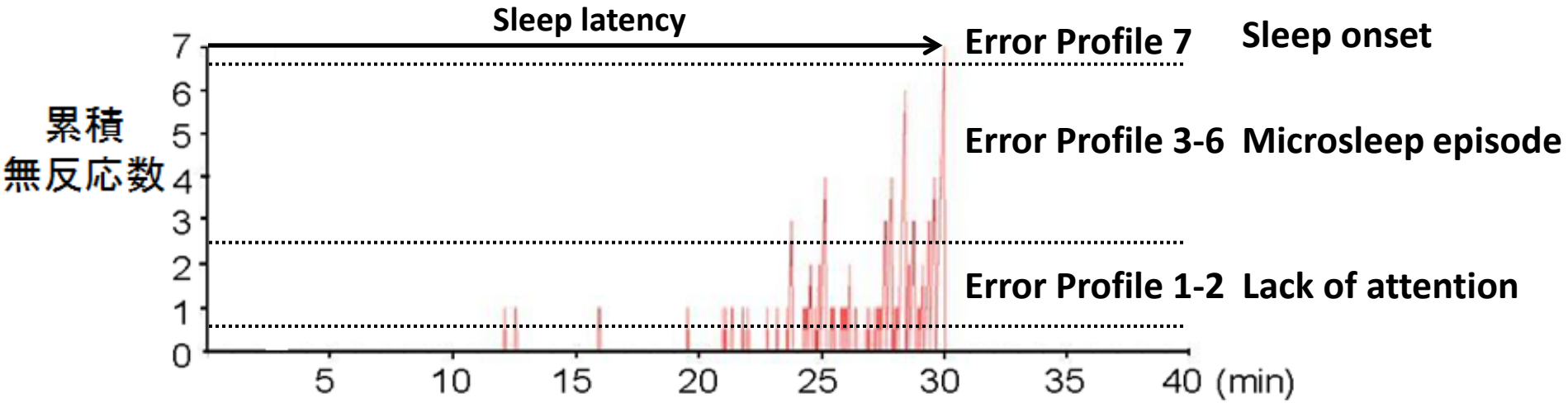
JSC

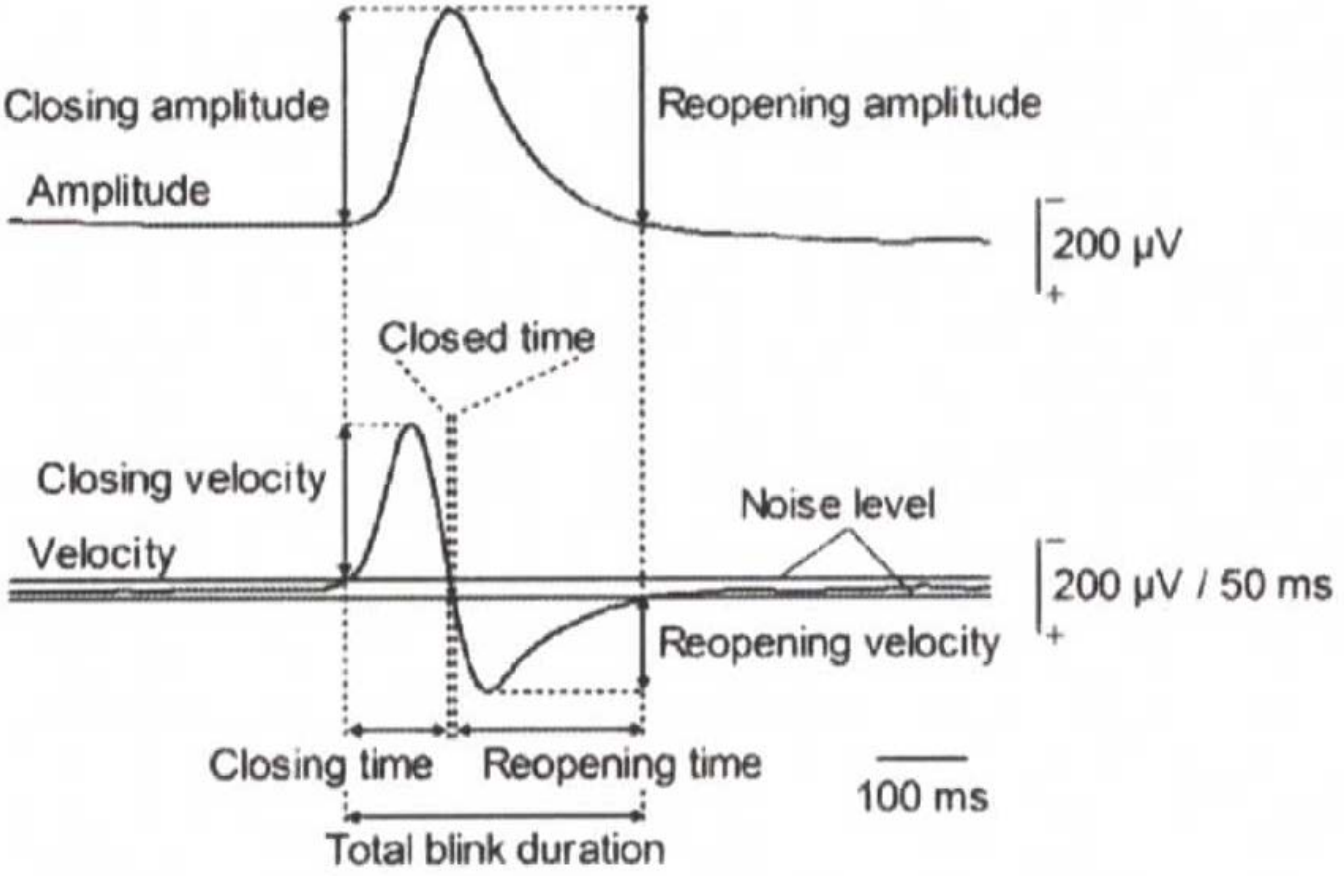
OSLER test (Oxford sleep resistance test)（Bennett & Davies, 1997）

A behavioral maintenance of wakefuleness test

Marker of sleepiness on Osler test

Number of consecutive loss of response (Mazza et al., 2002)





Schema of blink parameters. Upper and lower panels respectively show amplitude and velocity of a blink recorded using a vertical electrooculogram. The noise level of the velocity was set as ± 20 μV/50 ms.

Abe T, Inoue Y et al : Int J Psychophysiol. 2011; 82(3): 269–74

JSC

Subjective sleepiness and sleep latency of OSLER test.

	Before PSD		After PSD	
	10:00	14:00	10:00	14:00
Subjective sleepiness				
VAS	54.6±21.3	59.3±21.9	74.7±13.0	69.4±14.1
KSS-J	4.3±1.5	4.9±1.8	6.6±1.1	6.2±1.5
Objective sleepiness				
Sleep onset time on OSLER test	36.1±8.0	30.5±14.3	23.2±12.1	22.8±15.2
Rate of missed response (%)	4.1±4.8	10.7±9.0	11.8±7.8	17.6±10.7

VAS, visual analog scale: KSS-J, Japanese version of Karolinska sleepiness scale; OSLER: Oxford sleep resistance test; PSD: Partial sleep deprivation.

Abe T, Inoue Y et al : Int J Psychophysiol. 2011; 82(3): 269-74

JSC

Behavioral parameters and ocular variables among epochs with EPO, EP1-2, and EP3-6.

	EP0	EP1-2	EP3-6	ε	*F*	*p*
Behavioral Parameters						
Number of missed responses	0.0±0.0[a]	3.0±0.7[b]	7.6±1.8[c]	0.65	139.97	< 0.001
Response time (ms)	381±60[a]	509±102[b]	560±121[c]	1.00	28.52	< 0.001
Ocular Variables						
Relative velocity of saccade [deg/s^2]	2.49±0.29	2.57±0.35	2.46±2.43	0.69	1.01	0.37
Blink frequency [number /min]	9.6±6.1[a]	4.7±3.8[b]	3.0±3.3[c]	0.53	20.95	< 0.005
Closing time [ms]	126±5	127±6	128±5	0.82	0.97	0.390
Reopening time [ms]	221±25	213±28	214±32	0.85	0.68	0.500
Closure time during blink [ms]	11±6[a]	15±6[b]	19±8[b]	0.82	13.85	< 0.001
Blink duration [ms]	357±26	355±32	361±38	1.00	0.27	0.760
Closing AVR [μV/ΔμV/50 ms]	1.78±0.26	1.90±0.23	1.96±0.15	0.95	6.93	< 0.01
Reopening AVR [μV/ΔμV/50 ms]	3.31±0.61	3.48±0.68	3.80±1.07	0.59	4.55	0.060
PERCLOS [%]	7.5±3.9[a]	22.8±11.8[b]	34.7±17.1[c]	0.70	22.25	< 0.001
Proportion of SEM [%]	1.1±0.8[a]	6.2±4.4[b]	9.3±6.9[c]	0.97	12.39	< 0.005
Pupil diameter [mm]	9.6±1.3[a]	5.7±1.1[b]	5.0±0.9[c]	0.64	18.33	< 0.001

[a,b,c] Different character shows significant difference; EP, error profile; AVR, amplitude-velocity ratio; PERCLOS, percentage of eyelid closure time; SEM, show eye movement.

Abe T, Inoue Y et al : Int J Psychophysiol. 2011; 82(3): 269–74

JSC

覚醒水準と眼球指標

	EP0		EP1-2		EP3-6	p
行動指標						
無反応数	0.0 (0.0)	<	3.0 (0.7)	<	7.6 (1.8)	< 0.001
反応時間	381 (60)	<	509 (102)	<	560 (121)	< 0.001
眼球指標						
サッカード速度 [deg/s2]	2.49 (0.29)		2.57 (0.35)		2.46 (0.43)	0.37
瞬目頻度	9.6 (6.1)	>	4.7 (3.8)	>	3.0 (3.3)	< 0.005
閉瞼時間 [ms]	126 (5)		127 (6)		128 (5)	0.390
開瞼時間 [ms]	221 (25)		213 (28)		214 (32)	0.500
閉眼時間 [ms]	11 (6)	<	15 (6)		19 (8)	< 0.001
瞬目持続時間 [ms]	357 (26)		355 (32)		361 (38)	0.760
閉瞼相対速度（逆数）	1.78 (0.26)		1.90 (0.23)		1.96 (0.15)	< 0.01
開瞼相対速度（逆数）	3.31 (0.61)		3.48 (0.68)		3.80 (1.07)	0.060
PERCLOS [%]	7.5 (3.9)	<	22.8 (11.8)	<	34.7 (17.1)	< 0.001
緩徐眼球運動 [%]	1.1 (0.8)	<	6.2 (4.4)	<	9.3 (6.9)	< 0.005
瞳孔径 [mm]	6.4 (1.3)	<	5.7 (1.1)	<	5.0 (0.9)	< 0.001

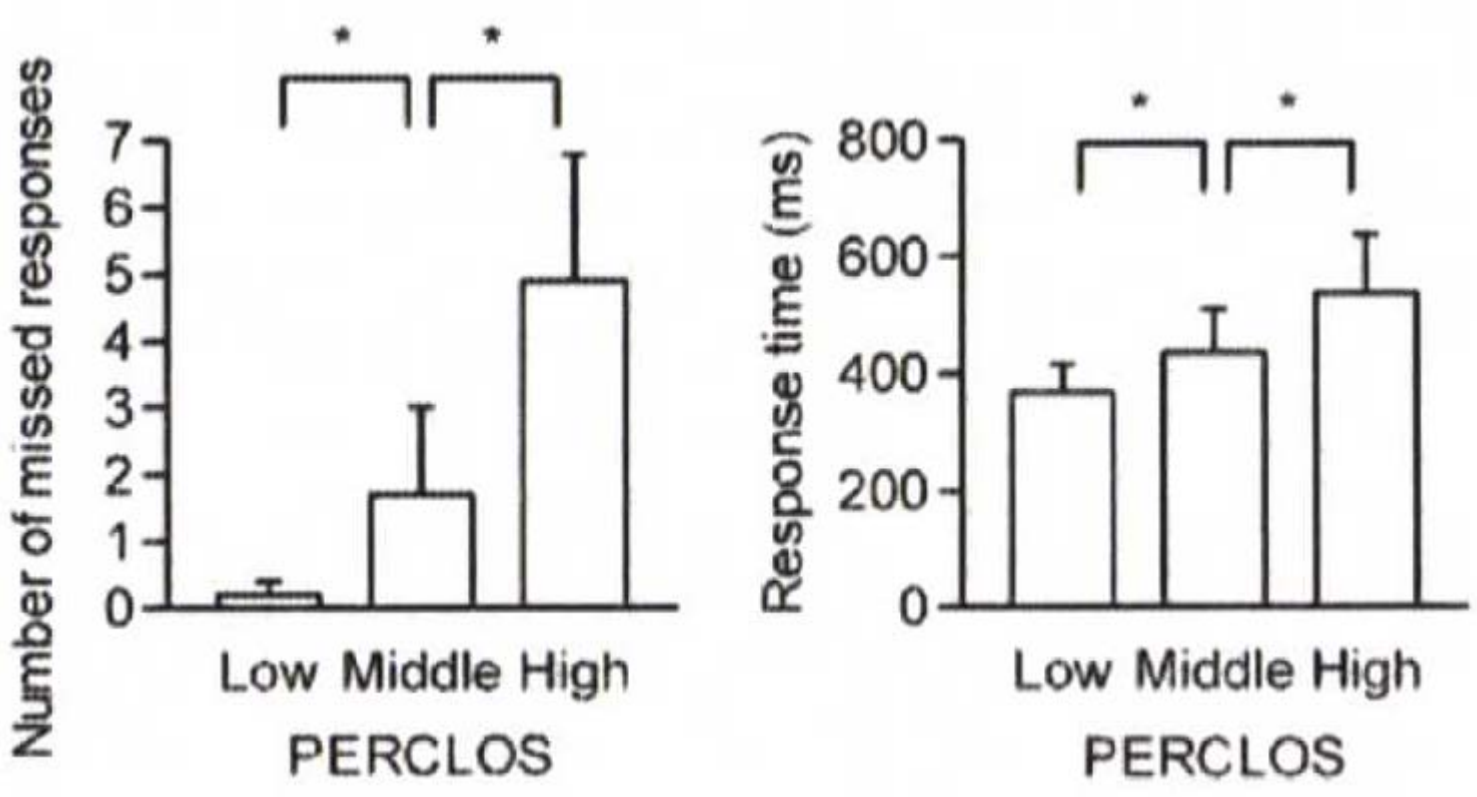
JSC

Area under the receiver operating characteristic curve, sensitivity, and specificity of ocular variables for discriminating between the EPO epoch and EP1-6 epoch and between the EPO-2 epoch and EP3-6 epoch.

Ocular variables	AUC	95% CI	*p*	Cut-off value	Specificity	Sensitivity
EP0 vs. EP 1-6						
Blink frequency	0.79	0.76-0.82	< 0.001	4.5	72.0	73.3
Closure time during blink	0.65	0.61-0.69	< 0.001	8.5	72.8	53.0
Pupil diameter	0.65	0.62-0.69	< 0.001	5.65	63.0	56.0
PERCLOS	0.85	0.82-0.87	< 0.001	11.5	77.5	76.0
%SEM	0.72	0.68-0.76	< 0.001	2.5	56.3	84.4
EP0-2 vs. EP 3-6						
Blink frequency	0.76	0.72-0.81	< 0.001	2.5	71.9	68.5
Pupil diameter	0.79	0.74-0.84	< 0.001	5.15	74.1	69.0
PERCLOS	0.92	0.89-0.94	< 0.001	22.5	80.5	85.5
%SEM	0.73	0.67-0.80	< 0.001	5.5	65.5	82.1

EP, error profile; ROC, receiver operating characteristic; AUC, area under the curve; CI, confidence interval; PERCLOS, percentage of eyelid closure time; SEM, show eye movement.

Abe T, Inoue Y et al : Int J Psychophysiol. 2011; 82(3): 269–74



Missed response and response time compared among PERCLOS levels.

Low, 0-11.5%; Middle, 11.5-22.5%; High, more than 22.5%. *p<0.05.

The increase in PERCLOS was associated with increase in missed responses and longer response time

Abe T, Inoue Y et al : Int J Psychophysiol. 2011; 82(3): 269-74

JSC

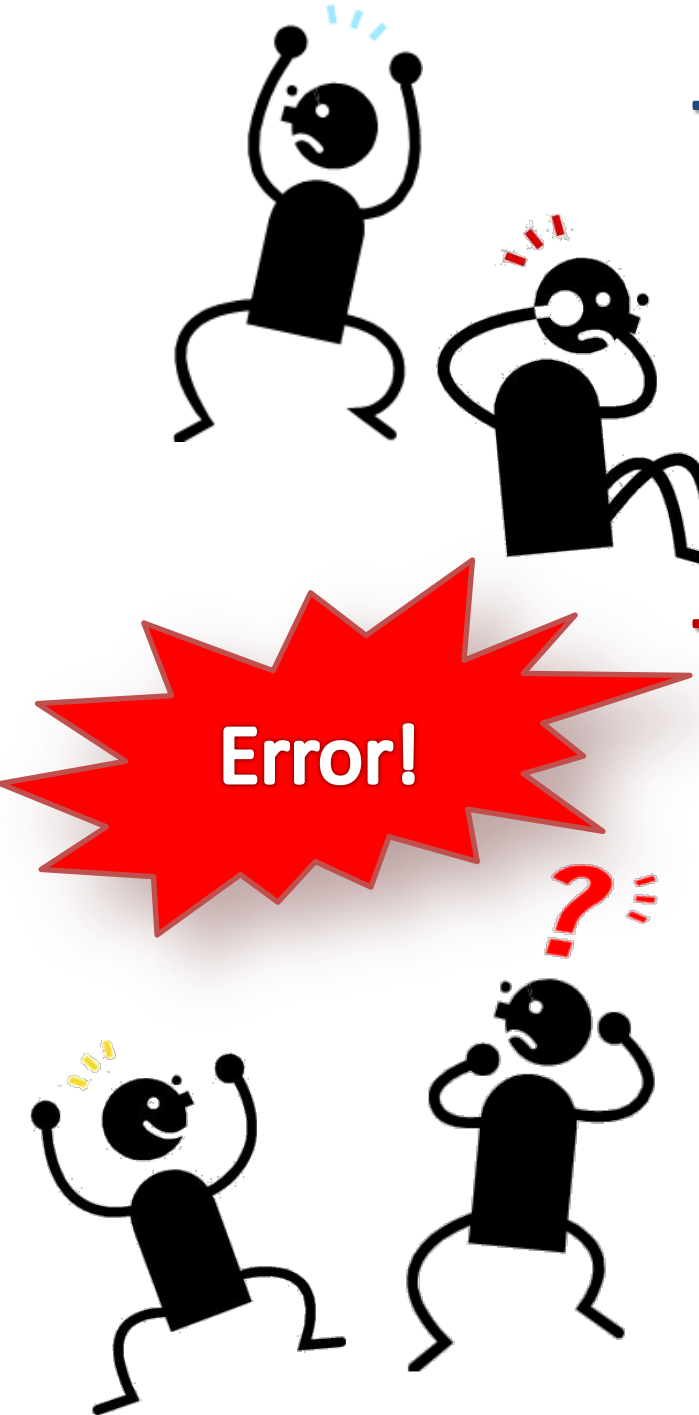
結論

- 無反応の有無を弁別する精度を比較したところ、眼球指標の中で、PERCLOSが最も優れていた。

- PERCLOSが11.5%未満の区間では、無反応はほとんど発生しなかった。本研究の結果は、PERCLOSEが覚醒水準低下を検出する高い精度を有していること、運転時のPERCLOSの値を低く保つことで眠気による事故を予防できる可能性があることを示している。

- PERCLOSによる無反応検出（3秒以上）の感度と特異度はそれぞれ、76.0%と77.5%であったことから、本計測法の精度を更に向上させる必要がある。

JSC



Towards decreased accident risk

- ✓Correction of error
- ✓Accurate subjective assessment of performance
- ✓Coping behavior

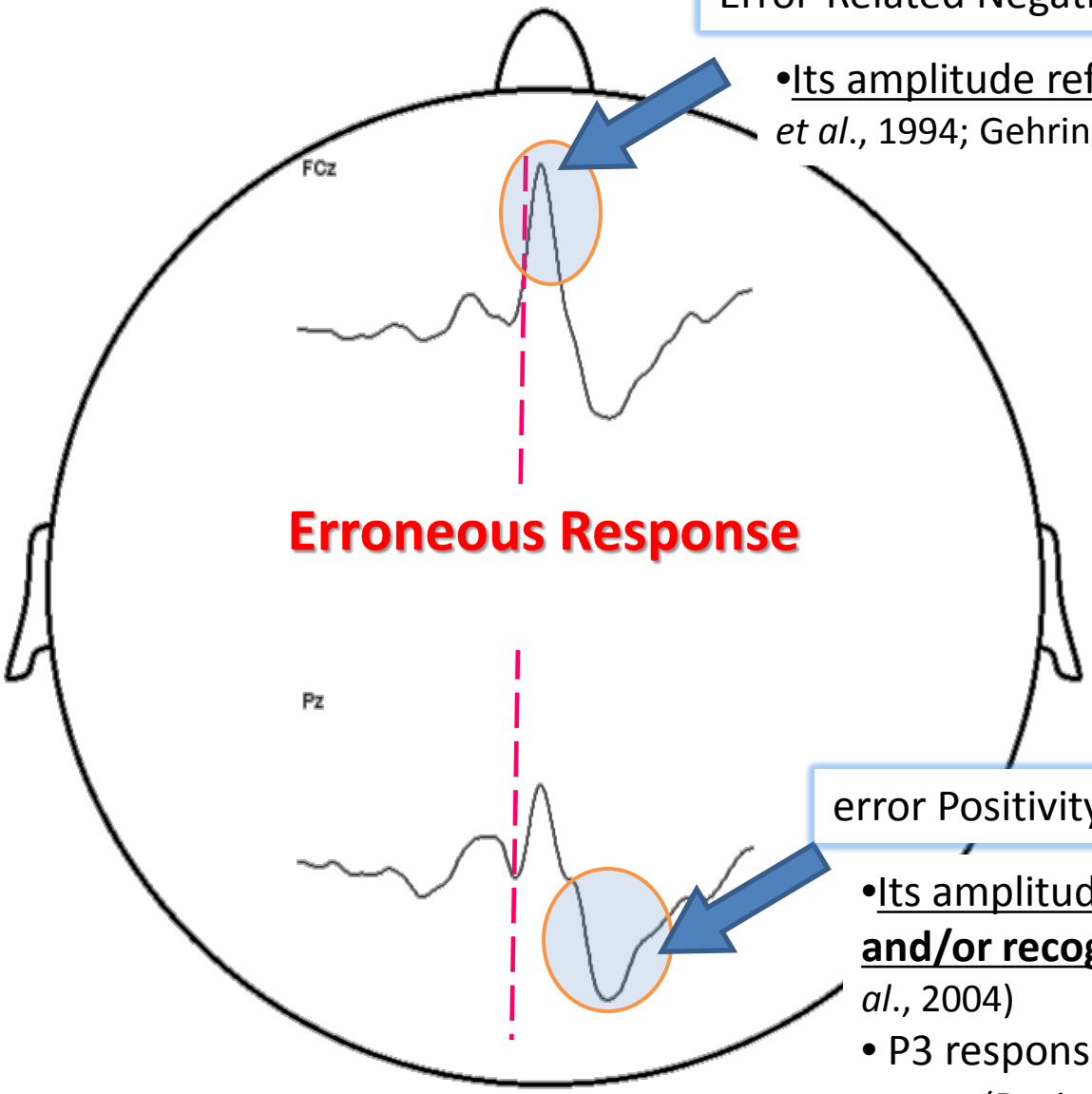
Towards increased accident risk

- ×Error without correction

  →accident!
- ×Overestimation of own performance
- ×No countermeasure

Error-Related Negativity/error Negativity (ERN/Ne)

•Its amplitude reflects **error detection** (Falkenstein *et al*., 1994; Gehring *et al*., 1993)

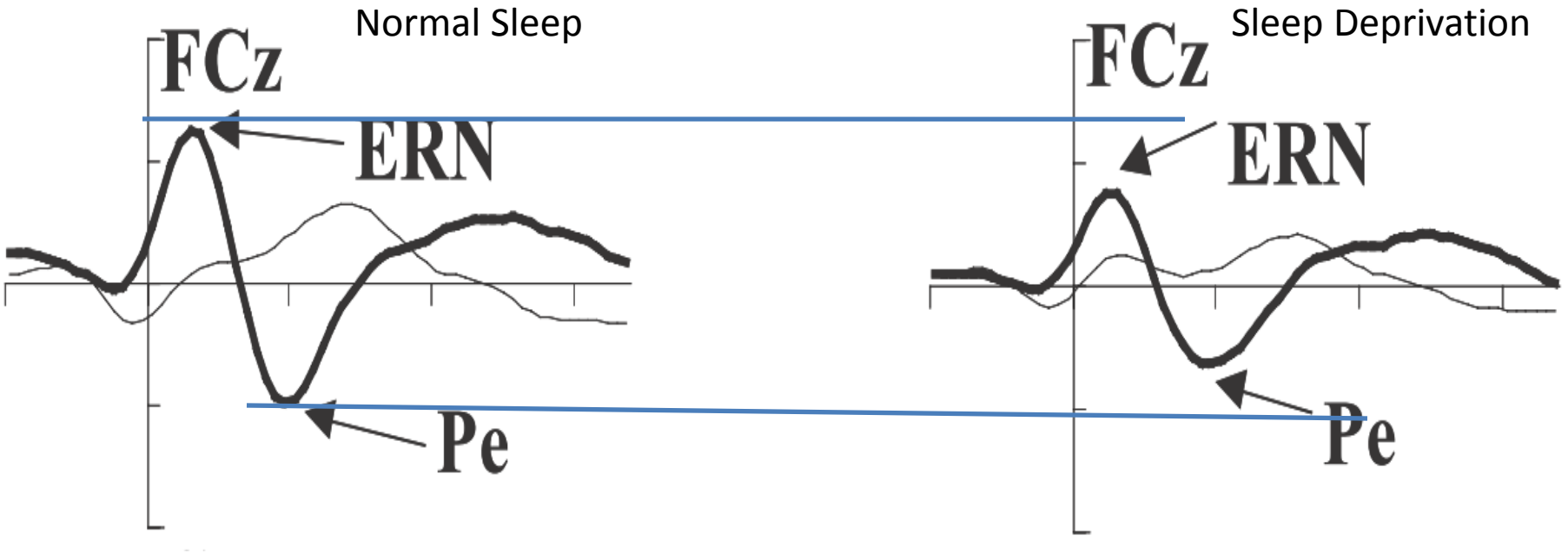


error Positivity (Pe)

•Its amplitude reflects **further evaluation and/or recognition of the error** (Falkenstein *et al*., 2004)

• P3 response to the internal detection of errors (Davies *et al*., 2001; Overbeek *et al*., 2005)

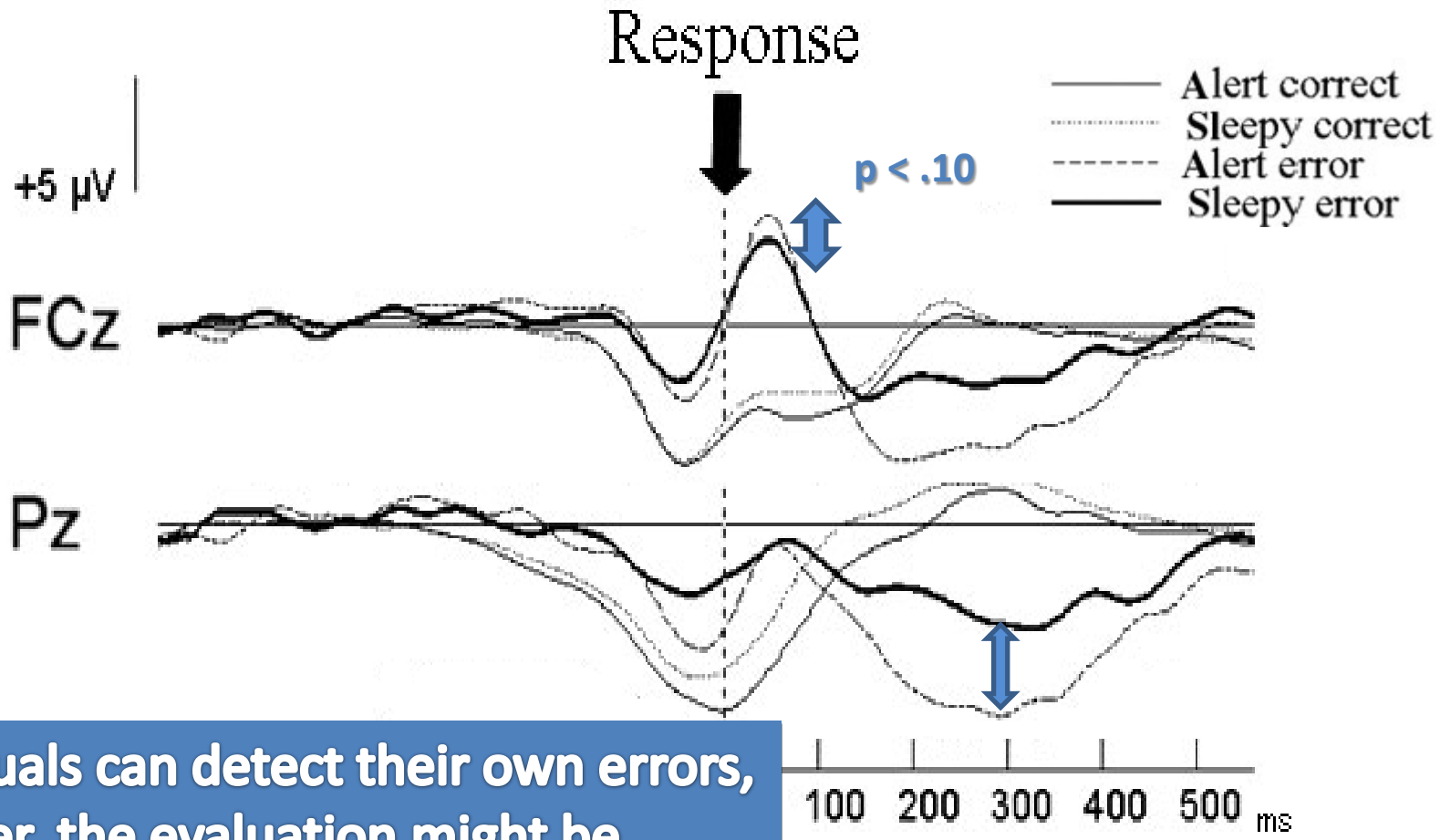
Error-monitoring functions following one-night sleep deprivation



One night of sleep deprivation impaired both the error detection and subjective error evaluation

Tsai *et al.*, 2005 *Sleep*

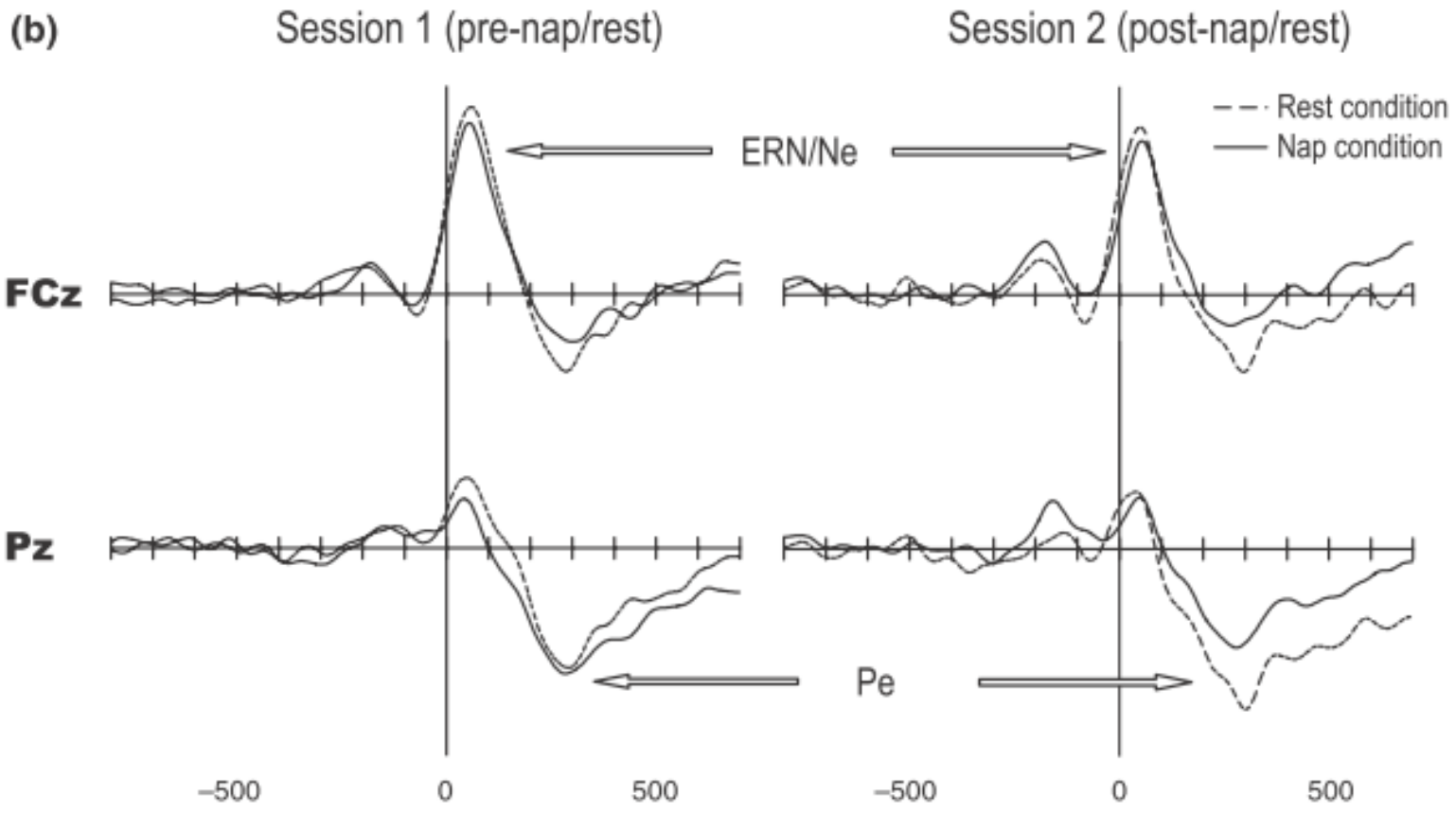
Error-monitoring functions during extended wakefulness (20h, 2AM)



Individuals can detect their own errors, however, the evaluation might be impaired during night work

Murphy *et al*., 2006 *J Sleep Res*

Error-monitoring functions immediately after the daytime 1-h nap (sleep inertia)

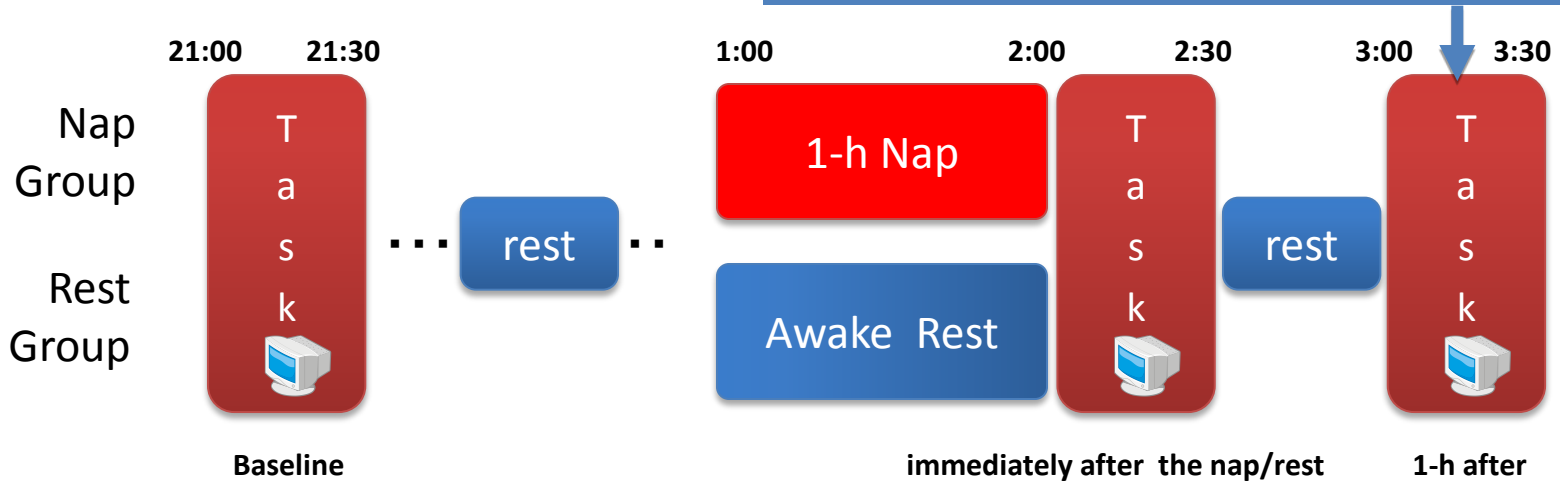


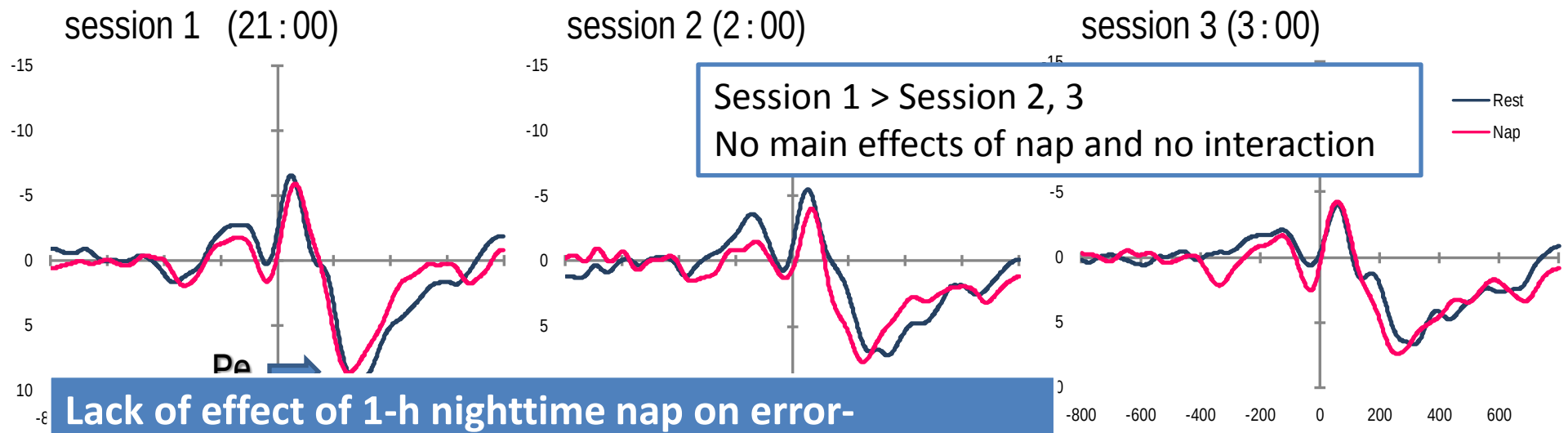
Error evaluation could not be improved during sleep inertia

Asaoka S *Inoue Y.*, 2010 *J Sleep Res*

The effects of nighttime nap during extended wakefulness

Response accuracy was higher in Nap Group compared to Rest Group



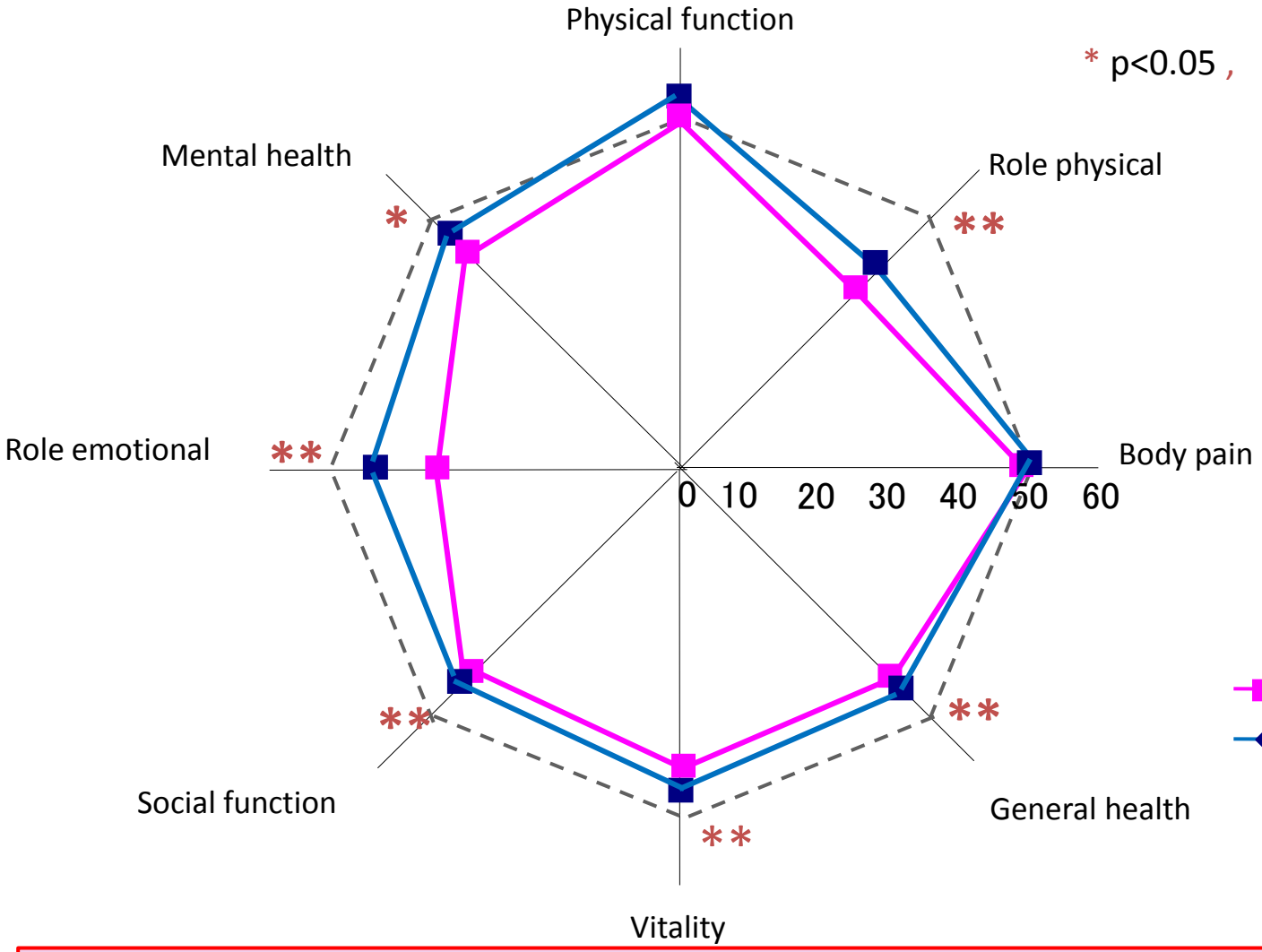


Session 1 > Session 2, 3
No main effects of nap and no interaction

Lack of effect of 1-h nighttime nap on error-monitoring functions

Asaoka *Inoue*., 2012 *SLEEP*

Health related quality of life in patients with CNS hypersomnia (In comparison with national-norm scores)

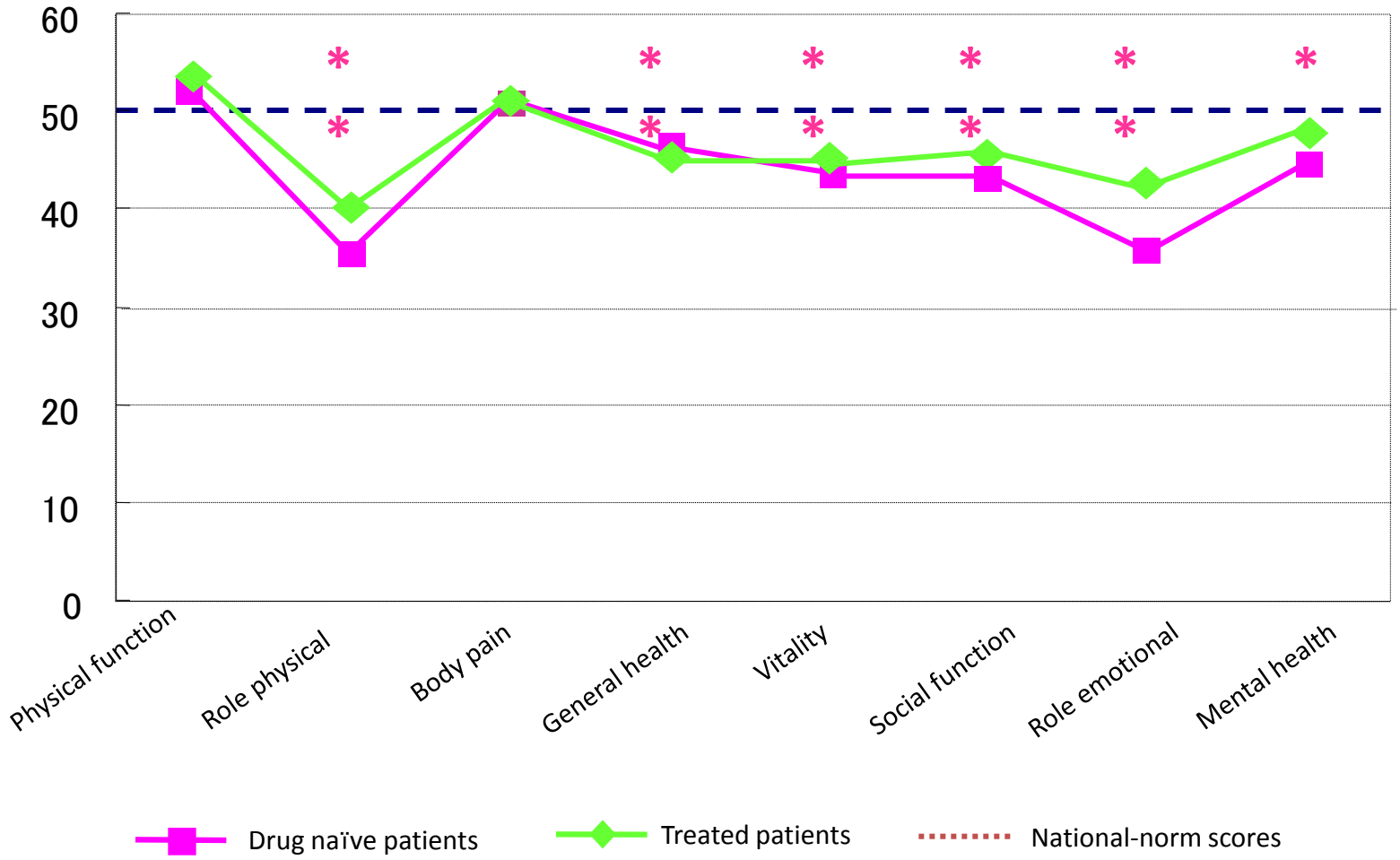


Ogawa A, Inoue Y et al.
Sleep Med (in press)

SF36 measures are almost equally deteriorated in both drug naive patients and treated patients.

過眠症患者のHRQOL

(In comparison with national-norm scores)



* p<.05　　** p<.01

*,**は治療後の国民標準値との比較です！！

The Comparison of Descriptive Variables Between Each Diagnostic Groups and Age- and BMI-Matched Control Groups

	SWD	Control	*z*	*P*	OSAS	Control	*z*	*P*
N	46	46	—	—	102	102	—	—
Age	39.80 (5.68)	39.80 (5.68)	0.00	n.s.	46.44 (8.92)	46.44 (8.92)	0.00	n.s.
BMI (kg/m^2)	24.30 (2.91)	24.27 (2.83)	−0.64	n.s.	27.10 (2.97)	27.07 (2.92)	−0.67	n.s.
ESS	13.17 (1.89)	3.54 (2.54)	−5.91	<0.001	7.73 (4.52)	3.87 (2.29)	−6.41	<0.001
SBP (mm Hg)	124.13 (11.38)	122.61 (11.41)	−0.65	n.s.	138.55 (17.65)	132.10 (14.06)	−2.85	<0.01
DBP (mm Hg)	76.96 (9.02)	77.20 (9.21)	−0.41	n.s.	86.27 (13.19)	81.12 (9.44)	−3.01	<0.01

The data of 14 OSAS and 2 SWD patients were eliminated from the analyses, because there were no matched control subjects. Values are expressed as mean (standard deviation).

n.s., not significant.

Asaoka S, Inoue Y et al. *J Occup Environ Med.* (2010)

JSC

Physical characteristics and other data of the cases for rear-end collision, single-car accidents and accidents of other types

	All accidents	*Rear-end collisions*	*Single-car accidents*	*Accidents of other types*		
Total (*n*)	1772	240	293	1239		
					F	*P*
Age (years)*	35.2 ± 15.5	33.7 ± 13.9[†,‡]	29.6 ± 14.0[†,§]	36.8 ± 15.7[‡,§]	27.68	<0.01
Body Mass Index (kg m^{-2})*	22.4 ± 3.3	22.6 ± 3.5	22.2 ± 3.3	22.4 ± 3.3	0.88	0.42
Sleep length of previous night (h)*	7.3 ± 1.6	7.0 ± 1.6[‡]	6.9 ± 2.2[§]	7.4 ± 1.5[‡,§]	9.79	<0.01
Length of time driving (min)[¶]	15 (5–35)	20 (10.8–50.8)[‡]	20 (10–50)[§]	15 (5–30)[‡,§]	32.72	<0.01
					χ^2	*P*
Male (%)	71.2	75.8 (1.7)	78.8 (3.2)	68.4 (−3.9)	15.43	<0.01
Time zone of occurrence						
Nap zone (%)**	15.2	17.5 (1.1)	8.5 (−3.5)	16.3 (2.0)	272.00	<0.01
Nighttime (%)**	17.7	12.1 (−2.4)	51.2 (16.5)	10.8 (−11.5)		
The other zone (%)**	67.2	70.4 (1.2)	40.3 (−10.7)	72.9 (7.8)		

*Data are given as mean ± standard deviation.
[†]Significant difference between rear-end collisions and single-car accidents.
[‡]Significant difference between rear-end collisions and accidents of other types.
[§]Significant difference between single-car accidents and accidents of other types.
[¶]Data are given as median (interquartile range).
**Data are given as percentage (adjusted standardized residual).

Abe T, Inoue Y et al. *J Sleep Res.* (2010)

JSC

Results of logistic regression analyses on associated factors for the existence of SWD

	Univariate Model					Multivariate Model (forward selection)				
	N	Adjusted odds ratio (95% CI)			p	N	Adjusted odds ratio (95% CI)			p
Family structure										
Living alone	571	1.00		(ref)		429				
Living with family (no children)	300	0.89	(0.64	- 1.22)	0.46	223				n.s.
Living with family (have children)	78	0.36	(0.18	- 0.74)	< 0.01	54				n.s.
Working as head nurse										
Yes	81	1.00		(ref)		58				
No	907	2.73	(1.35	- 5.55)	< 0.01	648				n.s.
Duration of experience in nursing work (years)										
< 3	224	1.00		(ref)		166	1.00		(ref)	0.05
3–6	264	1.76	(1.14	- 2.72)	0.01	193	1.32	(0.78	- 2.22)	0.30
6–10	219	2.45	(1.57	- 3.80)	< 0.01	164	1.81	(1.08	- 3.05)	0.02
≥ 10	280	1.05	(0.67	- 1.66)	0.81	183	0.95	(0.54	- 1.64)	0.84
Shift rotation										
3-shift	301	1.00		(ref)		204				
2-shift	692	1.39	(1.00	- 1.94)	0.05	502				n.s.
Currently engaged in consecutive night shifts										
No	806	1.00		(ref)		578				
Yes	171	1.56	(1.09	- 2.24)	0.02	128				n.s.
Missing nap opportunities during night work										
Rare or never	427	1.00		(ref)		325	1.00		(ref)	
Frequent or usual	513	1.79	(1.32	- 2.44)	< 0.01	381	1.86	(1.29	- 2.68)	< 0.01
Total time spent in work (hours/month)										
< 184.5	416	1.00		(ref)		348				
≥ 184.5	418	1.33	(0.97	- 1.83)	0.07	358				n.s.
Time spent in night work (hours/month)										
< 45.75	417	1.00		(ref)		336	1.00		(ref)	
≥ 45.75	416	1.84	(1.34	- 2.54)	< 0.01	370	1.49	(1.03	- 2.16)	0.04
Chronotype (diurnal type scale score)										
Morningness type (≥16)	484	1.00		(ref)		351	1.00		(ref)	
Eveningness type (<16)	441	1.60	(1.18	- 2.16)	< 0.01	355	1.65	(1.16	- 2.36)	< 0.01

JSC

Associated factors for dozing off at the wheel among OSAS drivers.

	Total	dozing off		Univariate relative risk			Multivariate relative risk		
	n	*n*	%	(95% CI)[*1]		*p*	(95% CI)[*1]		*p*
Age									
< 47	305	187	61.3						
≥ 47	311	169	54.3			*ns*			*ns*
Usual sleep length									
< 7 hr	312	176	56.4						
≥ 7 hr	296	174	58.8			*ns*			*ns*
ESS score [*2]									
< 11	256	89	34.8						
≥ 11, < 16	228	154	67.5	3.91	(2.68 - 5.70)	*< 0.0001*	3.79	(2.59 - 5.55)	*< 0.0001*
≥ 16	132	113	85.6	11.2	(6.44 - 19.3)	*< 0.0001*	9.87	(5.66 - 17.2)	*< 0.0001*
AHI [*3]									
< 40	297	143	48.1						
≥ 40	319	213	66.8	2.16	(1.56 - 3.00)	*< 0.0001*	1.68	(1.18 - 2.40)	*< 0.01*

[*1] Relative risks approximated with odds ratios. CI denotes confidence intervals

[*2] Epworth Sleepiness Scale before treatment

[*3] Apnea hypopnea index before treatment

Komada Y, Inoue Y et al. *Tohoku J Exp Med.* (2009)

JSC