Sleep and Depression

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Sleep Disturbance is Common

- Epidemiological survey indicates that 15~35% of the adult population complain of sleep quality disturbance.

Karacan et al., 1983; Lugaresi et al., 1983
Welstein et al., 1983; Mellinger et al., 1985

- Sleep quality complaints are particularly relevant to psychiatry.

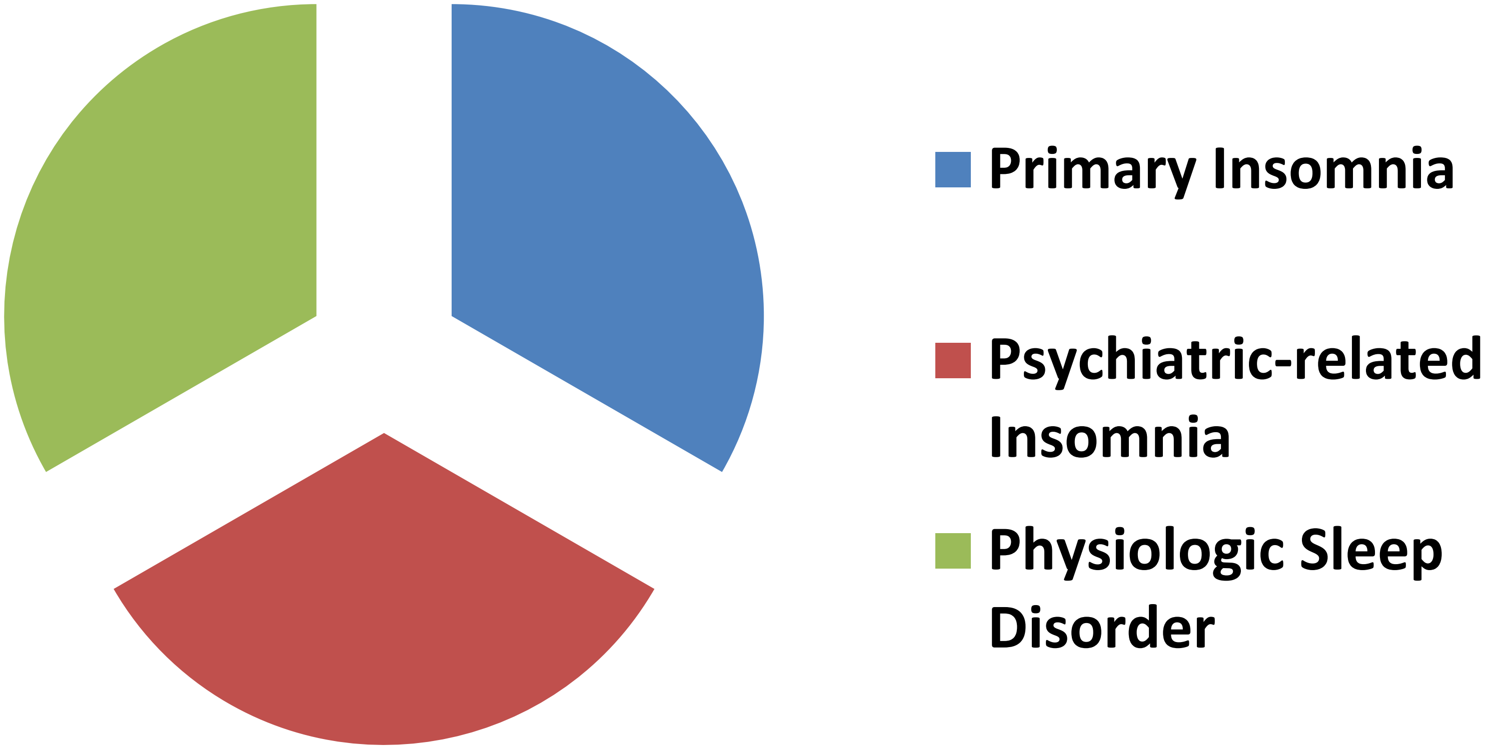
- Factors relating to anxiety and stress are one of the most important concomitants of sleep complaints in the general population.

Karacan et al., 1983

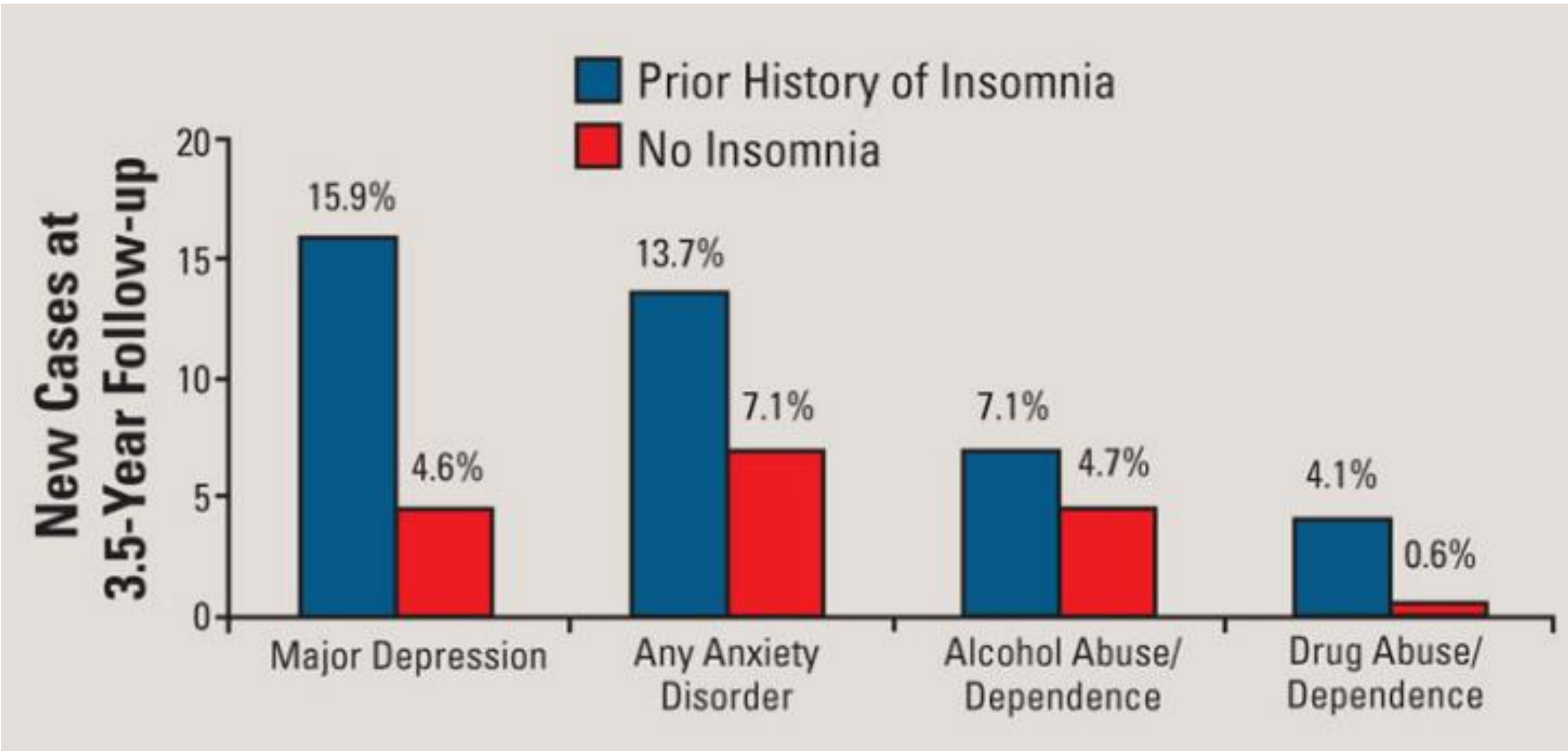
Distribution of Sleep Diagnoses

Insomnia associated with psychiatric disorders is the most prevalent type of insomnia seen in sleep disorders centers, accounting for **35%** of diagnoses.

Buysse et al., 1989



Insomnia Predicts Psychiatric Disorders



Breslau N, et al. *Biol Psychiatry*. 1996;39:411-418.

Sleep Complaints in Mood Disorders

- Sleep complaints are some of the earliest and most commonly reported symptoms of mood disorders.

- Specific sleep complaints include
  - **difficulty falling asleep**
  - **frequent nocturnal awakenings**
  - **early morning awakening**
  - **nonrestorative sleep**
  - disturbing dreams.

Insomnia Predicts Mood Disorders

- Sleep change is a robust predictor of recurrent mood episodes, and its persistence is associated with a more severe course.

- In patients with bipolar disorder, an increase *or* decrease of 3 hours or more of sleep suggested imminent onset of a recurrent mood episode.
  - Bauer M et al. Bipolar Disord 2006; 8:160-167.

Insomnia **Predicts** Mood Disorders

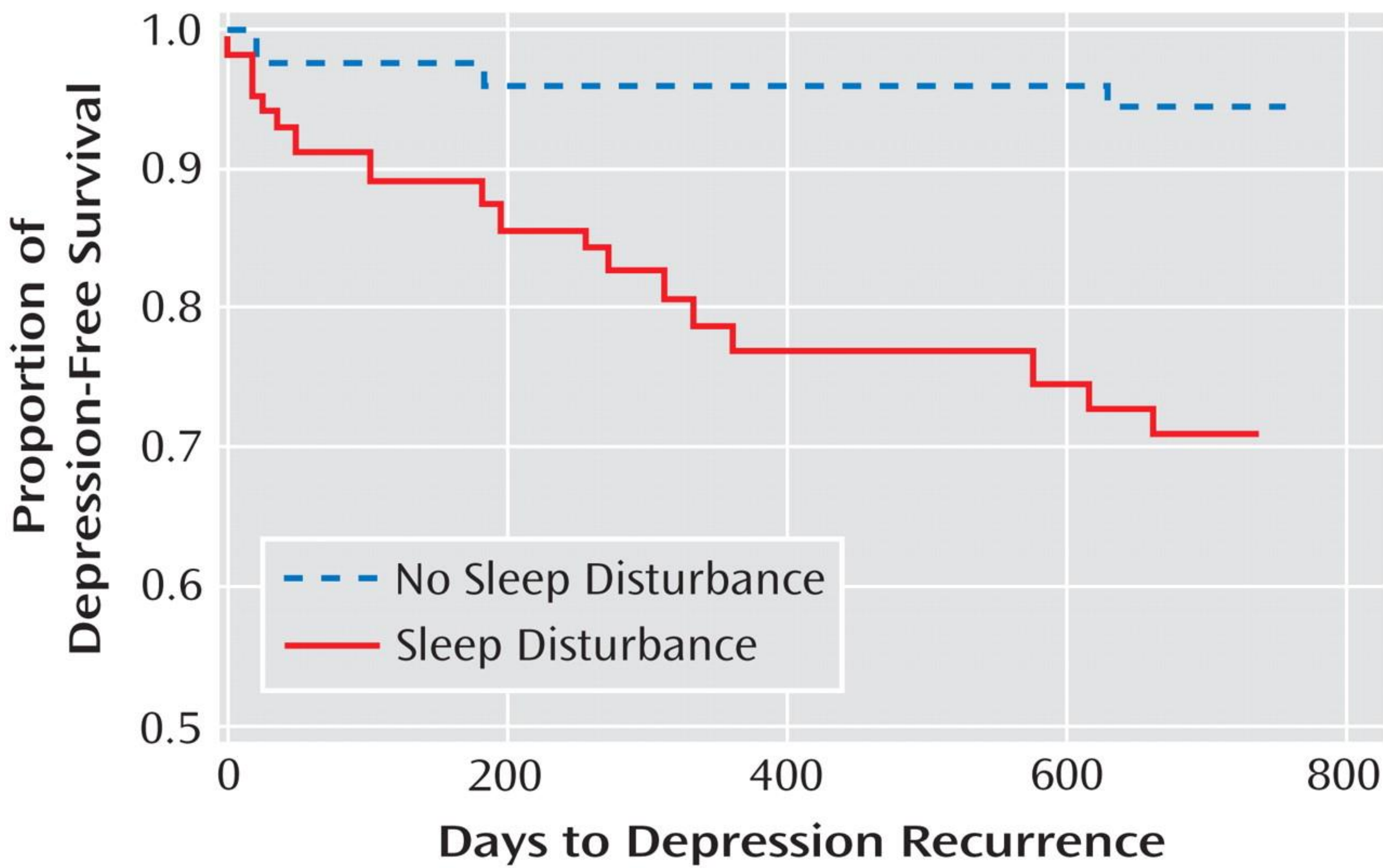
Table 6. Risk for New Major Depression Associated with Prior Sleep Disturbance: Controlling for the Effects of Other Prior Symptoms

	Odds Ratio (95% CI)	
	1	2
Gender (female)	2.4 (1.2–4.8)	2.1 (1.1–4.2)
T_1 Insomnia	3.4 (1.9–6.2)	2.1 (1.1–4.0)
T_1 Hypersomnia	2.1 (1.1–4.2)	1.3 (0.6–2.8)
T_1 Number of other symptoms[a]		1.3 (1.1–1.5)

Results from two successive multiple logistic regressions.
[a] From 15 criterion symptoms of major depression other than sleep disturbance.

Breslau N et al. Sleep. Biol Psychiatry 1996; 39(6):411-418.

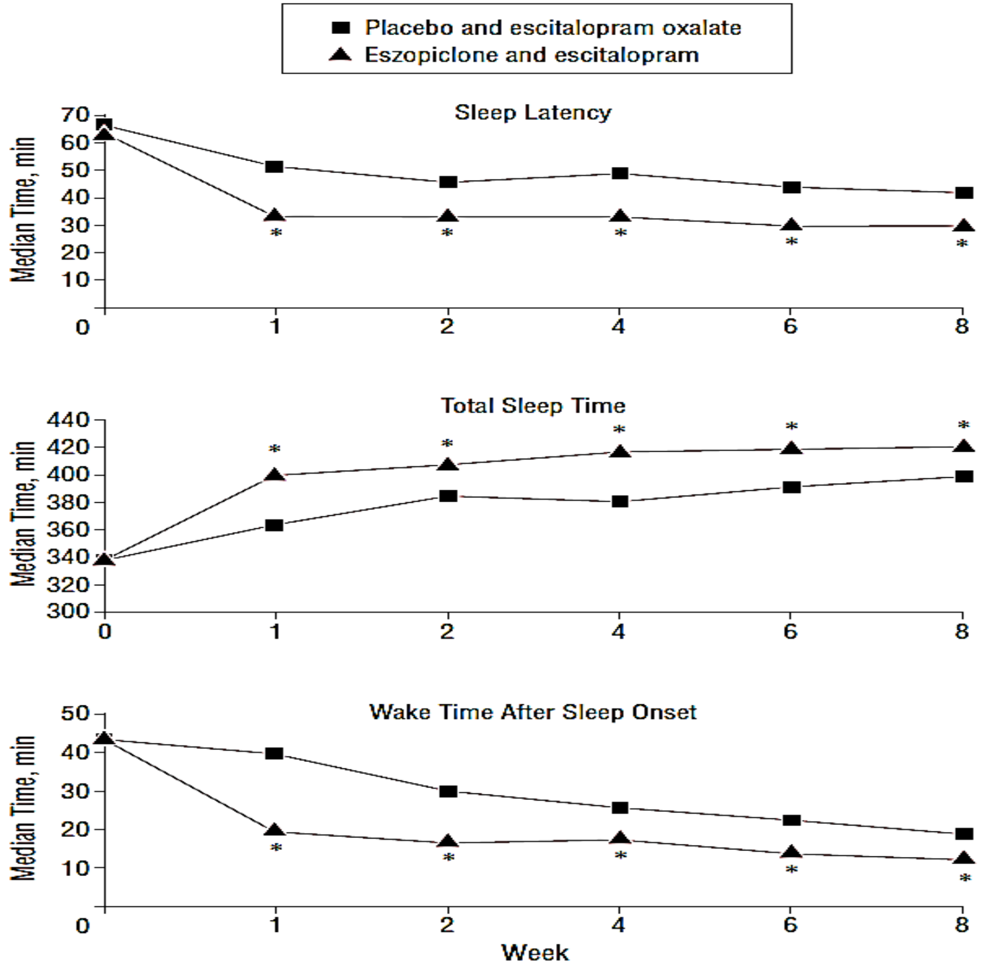
Insomnia Predicts Recurrence of Depression



Hyong Jin Cho et al. Am J Psychiatry 2008;165:1543-1550.

Sleep vs. Depression

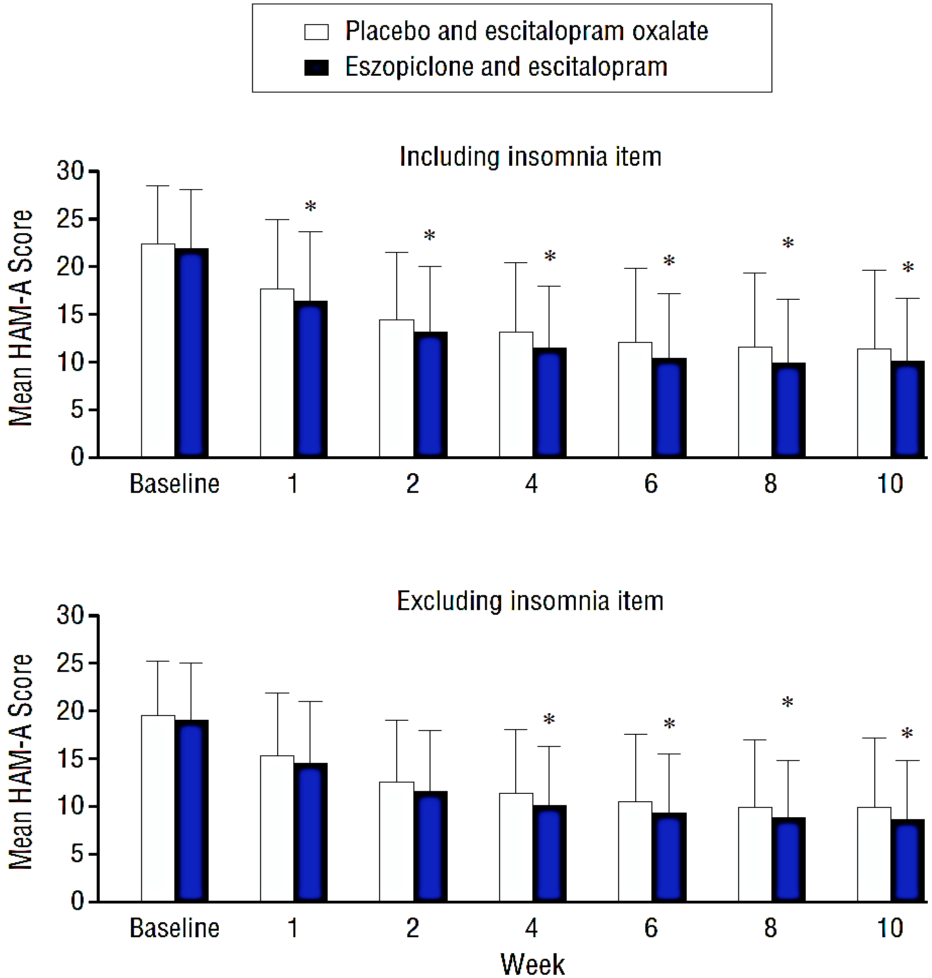
ONE Disorder or TWO Disorders?



Arch Gen Psychiatry. 2008;65(5):551-562

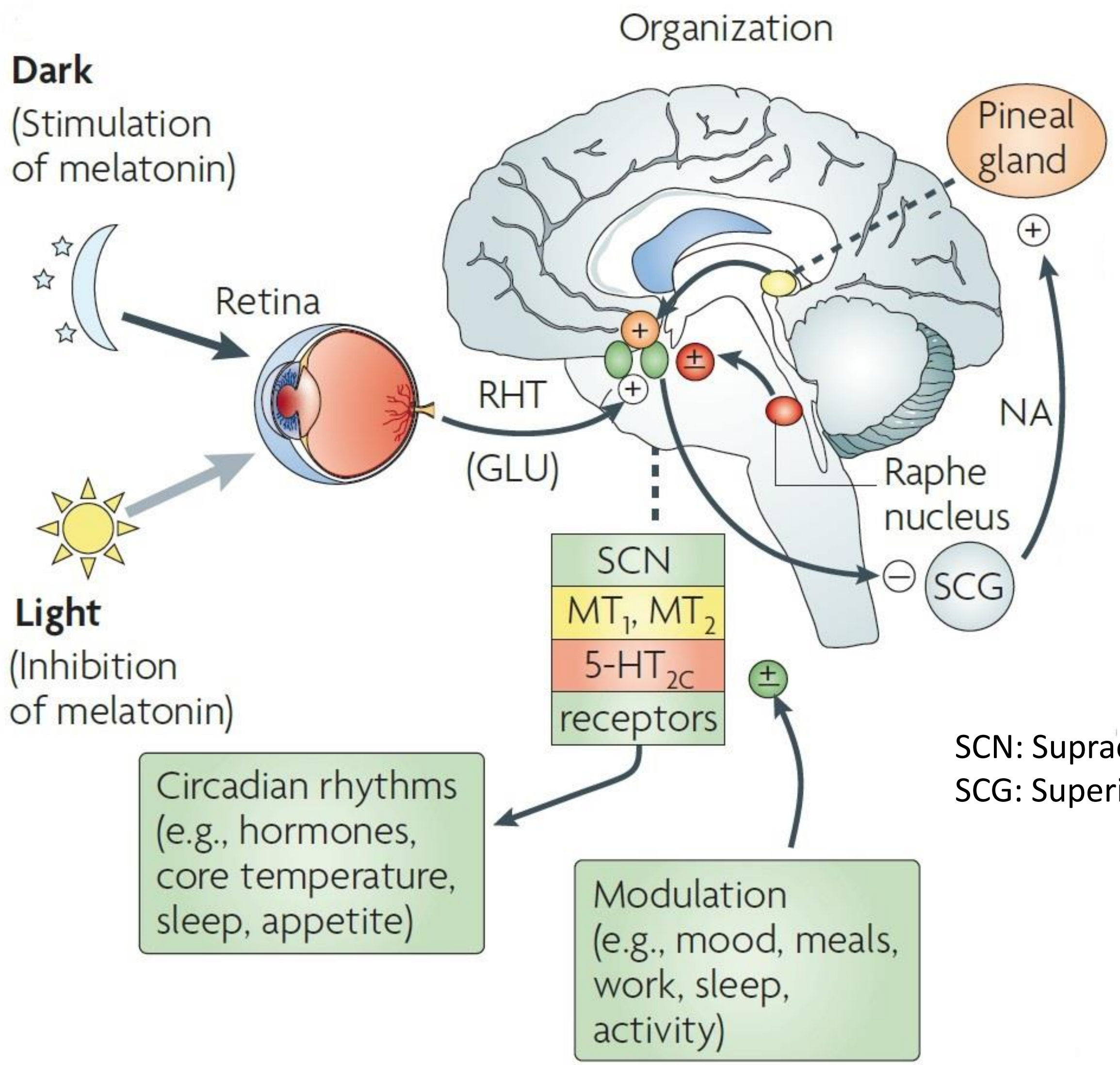
Sleep vs. Depression

ONE Disorder or TWO Disorders?



Arch Gen Psychiatry. 2008;65(5):551-562

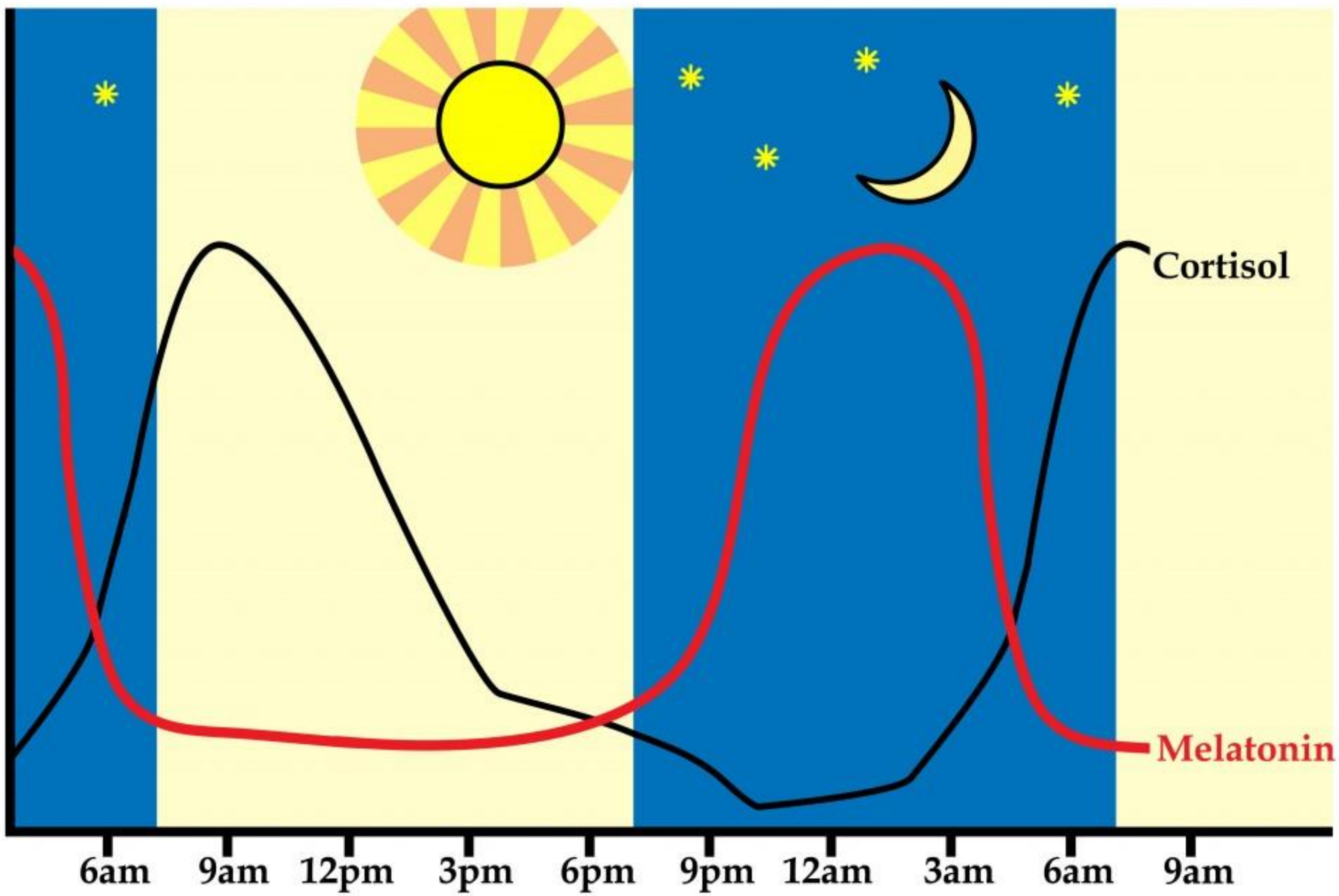
Our Internal Clock



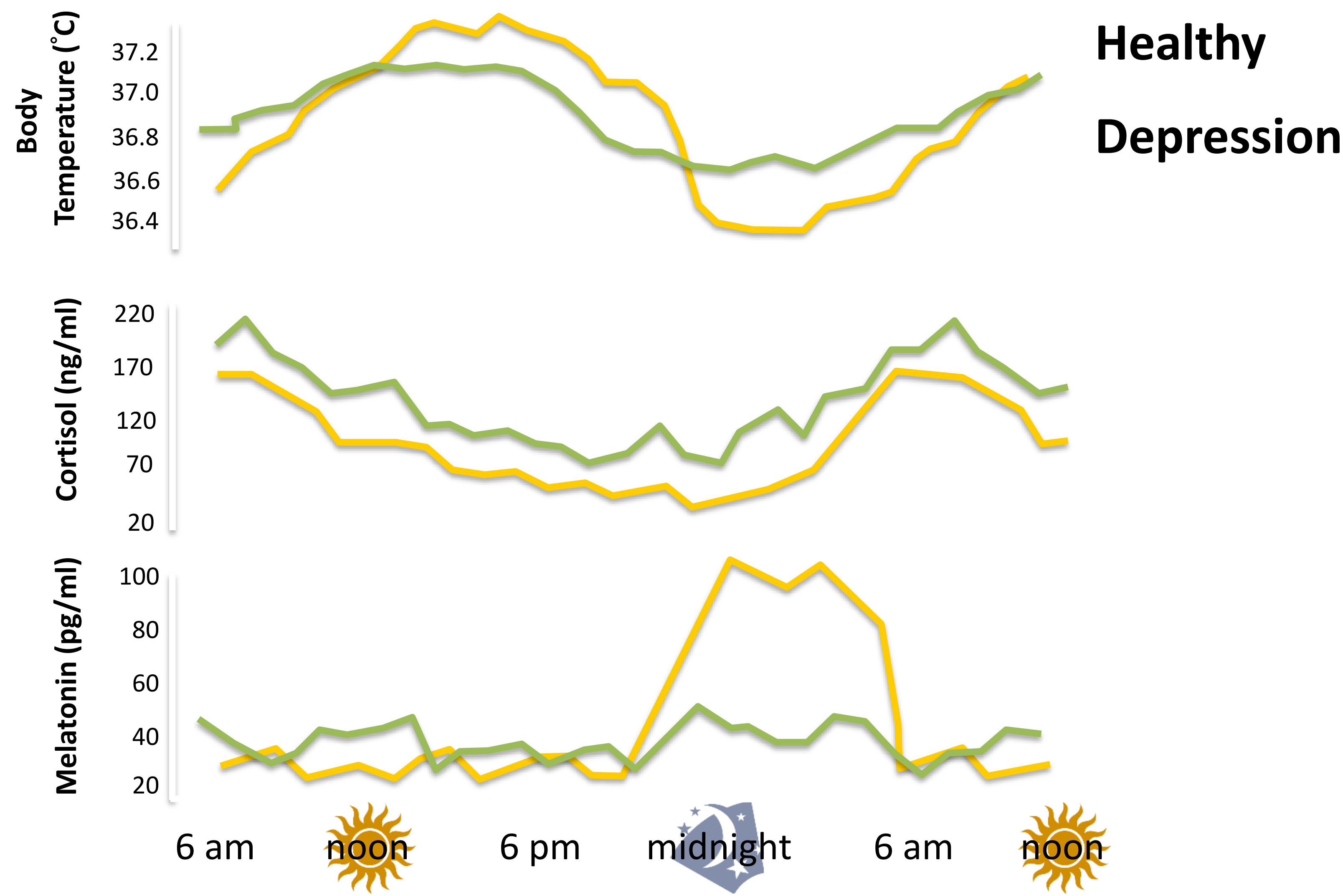
SCN: Suprachiasmatic Nuclei
SCG: Superior Cervical Ganglia

Bodinat C et al. *Nature Reviews*. 2010.

Circadian Rhythm



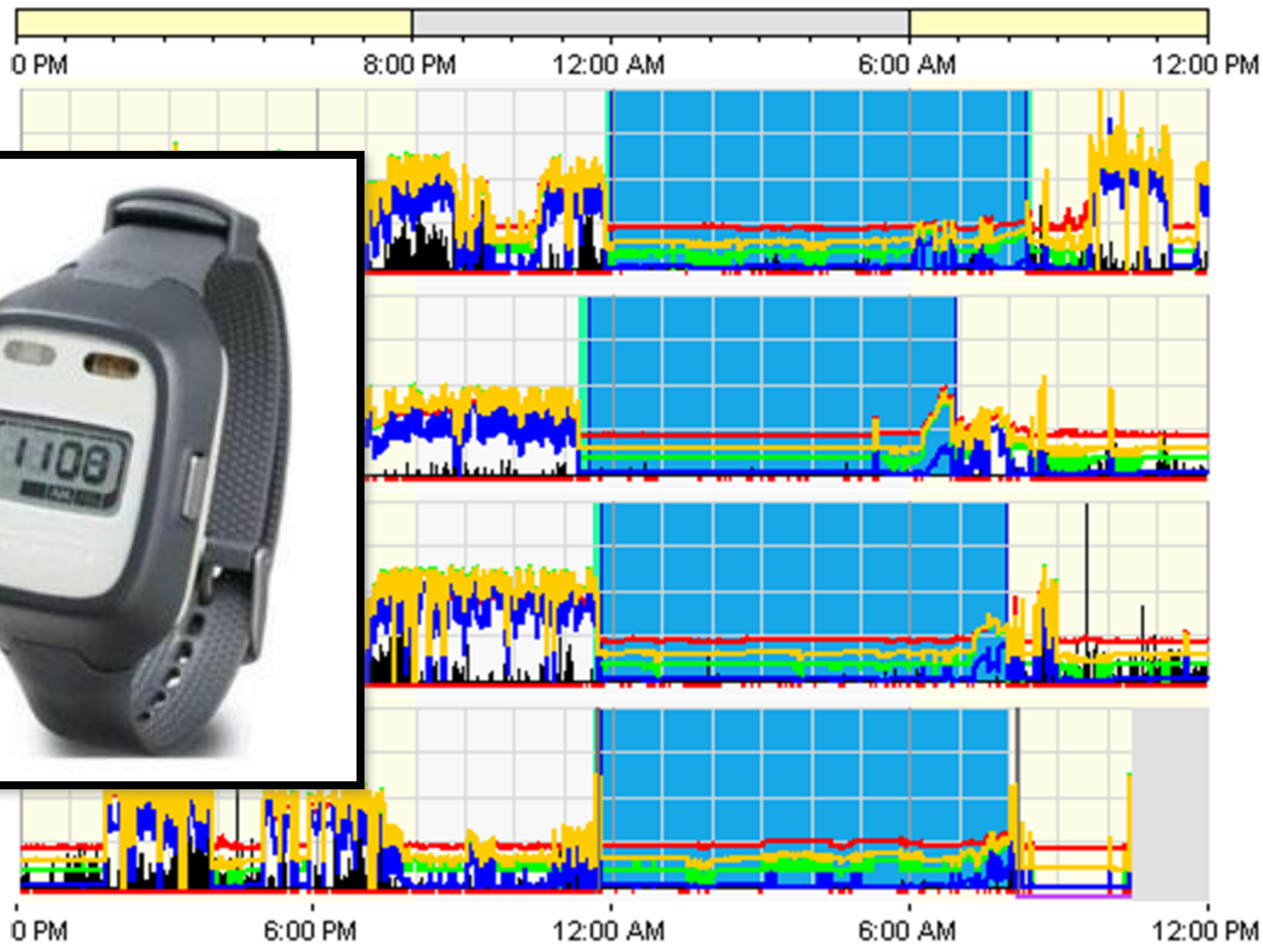
Disturbed Circadian Rhythm in Depression



Souêtre E et al. *Psychiatry Res*. 1989.

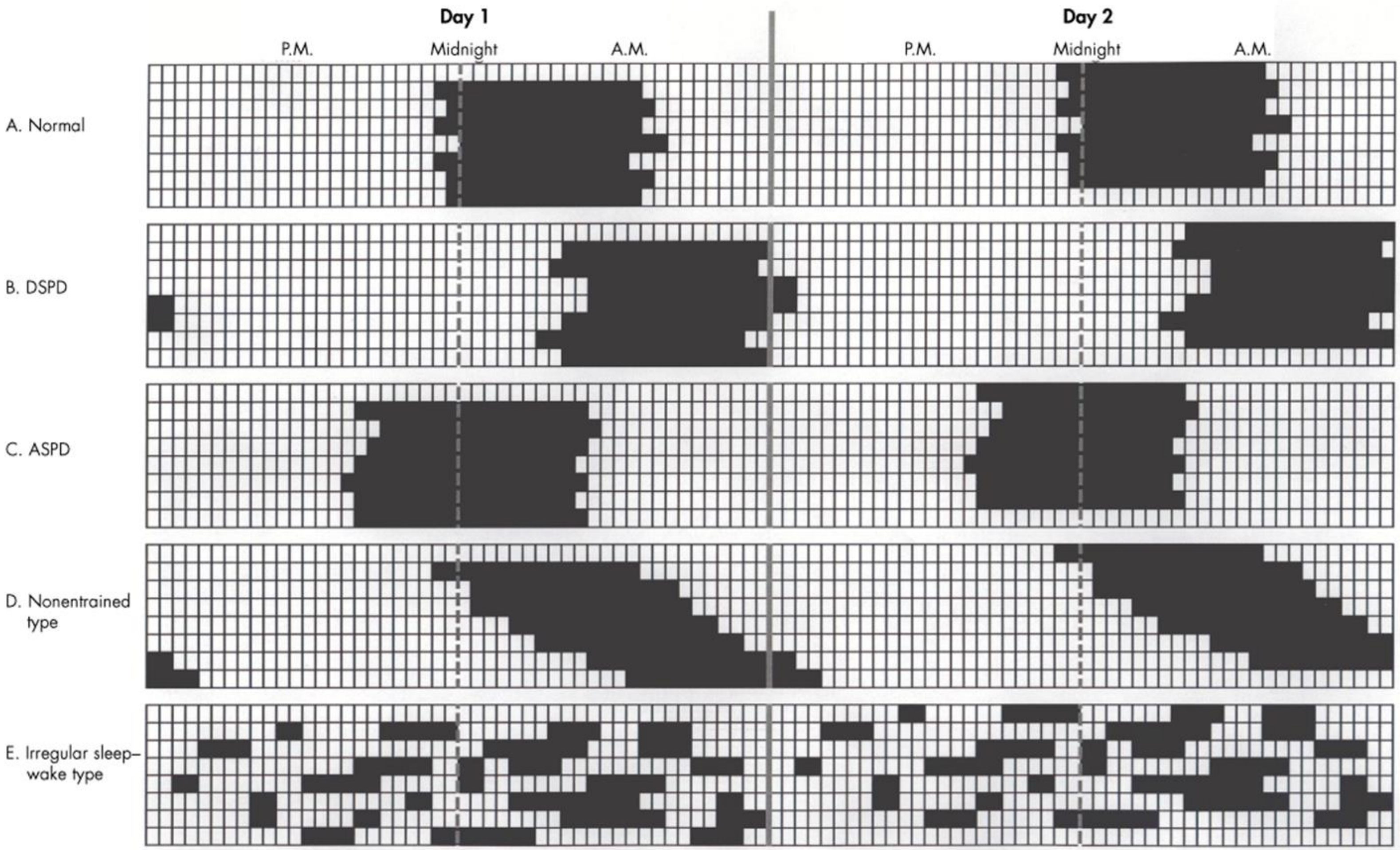
Actigraphy

1108
AM



0 PM
8:00 PM
12:00 AM
6:00 AM
12:00 PM
0 PM
6:00 PM
12:00 AM
6:00 AM
12:00 PM

Owl or Lark?


Day 1
Day 2
P.M.
Midnight
A.M.
P.M.
Midnight
A.M.
A. Normal
B. DSPD
C. ASPD
D. Nonentrained type
E. Irregular sleep–wake type

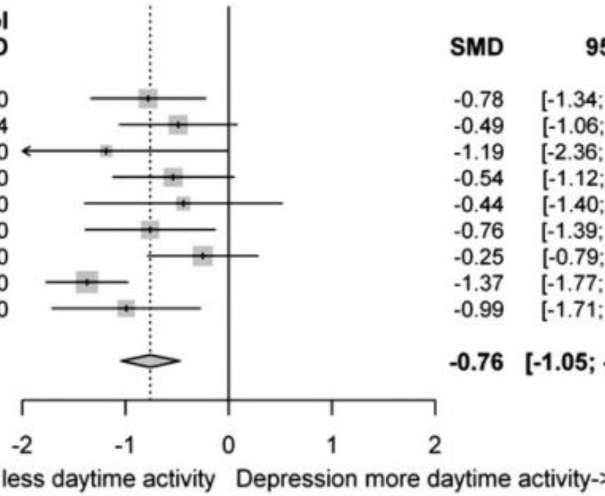
Wearable Devices

Actigraphy Monitoring in Depression

a

Study	Depression Total	Depression Mean	Depression SD	Control Total	Control Mean	Control SD	SMD	95%-CI	W(random)
Berle 2010	23	93.300	60.000	32	142.00	62.600	-0.78	[-1.34; -0.22]	12.8%
Faurholt-Jepsen 2012	20	0.085	0.059	31	0.11	0.044	-0.49	[-1.06; 0.08]	12.5%
Foster 1978	7	22.400	9.100	7	35.20	11.000	-1.19	[-2.36; -0.02]	4.8%
Glod 1992	26	11.000	2.230	21	12.00	1.150	-0.54	[-1.12; 0.05]	12.2%
Korszun 2002	5	182.000	19.000	28	192.00	22.600	-0.44	[-1.40; 0.52]	6.6%
Teicher 1997	25	638.000	133.000	18	726.00	78.000	-0.76	[-1.39; -0.13]	11.3%
Todder 2009	27	65.000	15.600	27	69.00	15.600	-0.25	[-0.79; 0.28]	13.3%
Volker 2003	58	6.900	3.400	64	11.60	3.400	-1.37	[-1.77; -0.98]	16.8%
Winkler 2005	17	367.000	125.000	17	637.00	354.000	-0.99	[-1.71; -0.28]	9.7%
Random effects model	**208**			**245**			**-0.76**	**[-1.05; -0.47]**	**100%**

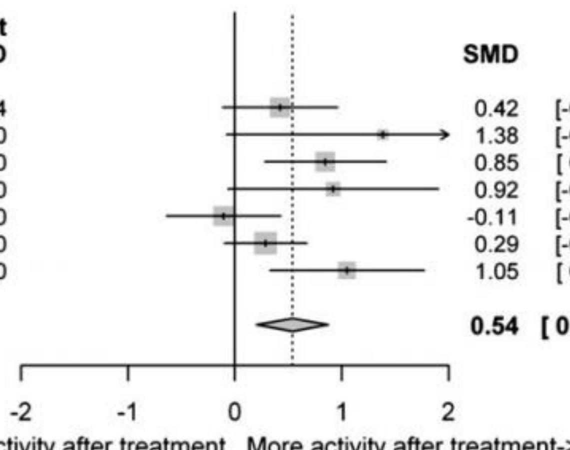
Heterogeneity: I-squared=47.5%, p=0.0547



b

Study	Post treatment Total	Post treatment Mean	Post treatment SD	Pre treatment Total	Pre treatment Mean	Pre treatment SD	SMD	95%-CI	W(random)
Baune 2007	27	17.0	8.86	27	13.8	5.74	0.42	[-0.12; 0.96]	17.4%
Godfrey 1984	5	541.0	175.00	5	273.0	175.00	1.38	[-0.08; 2.85]	4.6%
Raoux 1994	26	1560.0	487.00	26	1140.0	491.00	0.85	[0.28; 1.42]	16.6%
Royant Parola 1986	9	64.3	13.40	9	47.6	20.50	0.92	[-0.07; 1.90]	8.6%
Todder 2009	27	63.0	20.80	27	65.0	15.60	-0.11	[-0.64; 0.43]	17.6%
Volker 2002	52	8.0	3.60	52	7.0	3.30	0.29	[-0.10; 0.67]	22.3%
Winkler 2005	17	565.0	229.00	17	367.0	125.00	1.05	[0.33; 1.77]	12.9%
Random effects model	**163**			**163**			**0.54**	**[0.20; 0.87]**	**100%**

Heterogeneity: I-squared=49.1%, p=0.0668



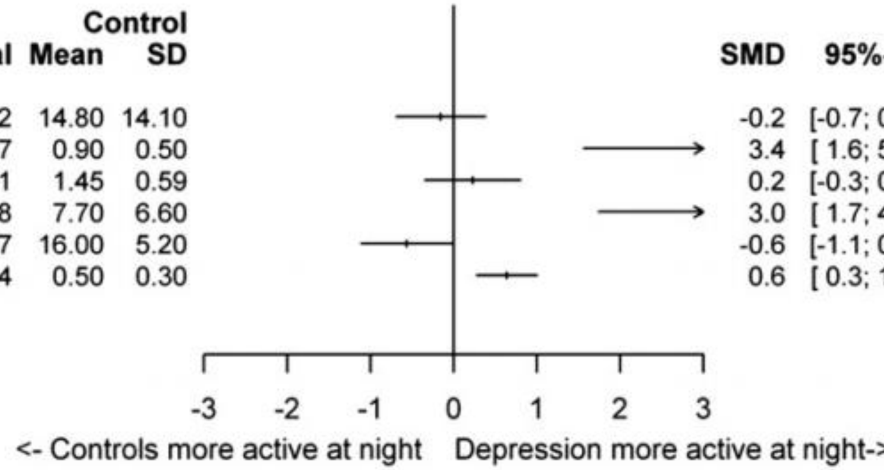
Burton C et al. J Affect Disord. 2013;145(1):21-8

Actigraphy Monitoring in Depression

c

Study	Depression Total	Depression Mean	Depression SD	Control Total	Control Mean	Control SD	SMD	95%-CI
Berle 2010	23	12.70	12.20	32	14.80	14.10	-0.2	[-0.7; 0.4]
Foster 1978	7	3.30	0.80	7	0.90	0.50	3.4	[1.6; 5.2]
Glod 1992	26	1.65	1.03	21	1.45	0.59	0.2	[-0.3; 0.8]
Korszun 2002	5	35.90	19.40	28	7.70	6.60	3.0	[1.7; 4.2]
Todder 2009	27	13.00	5.20	27	16.00	5.20	-0.6	[-1.1; 0.0]
Volker 2003	58	0.80	0.60	64	0.50	0.30	0.6	[0.3; 1.0]

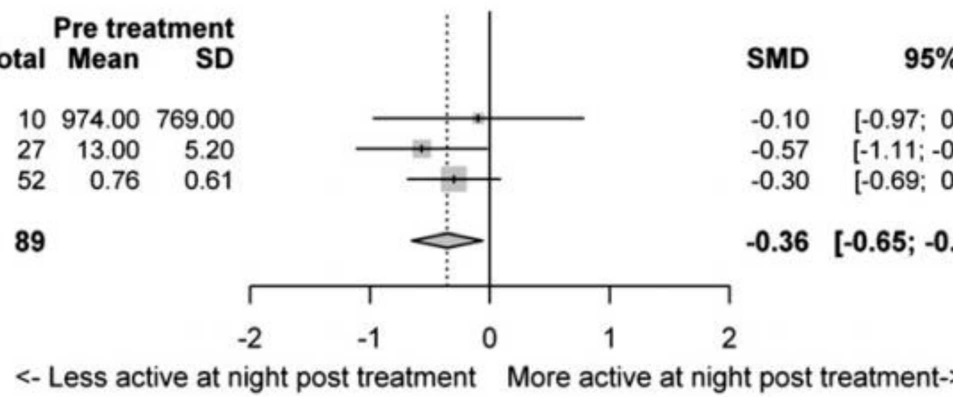
Heterogeneity: I-squared=88.9%, p<0.0001



d

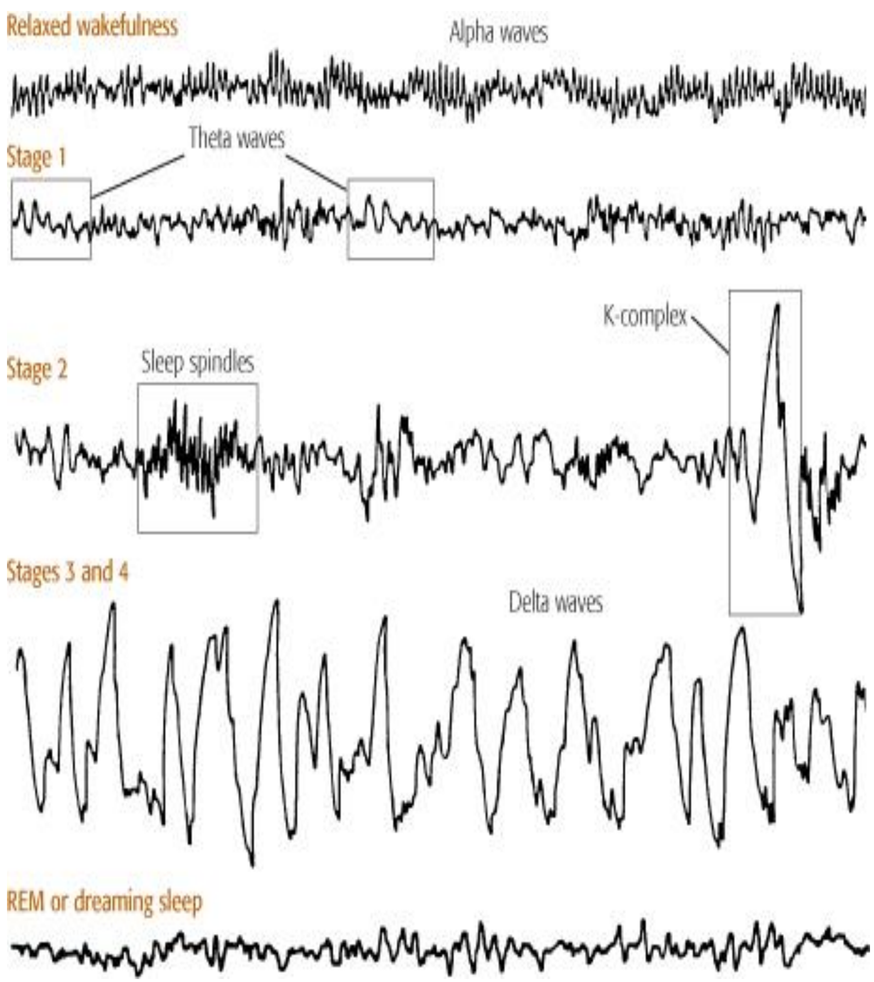
Study	Post treatment Total	Post treatment Mean	Post treatment SD	Pre treatment Total	Pre treatment Mean	Pre treatment SD	SMD	95%-CI	W(random)
Baune 2006	10	904.00	616.00	10	974.00	769.00	-0.10	[-0.97; 0.78]	11.4%
Todder 2009	27	10.00	5.20	27	13.00	5.20	-0.57	[-1.11; -0.02]	29.6%
Volker 2002	52	0.61	0.35	52	0.76	0.61	-0.30	[-0.69; 0.09]	58.9%
Random effects model	**89**			**89**			**-0.36**	**[-0.65; -0.06]**	**100%**

Heterogeneity: I-squared=0%, p=0.6054



Burton C et al. J Affect Disord. 2013;145(1):21-8

EEG Sleep Stages

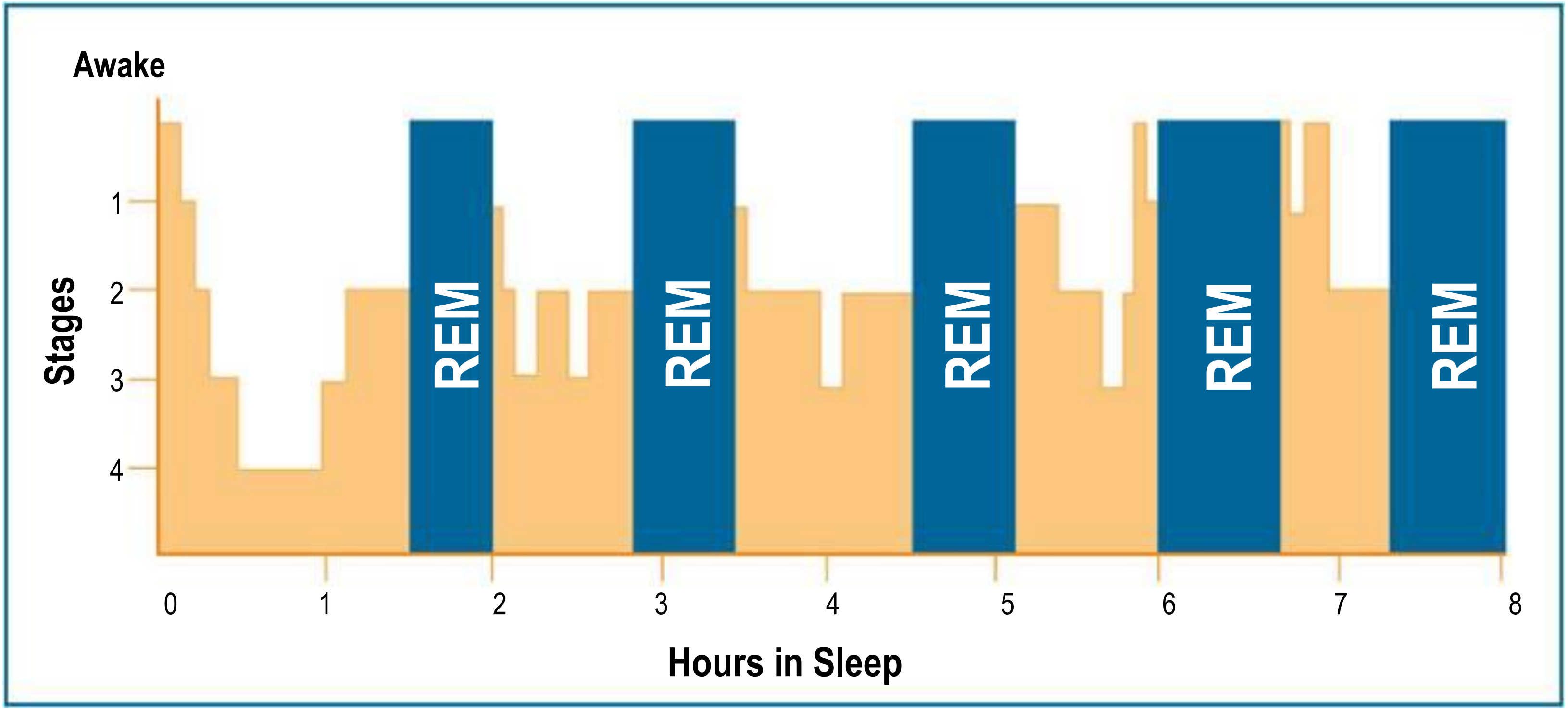


- Slow wave sleep is correlated with **restorative** function of sleep
- Slow wave sleep is considered as **deep** sleep

Picture taken from www.aolhealth.com

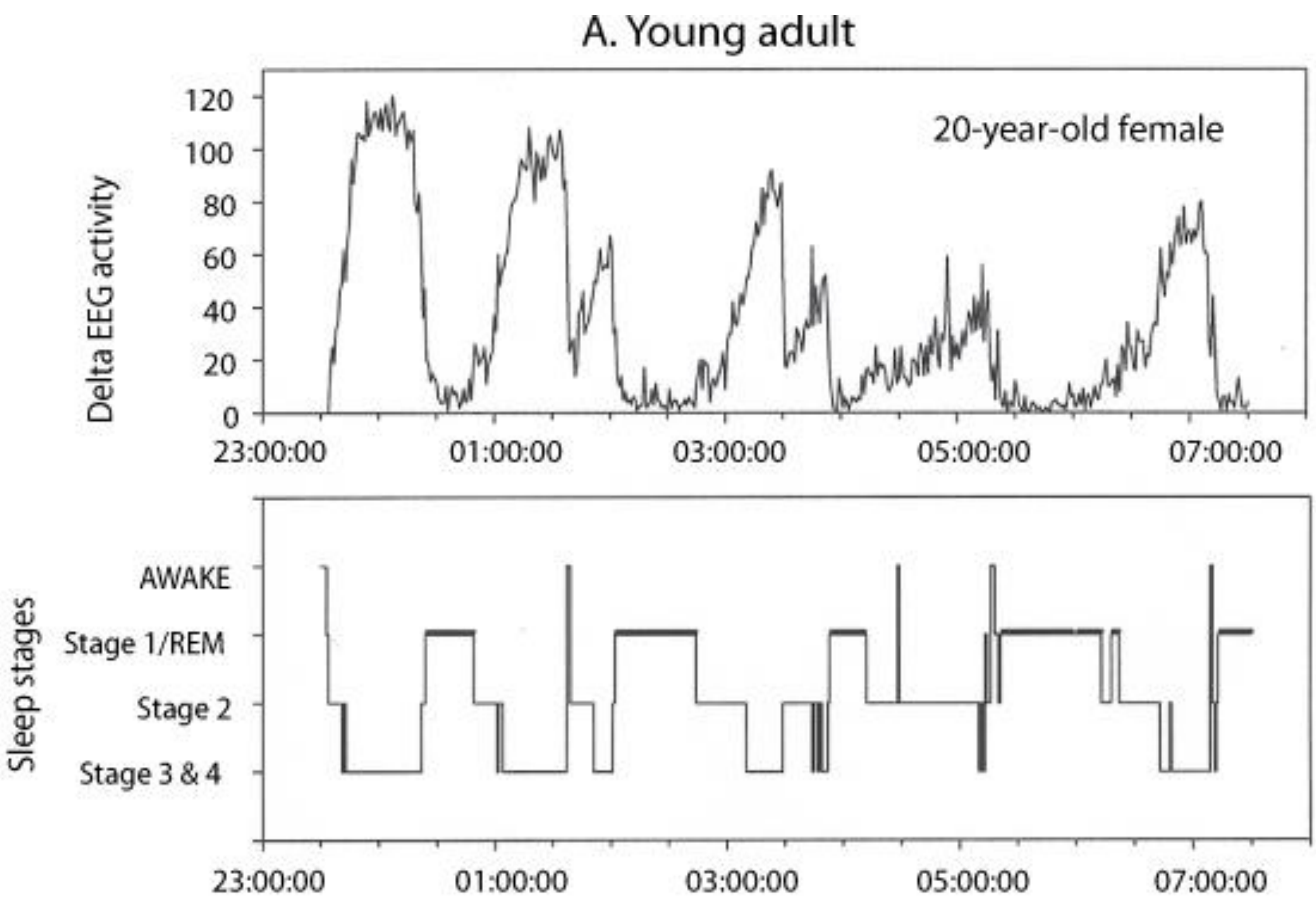
Hobson JA (2005) Nature 437, 1254-1256

The Sleep Cycle in Adults

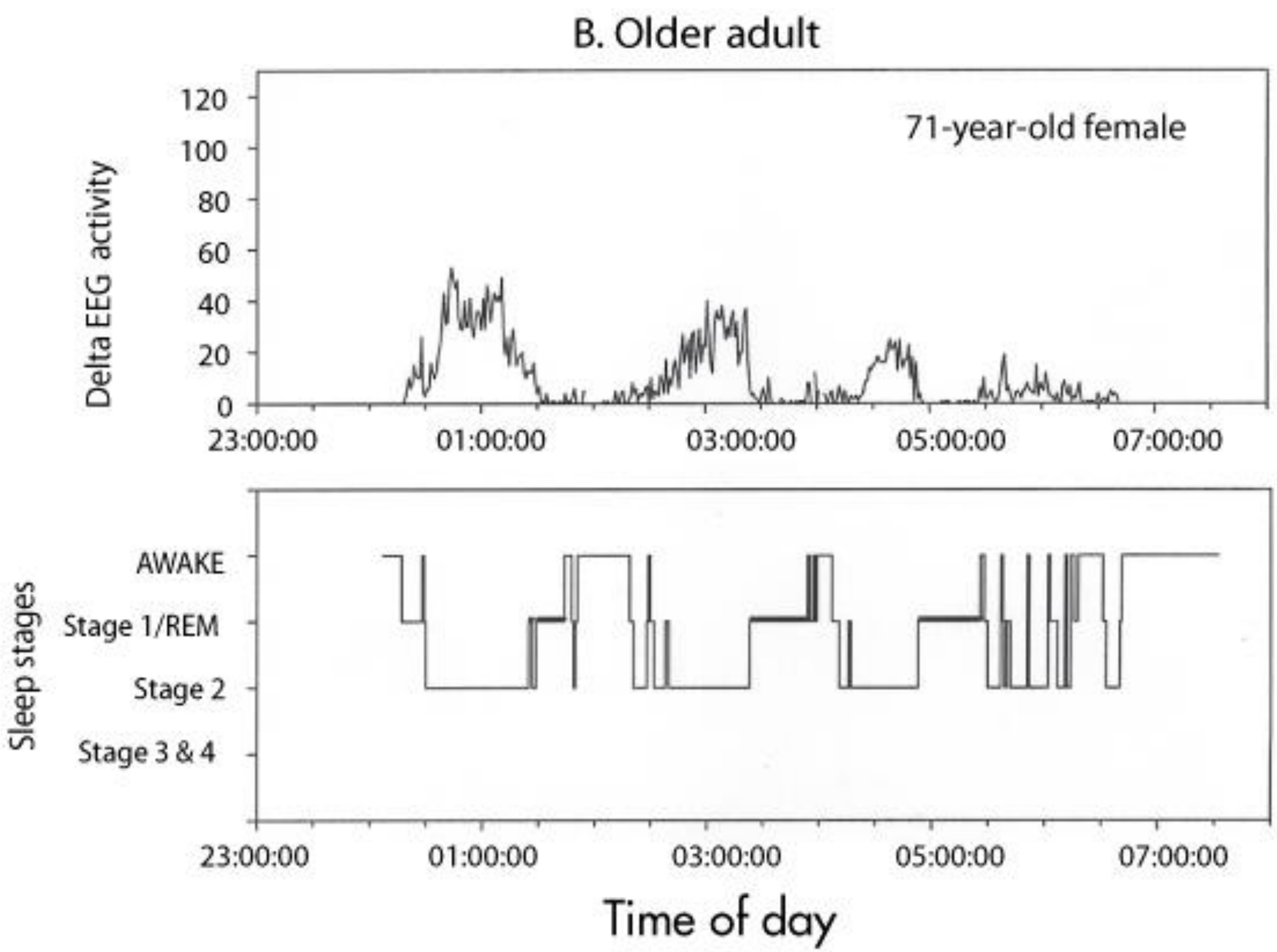


National Sleep Foundation

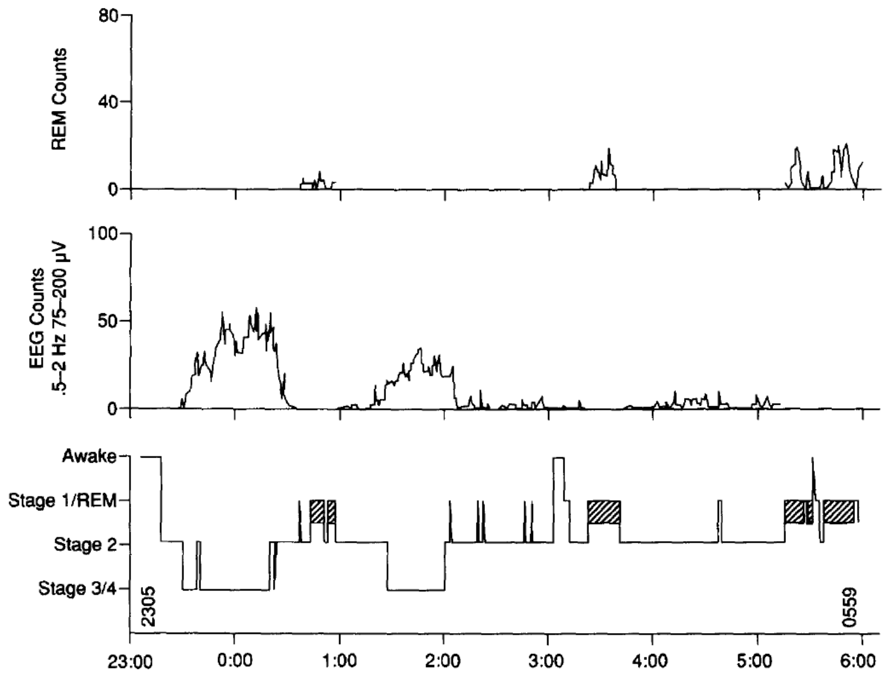
Slow Wave Sleep (Healthy)

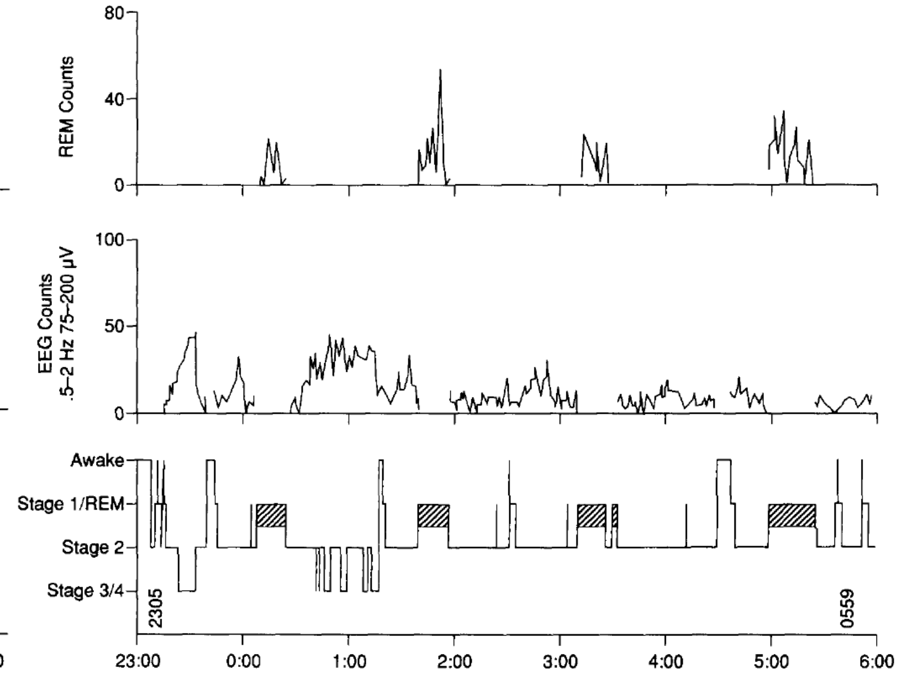


Slow Wave Sleep (Healthy)



Disturbed Slow Wave Sleep in Depression

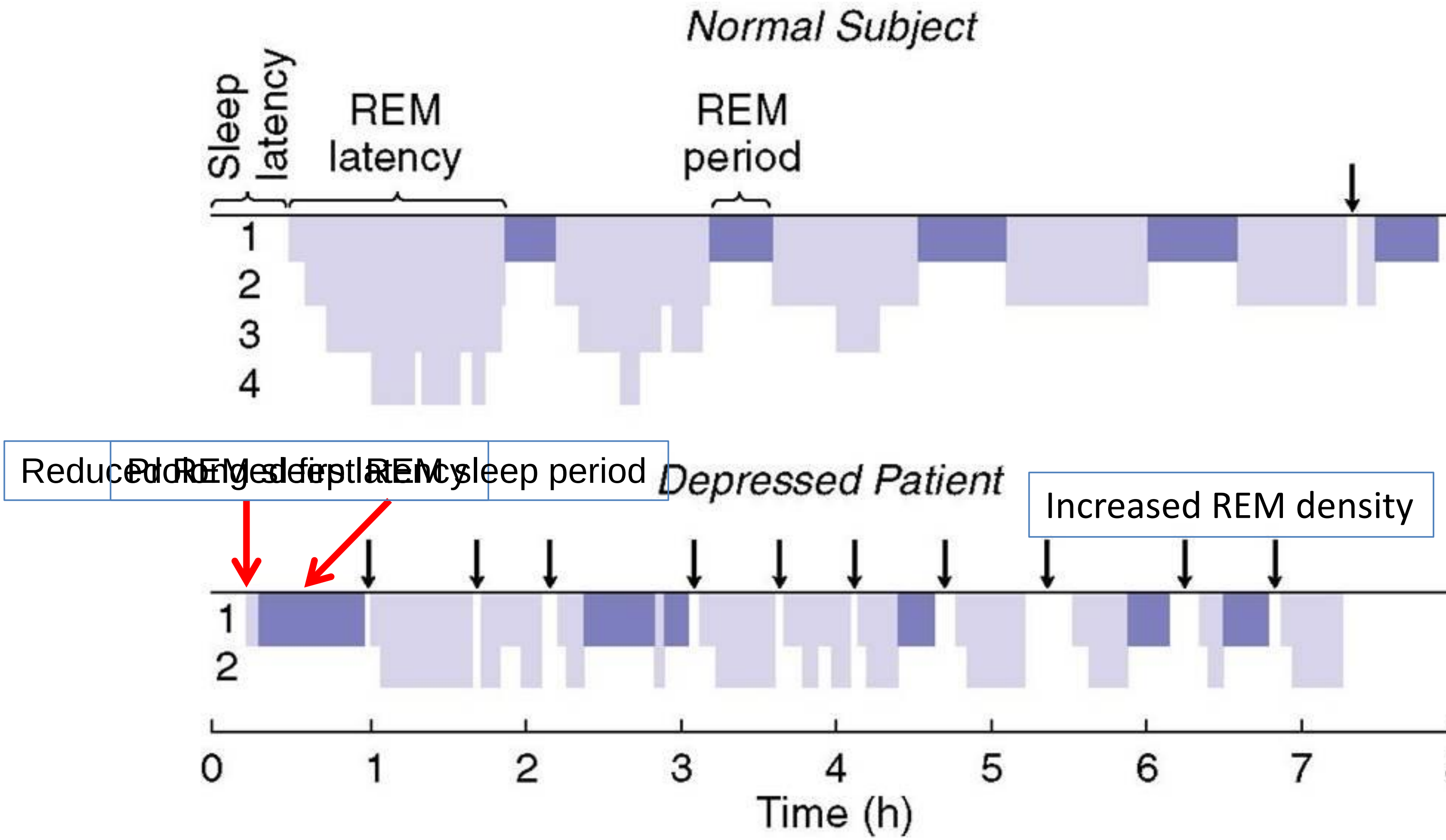




Healthy Control **Depression**

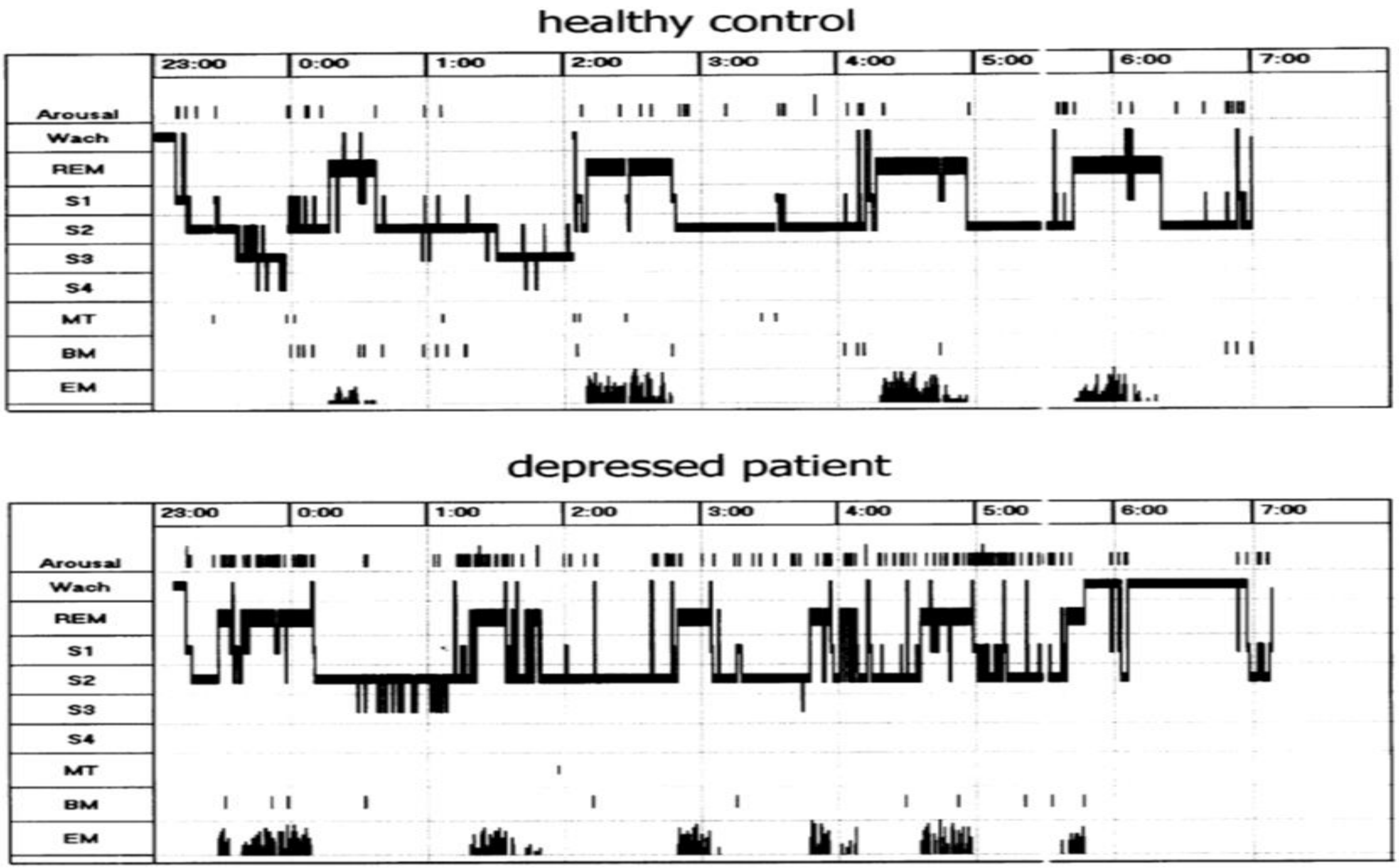
Kupfer DJ. Biol Psychiatry 1995; 38(6):391-403.

Disturbed REM in Depression



Riemann D et al. Biological Psychology 2001;57:67-103.

Disturbed Wake/Arousal in Depression



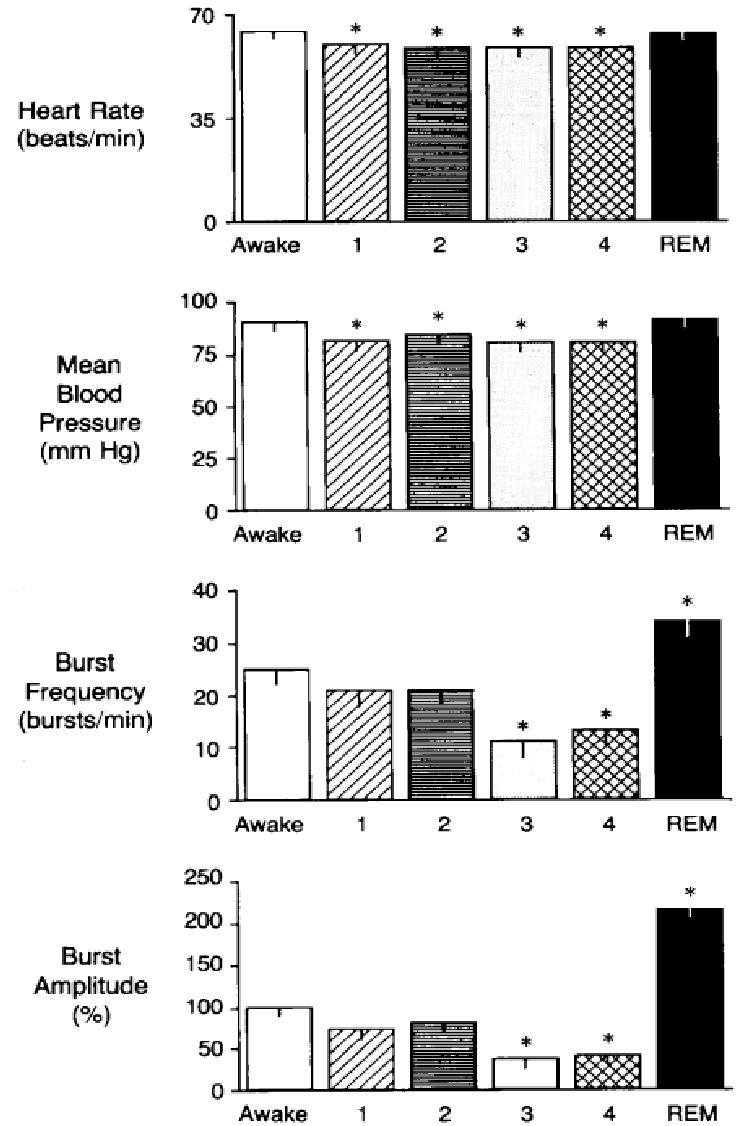
Lancet Neurol 2015; 14: 547–58

Sleep and Autonomic Nervous System

- Sympathetic activity was lower during sleep than wakefulness.

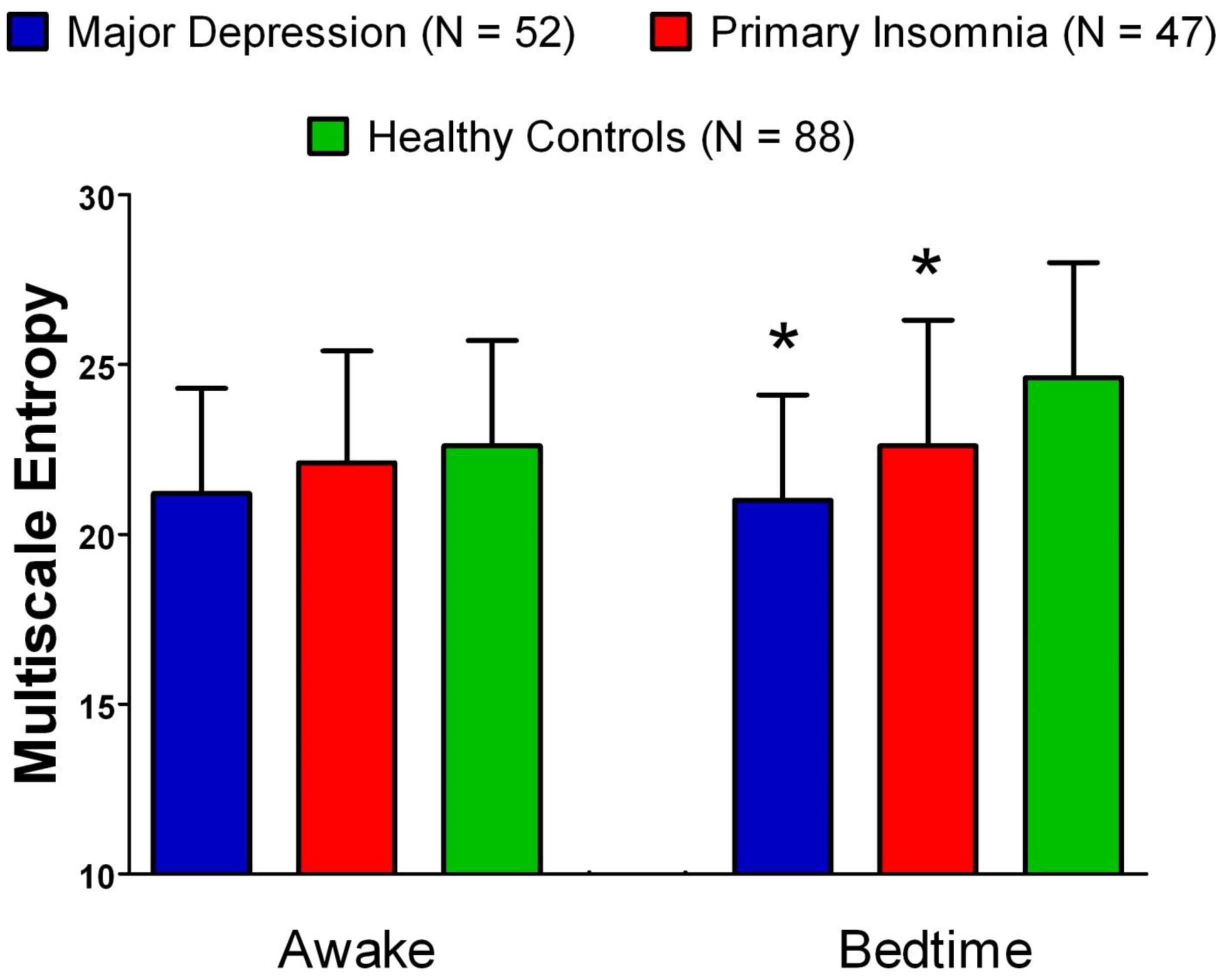
- Sympathetic activity
  - AW = REM = N1 > N2 > SWS

- Parasympathetic activity
  - SWS > N2 > N1 = REM = AW



Somers et al., 1993; Bonnet and Arand et al., 1998; M. de Zambotti et al., 2011

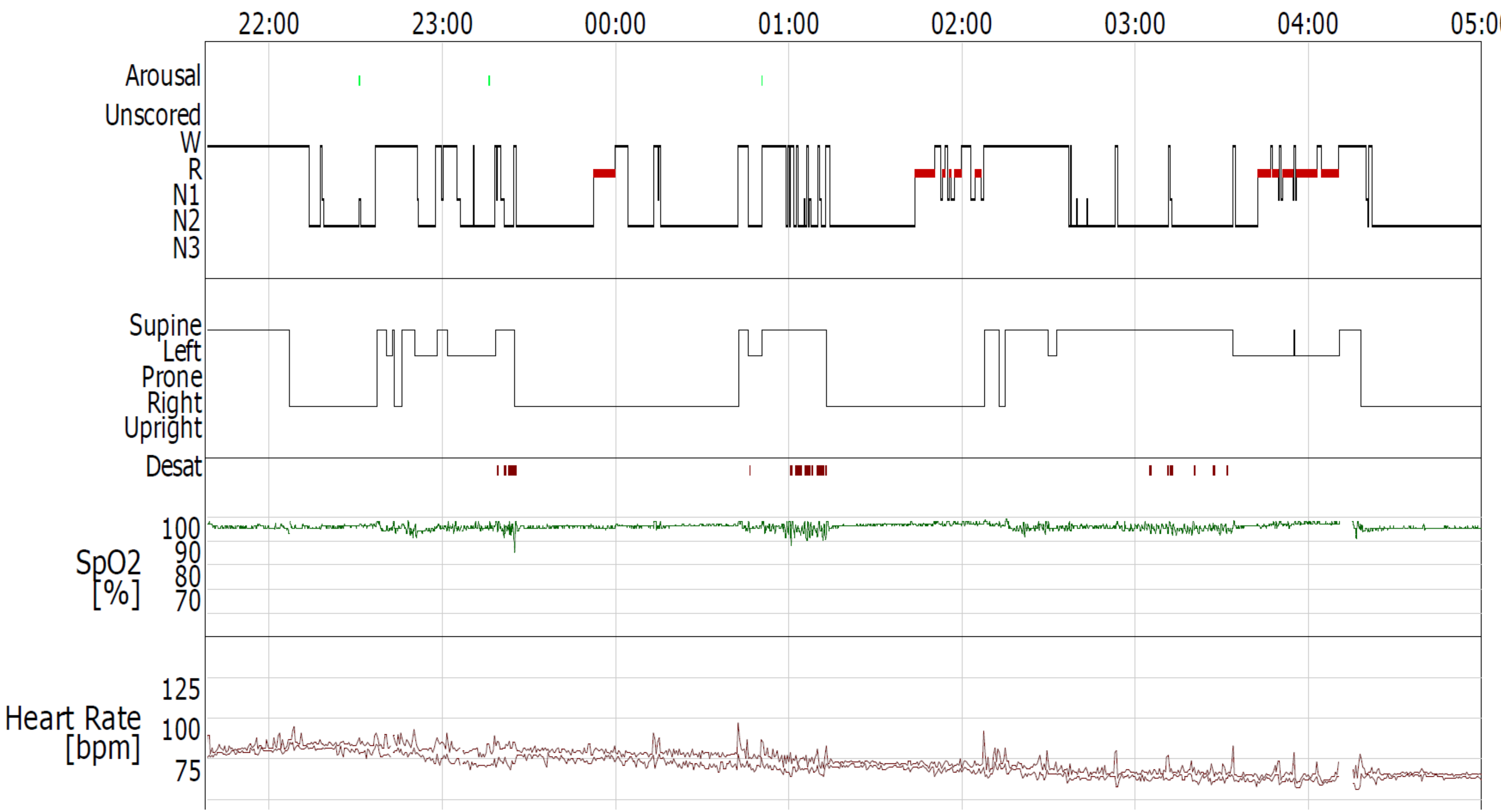
Disturbed Autonomic Regulation in Depression



Yang AC et al. **Journal of Affective Disorders** 2011;131:179-185

Good Sleeper

Poor Sleeper
(Major Depression)



Summary

- Sleep has an unique role in the pathophysiology of the depression.
- Disturbance in autonomic function is the key to understand the sleep disturbance associated with depression.