Miles to go before I sleep: Sleep problems in Rheumatic Diseases

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Overview

- Sleep
- Sleep Disorders in Rheumatic Diseases
  - Insomnias
  - Sleep-related breathing disorders
  - Sleep-related movement disorders
  - Circadian rhythm disorders
- Effect of Sleep on Inflammation and Pain
- Treating and Managing Sleep Problems

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What is Sleep?

- A period of reduced activity
- Associated with a typical posture, such as lying down with eyes closed
- Results in a decreased responsiveness to external stimuli
- A state that is relatively easy to reverse (distinguishes sleep from hibernation and coma)

"I don't think he's sleeping, I think he's faking."

http://healthysleep.med.harvard.edu

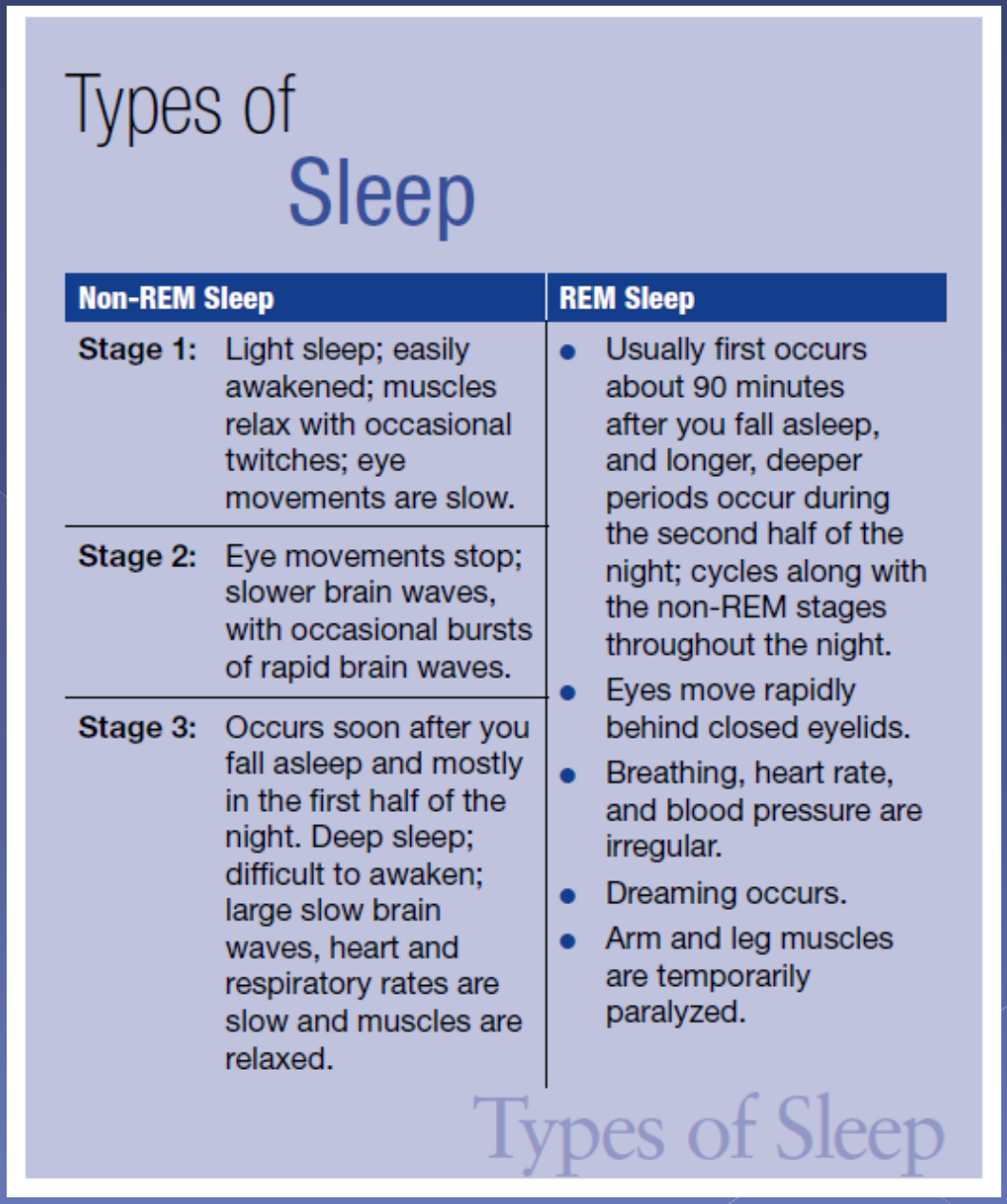
Sleep varies across different species but all animals sleep

- Sleep quantity
- Sleep postures
  - Standing
  - Curled up
  - Hanging upside down
- Decreased responsiveness
  - Unihemispheric sleep: One side of the brain sleeps while the other side is awake
    - Birds
    - Aquatic mammals

Species	Average Sleep Time (hrs/day)
Giraffe	1.9
Horse	2.9
Elephant	3.5
Cow	3.9
Goat	5.3
Pig	7.8
Dog	10.6
Cat	12.1
Brown bat	19.9

http://science.education.nih.gov/supplements/nih3/sleep/guide/info-sleep.htm

- Two basic types of sleep
  - Non-REM
  - REM
- Typically, sleep begins with non-REM sleep
- Sleep stages repeat as you sleep. REM stage becomes longer, and stage 3 sleep becomes shorter
- REM sleep stimulates the brain regions you use to learn and make memories



http://www.nhlbi.nih.gov/health/public/sleep/healthy_sleep.pdf

What is Sleep Deprivation?

- Don't get enough sleep
  - Amount of sleep varies, depending on individual and age
  - Over a lifespan, the amount of time we need to sleep declines
    - Newborn: 16-20 hrs/day
    - 1-4 yr old: 11-12 hrs/day
    - Adolescent: 9 hrs/day
    - Adults: 7-8 hrs/day

http://healthysleep.med.harvard.edu

What is Sleep Deficiency?

- Broader concept than sleep deprivation
- Includes:
  - Don't get enough sleep (sleep deprivation)
  - Have a sleep disorder that prevents getting enough sleep or causes poor sleep quality
  - Sleep at the wrong time of day
  - Not getting all the types of sleep your body needs

http://www.nhlbi.nih.gov/health/health-topics/topics/sdd/why.html

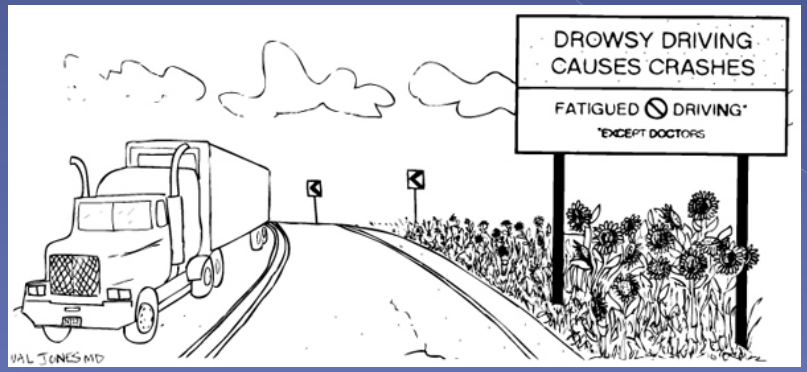
Sleep Deficiency

- 7 out of 10 adults experience problems that affect sleep quality
- Sleep problems are particularly prevalent among adult women
  - ½ report sleep disturbances during menstrual periods
  - ¾ report disturbed sleep during pregnancy
  - Many experience disrupted sleep during menopause (due to lower progesterone levels)
- Older adults are less able to maintain sleep

http://healthysleep.med.harvard.edu

Why is Sleep Important?

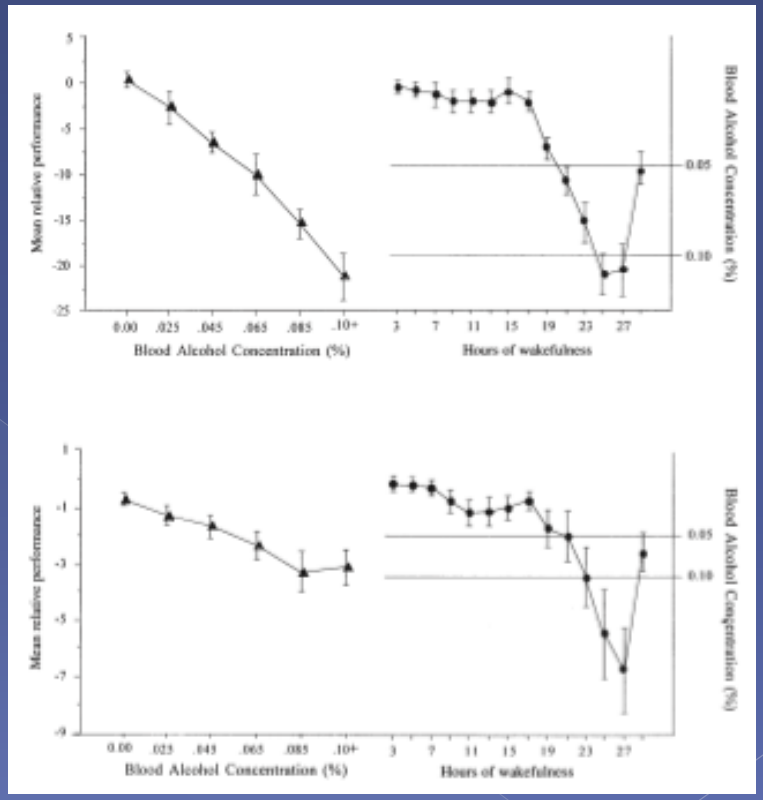
- After several nights of losing sleep (at a loss of just 1-2 hrs per night), function is impaired as much as not sleeping at all for 1-2 nights
- Per year, sleepiness is a factor in >100,000 car accidents, including 1,500 deaths



http://www.nhlbi.nih.gov/health/health-topics/topics/sdd/why.html

Why is Sleep Important?

- Sleep deficiency impairs driving ability as much as driving drunk
- Participants who had been awake 20-25 hrs performed similarly to participants with a blood alcohol level of 0.10



Lamond and Dawson. J Sleep Res, 1999.

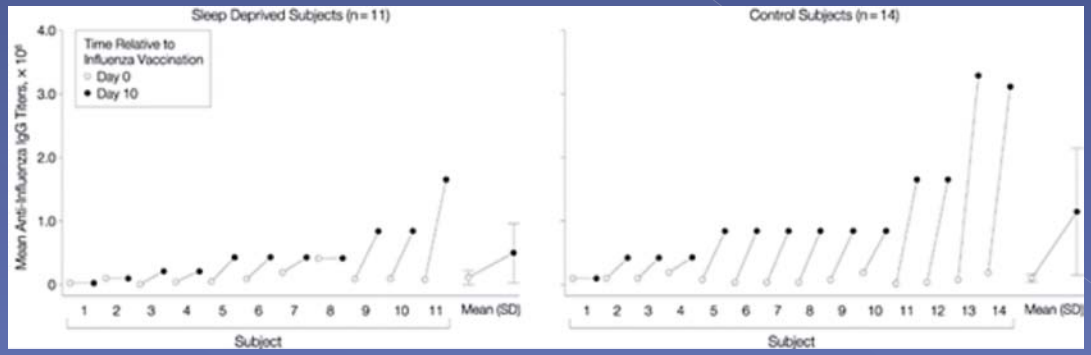
Why is Sleep Important?

- Physical Health
  - Obesity
    - Associated with higher ghrelin (makes you hungry) and lower leptin (makes you feel full) levels
  - Diabetes
    - Affects how your body reacts to insulin
  - Cardiovascular disease
    - Affects healing and repair of blood vessels and heart
  - Immune system
    - Decreases body's ability to fight infection

http://www.nhlbi.nih.gov/health/health-topics/topics/sdd/why.html

Effect of sleep deprivation on response to vaccination

- 25 healthy young men (mean age 23 yrs)
  - 11 sleep restricted to 4 hrs x 6 nights and then extended to 12 hrs x 7 nights for recovery
  - 14 continued usual sleep patterns (7.5-8.5 hrs/night)
  - All participants were vaccinated on day 5
  - Anti-influenza IgG antibodies were measured at 10 days after vaccination



Spiegel et al. JAMA, 2002.

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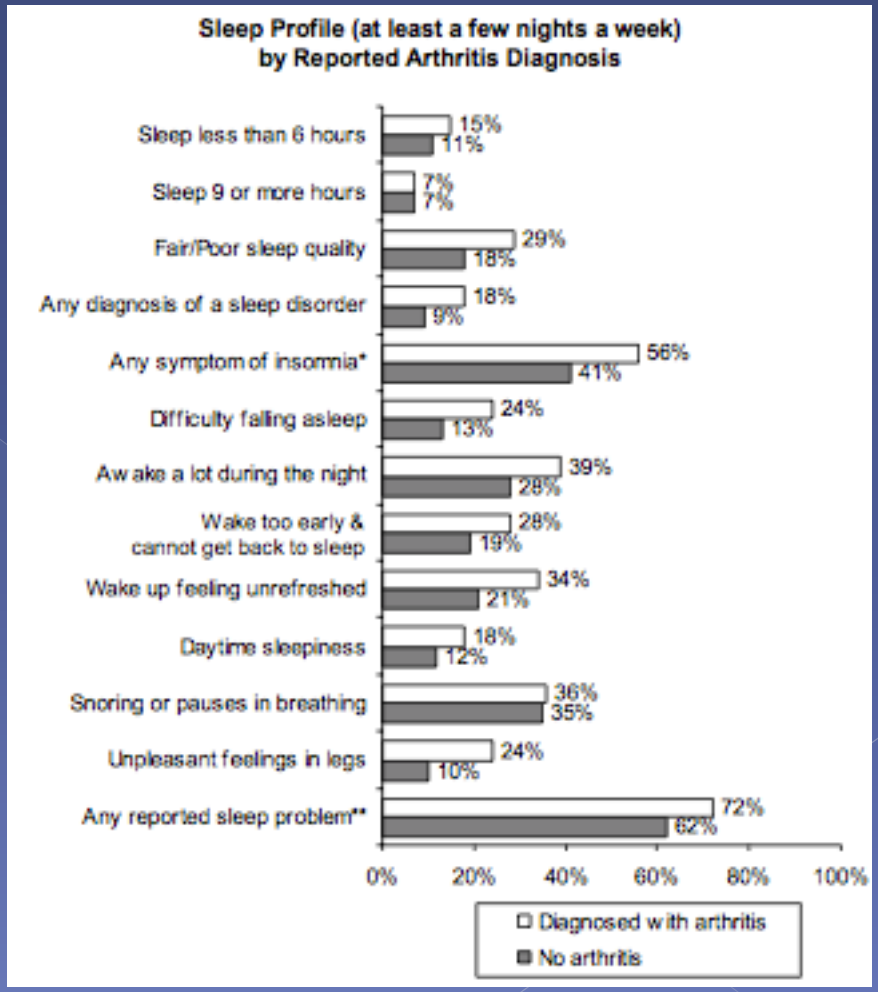
Categories of Sleep Disorders

- Insomnias
  - Disorders initiating and maintaining sleep
- Sleep-related breathing disorders
  - Obstructive sleep apnea
- Sleep-related movement disorders
  - Restless leg syndrome
- Circadian rhythm sleep disorders
  - Delayed or advanced sleep phase disorders

Buenaver LF and Smith MT. Curr Treatment Options Neurol 2007.

Insomnia in Arthritis Patients

- Older adults with arthritis are
  - More likely to report sleep problems (72% vs. 62%)
  - More likely to report insomnia (56% vs. 41%)
  - More likely to be awake during the night
  - Wake up feeling unrefreshed



2003 Sleep in America Poll

Insomnia in RA

- In a study of 145 RA patients, the most common sleep abnormality was sleep fragmentation
- The most common causes for sleep disturbance were
  - "Need to use the washroom" (51%)
  - "Pain" (33%)

Taylor-Gjevre et al. Musculoskeletal Care, 2011.

Insomnia in RA

- In a study of 41 RA patients and 19 controls evaluated by home sleep studies, RA pts
  - Greater difficulties falling asleep
    - Longer sleep latencies: 30.5 vs. 12.1 min
  - Worse quality of sleep
  - More non-restorative sleep
  - More daytime sleepiness

Drewes AM et al. Br J Rheumatol 1998.

Insomnia in Lupus

Determinants of Sleep Quality in Women With Systemic Lupus Erythematosus

DEBORAH DA COSTA, SASHA BERNATSKY, MARIA DRITSA, ANN E. CLARKE, KABERI DASGUPTA, ANAHITA KESHANI, AND CHRISTIAN PINEAU

- In a study of 100 female SLE patients who completed the Pittsburgh Sleep Quality Index:

Table 2. Pittsburgh Sleep Quality Index Scores in women with systemic lupus erythematosus (SLE)*

	SLE (n = 100)	Healthy controls† (n = 52)	Insomniacs† (n = 45)
Global score	6.98 ± 4.03‡	2.67 ± 1.70	10.38 ± 4.57
Component score			
Sleep quality	1.21 ± 0.80‡	0.35 ± 0.48	1.96 ± 0.93
Sleep latency	1.22 ± 1.15§	0.56 ± 0.73	1.42 ± 1.01
Sleep duration	0.93 ± 1.00‡	0.29 ± 0.50	1.51 ± 1.20
Sleep efficiency	0.63 ± 1.00‡	0.10 ± 0.30	1.47 ± 1.24
Sleep disturbance	1.51 ± 0.67§	1.00 ± 0.40	1.40 ± 0.62
Use of sleep medications	0.45 ± 0.98‡	0.04 ± 0.28	1.20 ± 1.31
Daytime dysfunction	1.15 ± 0.83‡	0.35 ± 0.48	1.42 ± 0.94

Insomnia in Lupus

- Depressed mood, prednisone use and lack of exercise may contribute to poor sleep quality in SLE

Table 4. Results of regression models predicting sleep quality*

	Model 1 Demographic		Model 2 Disease related		Model 3 Exercise		Model 4 Psychosocial		Full Model	
	Beta	*P*	Beta	*P*	Beta	*P*	Beta	*P*	Beta	*P*
Age	0.16	0.118	0.22	0.39	0.14	0.127	0.08	0.374	0.13	0.169
Education	−0.11	0.253	−0.02		0.05	0.609	0.01	0.922	0.06	0.484
Disease duration			−0.06						−0.01	0.964
SLICC/ACR-DI			0.07						0.05	0.649
SLAM-R			−0.02						−0.10	0.358
HAQ Index			0.39						0.17	0.190
Pain			−0.09						−0.12	0.296
Prednisone use			0.28						0.18	0.055
Exercise					−0.40	0.001			−0.17	0.088
CES-D							0.51	0.001	0.44	0.001
R^2	0.04		0.26		0.17		0.31		0.41	
Adjusted R^2	0.02		0.20		0.14		0.29		0.34	

Da Costa et al. Arthritis Rheum, 2005.

Sleep-Related Breathing Disorders

- Sleep apnea: disorders characterized by one or more pauses in breathing or shallow breaths when sleeping
  - Obstructive sleep apnea:
    - Most common cause of sleep apnea
    - Occurs when the airway collapses or becomes blocked during sleep

Taylor-Gjevre et al. Ther Adv Musculoskelet Dis, 2011
Iaboni A et al. J Rheumatol, 2006.

Do Rheumatoid Arthritis Patients Have a Higher Risk for Sleep Apnea?

STEPHANIE R. READING, CYNTHIA S. CROWSON, RICHARD J. RODEHEFFER, PATRICK D. FITZ-GIBBON, HILAL MARADIT-KREMERS, and SHERINE E. GABRIEL

- 23% of RA patients had a diagnosis of OSA
- 50% of RA patients were at high risk for sleep apnea
- This risk was significantly higher than controls (31%)

Table 1. Characteristics of study subjects with and without RA, and risk of sleep apnea. Values are number (%) unless otherwise indicated.

	Subjects		
	Non-RA, n = 328	RA, n = 164	p
Female	236 (72)	118 (72)	1.00
Age years, mean ± SD	64.0 ± 10.5	62.9 ± 12.2	0.31
Body mass index, kg/m^2, mean ± SD	28.2 ± 5.5	28.4 ± 5.5	0.62
High blood pressure	136 (42)	61 (37)	0.17
Smoking, current or former	138 (44)	76 (46)	0.64
Diagnosed with obstructive sleep apnea	31 (9)	23 (14)	0.13
Berlin Questionnaire Score			
High risk of sleep apnea	101 (31)	82 (50)	< 0.001
Low risk of sleep apnea	227 (69)	82 (50)	
Berlin Questionnaire Subscales			
Category 1: Snoring	144 (44)	80 (48)	0.31
Category 2: Fatigue	41 (13)	63 (38)	< 0.001
Category 3: Comorbidities	178 (54)	97 (59)	0.37

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- Compared to RA patients at low risk for sleep apnea, RA patients at high risk
  - More likely to be male
  - More likely to have high blood pressure
  - More likely to be overweight/obese

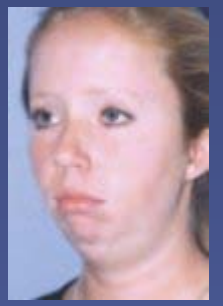
Table 2. Characteristics and risk factors according to risk of obstructive sleep apnea (OSA) in patients with RA. Values are number of patients (%) unless otherwise noted.

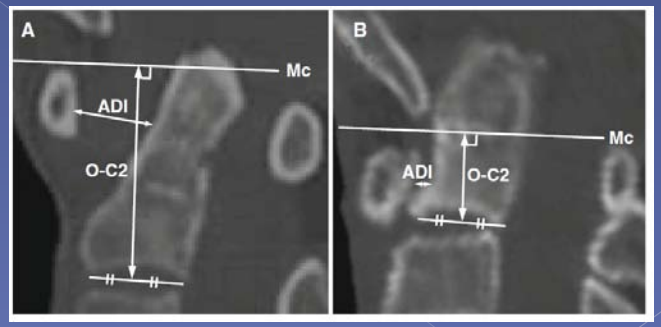
	Low Risk of Sleep Apnea, n = 82	High Risk of Sleep Apnea, n = 82	p
Female	68 (83)	50 (61)	0.002
Age, years, mean ± SD	62.6 ± 11.7	63.2 ± 12.8	0.74
High blood pressure	18 (22)	43 (52)	< 0.001
Smoking, current or former	33 (40)	43 (52)	0.12
Rheumatoid factor positive	55 (67)	55 (67)	1.00
Diagnosed with OSA	7 (9)	16 (20)	0.04
Treatment of OSA with CPAP	3 (4)	5 (6)	0.46
Body mass index (BMI)	26.7 ± 5.0	30.2 ± 5.4	< 0.001
Underweight, BMI ≤ 18.5 kg/m^2	3 (4)	4 (5)	0.70
Overweight, BMI ≥ 25 kg/m^2	45 (55)	63 (77)	0.003
Obese, BMI ≥ 30 kg/m^2	18 (22)	47 (57)	< 0.001

CPAP: continuous positive airway pressure.

Mechanisms of Sleep Apnea in Rheumatoid Arthritis

- Temporomandibular joint destruction
  - Retrognathia: (abnormal posterior positioning of the maxilla or mandible)
- Occipitocervical spine disease
  - Increased pressure on the soft tissues surrounding the airway
  - Compression of cranial nerves that control the airway dilator muscles





Alomoudi. Med Sci Monit, 2006.
Shoda et al. Eur Spine J, 2009.

Sleep-Related Breathing Disorders in Lupus

- Compared to healthy controls, SLE patients had significantly higher respiratory distress indices and lower minimum oxygen saturations

Table 2. Sleep-related respiratory abnormalities and movement in patients with SLE*

	RDI	SaO_2<90T	SaO_2<90I	SaO_2Min
SLE patients				
1	3.62	1.25	0.10	86.20
2	25.30	16.25	2.69	82.00
3	9.55	10.35	2.53	82.60
4	4.10	37.40	0.97	83.95
5	3.32	0.50	0.34	86.40
6	3.25	8.60	1.36	82.80
7	7.12	9.30	0.59	82.55
8	30.07	234.80	19.47	59.00
9	6.07	0.45	0.24	87.55
10	10.82	281.30	4.55	77.15
11	5.95	0.05	0.00	89.45
12	2.65	0.80	0.36	85.10
13	9.20	61.15	4.28	82.25
14	2.80	94.45	2.35	81.65
Mean ± SD	8.84 ± 8.46†	54.05 ± 91.13	2.84 ± 5.02	82.05 ± 7.29‡
Healthy controls				
Mean ± SD	1.89 ± 2.09	13.72 ± 45.32	0.44 ± 1.37	89.44 ± 3.38

Valencia-Flores et al. Arthritis Rheum, 1999.

Treatment for Sleep Apnea

- Controlling inflammatory disease
  - Pilot study of 8 obese, male RA patients, treated with etanercept, showed significant decrease in sleepiness and in the number of apneas/hypopneas per hour
- Behavioral changes
  - Sleeping on your side
  - Losing weight
  - Using an oral mouthpiece
- Continuous positive airway pressure (CPAP)
- Surgery
  - Total TMJ replacement
  - Occipito-cervical fusion

Vgontzas et al. J Clin Endocrinol Metab, 2004.
Ataka et al. Spine, 2010.
Mishima et al. Int J Oral Maxillofac Surg, 2003.

Sleep-Related Movement Disorders

- Restless leg syndrome:
  - An urge to move the legs
    - Usually accompanied by uncomfortable sensations in the legs
    - Any unpleasant sensations that worsen during periods of rest
    - Any unpleasant sensations that worsen at night

Gjevre and Taylor Gjevre. Autoimmune Diseases, 2013.

Risk for Restless Leg Syndrome

- Compared to a prevalence of 2-6% in controls, the prevalence of restless leg syndrome in RA is 20-35%
- RA confers a similar risk for restless leg syndrome as obesity, and higher risk than smoking and age ≥ 50 yrs

Table 2 Univariate and multivariate effects of variables on restless leg syndrome (RLS) in female patients ($n = 60$)

	Univariate (95 % CI)	Multivariate (95 % CI)
Age ≥ 50 years	1.62* (0.48, 5.23)	1.26* (0.53, 5.25)
Regular smoker	1.15* (0.35, 4.27)	1.24* (0.44, 7.54)
Obesity (BMI ≥ 30)	3.33* (0.98, 10.14)	5.41* (1.70, 21.6)
With RA (compared to control)	4.21* (1.12, 13.46)	5.61* (1.25, 24.87)

Ishaq et al. Modern Rheumatol, 2013.

Restless Leg Syndrome in RA

- Among RA patients, measures of increased disease activity are associated with greater risk for RLS

Demographic details and indices of disease activity and severity in RA patients with and without restless legs syndrome (RLS)

	RLS (n = 46)	RA controls (n = 41)
Male:female	8:38†	16:25
Age (yr)	61.1 ± 7.5	59.4 ± 11.7
Clinical indices:		
Duration of RA (yr)	14.8 ± 8.4	11.3 ± 10.2
Disease modifying therapy ever	n = 24	n = 14
Oral corticosteroid therapy ever	n = 22†	n = 10
Early morning stiffness (min)	57 ± 71	37 ± 54
Ritchie articular index	7.1 ± 3.9***	3.5 ± 2.5
Visual analogue score for pain	4.5 ± 2.0**	2.9 ± 2.0
Number of lower limb joints involved	2.6 ± 1.1***	1.3 ± 0.8
Steinbroker functional grade	1.3 ± 0.7	1.1 ± 0.4
Laboratory indices:		
Haemoglobin (g/dl)	11.6 ± 2.2***	14.5 ± 1.6
ESR (mm/h)	43 ± 30	33 ± 19
CRP (mg/l)	33 ± 39	18 ± 34
SCAT score‡	6.7 ± 3.9	6.4 ± 3.4
Serum ferritin (μg/l)	152 ± 414**	408 ± 241
Steinbroker radiologicl grade	2.8 ± 0.9*	2.3 ± 0.9*
Atlanto-axial subluxation >3 mm	n = 14†	n = 3

Reynolds et al. Br Med J, 1986.
Salih et al. Br J Rheumatol, 1994.

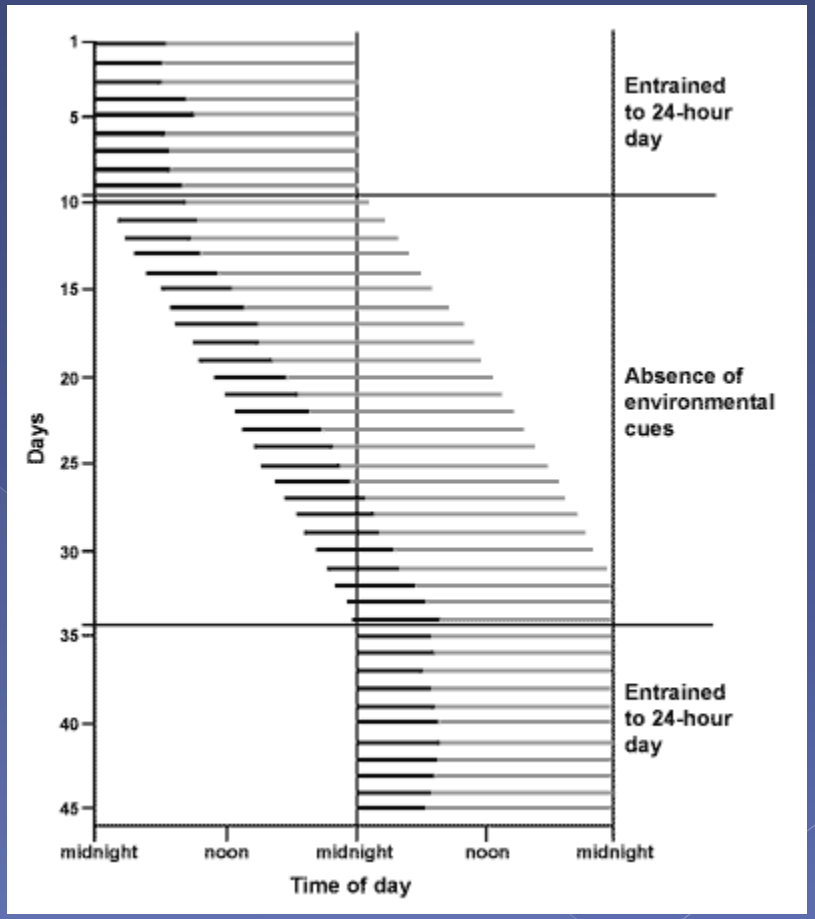
Treatment for Restless Leg Syndrome

- If mild/intermittent symptoms
  - Sleep hygiene
- If moderate/severe symptoms
  - Dopamine specific agent
    - Ropinrole
    - Pramipexole
  - Anticonvulsants
    - Gabapentin

Hening and Caivano. Semin Arthritis Rheum, 2008.

Circadian Rhythms

- Suprachiasmatic nucleus is the body's internal clock
- The body clock typically produces a 24+ hour rhythm, called the circadian rhythm
- When it gets dark, your body releases melatonin, which helps you feel drowsy
- As the sun rises, the body produces cortisol, which prepares you to wake up



Straub and Cutolo. Arthritis Rheum, 2007.

http://science.education.nih.gov/supplements/nih3/sleep/guide/info-sleep.htm

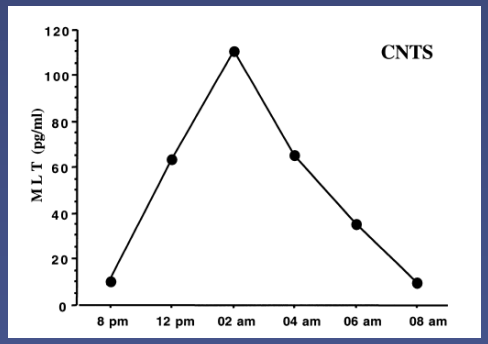
Circadian Rhythms in Rheumatic Diseases

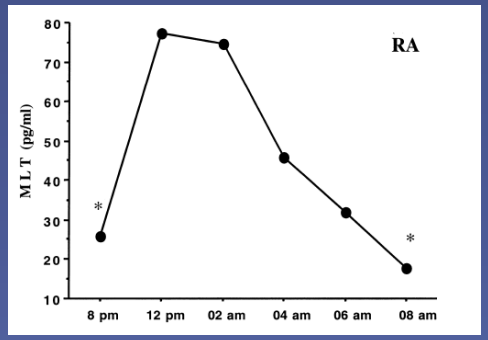
- Hormones involved in regulating the circadian rhythm may be dysregulated among RA patients with high disease activity
  - Melatonin
  - Cortisol

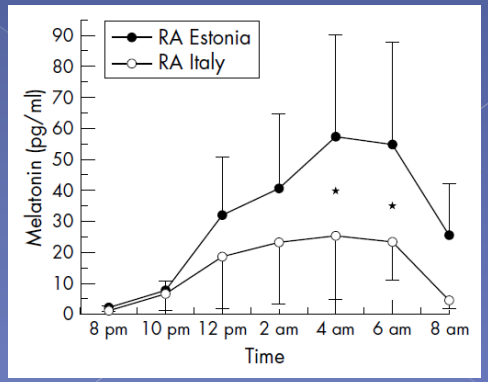
http://www.mhealthtalk.com/2012/04/how-light-affects-melatonin-and-sleep/

Circadian Rhythms in Rheumatic Diseases

- In healthy controls, melatonin levels increase ~ 8 pm, peak at 2 am, decrease until 8 am
- In RA patients, melatonin levels
  - Peak earlier (10-12 pm)
  - May be higher at the beginning & end of the night
- Among RA patients, melatonin levels may be affected by geography (light exposure)





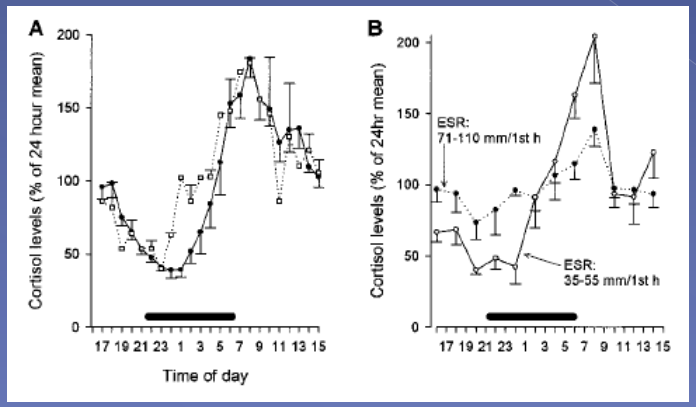


Straub and Cutolo. Arthritis Rheum, 2007.
Cutolo et al. Ann Rheum Dis, 2005.

Circadian Rhythms in Rheumatic Diseases

- In healthy controls (and RA patients with low disease activity), cortisol levels dip at midnight and peak at 8:00 am
- In RA patients with high levels of inflammation, there is flattening of the response curve

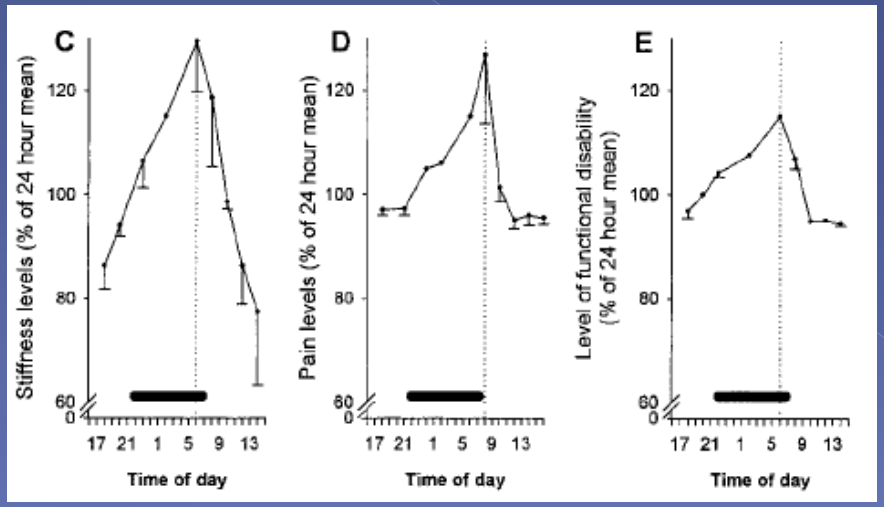
Healthy RA



Straub and Cutolo. Arthritis Rheum. 2007.

Circadian Rhythms in Rheumatic Diseases

- Variations in hormone levels may be associated with changes in disease symptoms during the day
  - Stiffness, pain levels and functional disability peak from 6 am-8 am, the time when the cortisol peak inappropriately flattens among RA pts with high disease activity



Straub and Cutolo. Arthritis Rheum, 2007

Circadian Rhythm Disorders in Other Chronic Diseases

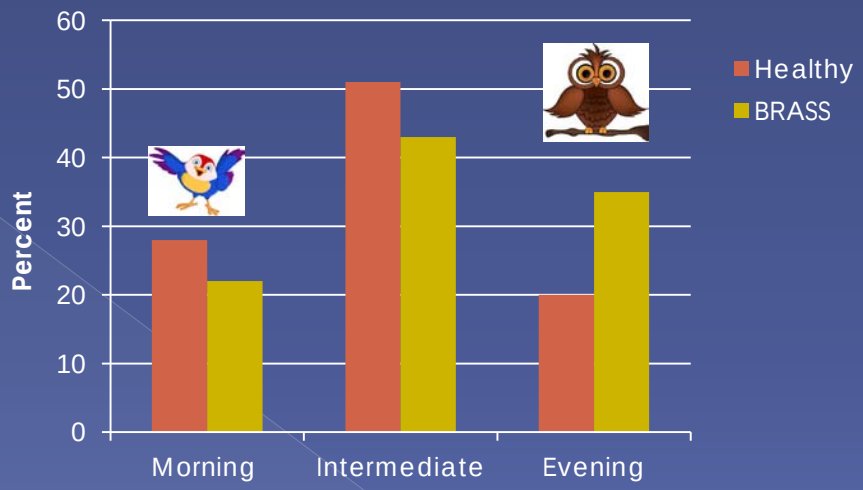
- Although there are data that circadian rhythm hormones are dysregulated in RA, there is no data about circadian rhythm sleep disorders in RA

Circadian Rhythm Sleep Disorders in RA (Larks vs. Owls)

- Phase 1:
  - Mailed Morningness-Eveningness Questionnaire to BRASS patients scoring high on the MOS Sleep Problems Index
  - 190 RA patients completed

Circadian Rhythm Sleep Disorders in RA (Larks vs. Owls)

- In BRASS,
  - 22% were morning
  - 43% were intermediate
  - 35% were evening
- Compared to reports of chronotypes in the literature
  - RA patients appear to be shifted towards evening



Circadian Rhythm Sleep Disorders in RA (Larks vs. Owls)

	Morning	Intermediate	Evening
DAS28-CRP	3.0 (1.2)	3.1 (1.4)	3.1 (1.4)
Tender joint count	3.4 (5.5)	4.4 (6.0)	4.5 (5.4)
Swollen joint count	3.1 (4.9)	3.5 (5.1)	3.3 (4.4)
Sleep problems index	39.0 (12.7)*,†	44.8 (16.4)	45.7 (15.3)
Mental health index (0-100; higher numbers = better mental health)	78.1 (14.6)†	71.1 (18.0)	69.3 (17.0)
MDHAQ anxiety (0-3; higher numbers = more anxiety)	0.5 (0.7)	0.6 (0.7)	0.6 (0.6)
MDHAQ depression (0-3; higher numbers = more depression)	0.4 (0.6)	0.4 (0.6)	0.6 (0.6)

* $P < 0.05$ when compared to intermediate category

† $P < 0.05$ when compared to evening category

Circadian Rhythm Sleep Disorders in RA (Larks vs. Owls)

- Phase 2:
  - 1-week sleep diary
  - 27 participants have completed
  - Need 73 more patients to complete

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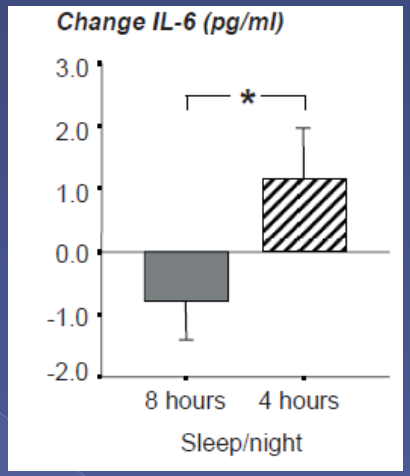
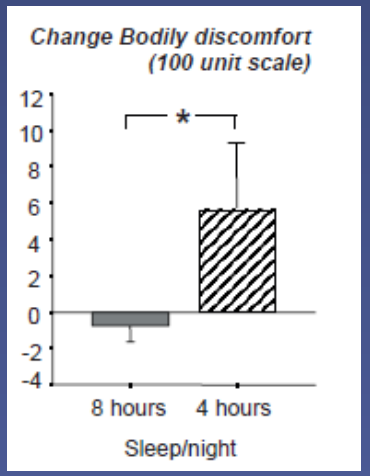
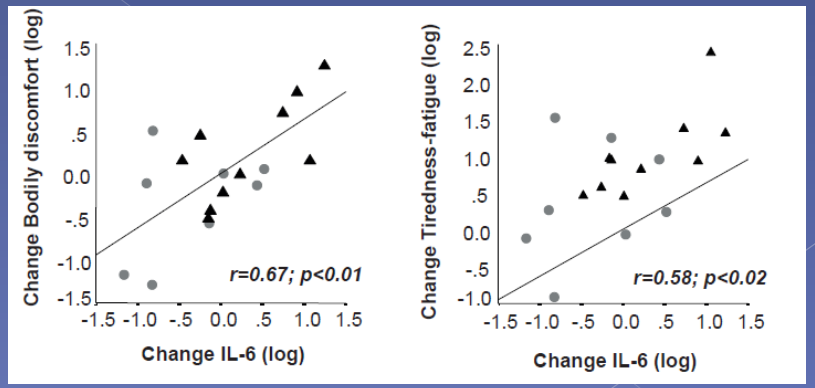
- Effect of Sleep on Inflammation and Pain
- Treating and Managing Sleep Problems

Impact of Sleep on Inflammation

- Compared to participants sleeping 8 hrs/night x 12 nights, participants sleeping 4 hrs/night x 12 nights had significantly greater:
  - Increases in IL-6
  - Increases in bodily discomfort
  - Increases in fatigue
- Changes in IL-6 were significantly associated with:
  - Changes in bodily discomfort
  - Changes in fatigue



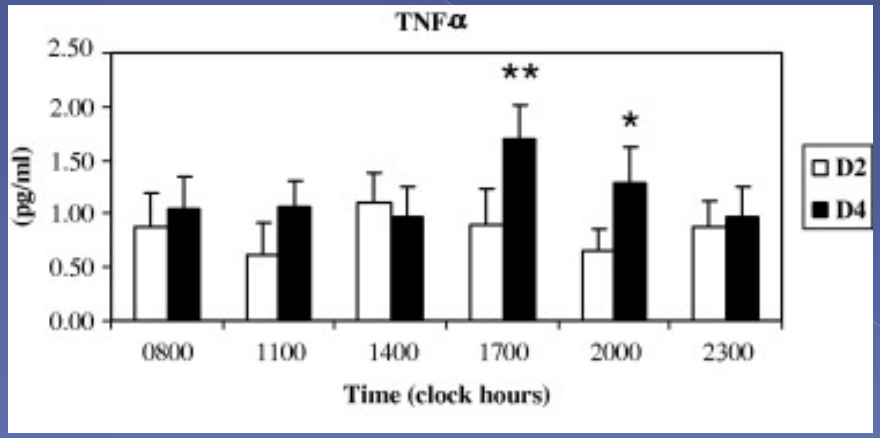




Haack et al. Sleep, 2007.

Impact of Sleep on Inflammation

- Among 12 healthy men, 34-37 hours of sleep deprivation was associated with an increase in TNF-alpha levels



Chennaoui et al. Cytokine, 2011.

Impact of Sleep on Pain:
Data from BWH

ARTHRITIS & RHEUMATISM
Vol. 65, No. 1, January 2013, pp 59–68
DOI 10.1002/art.37733

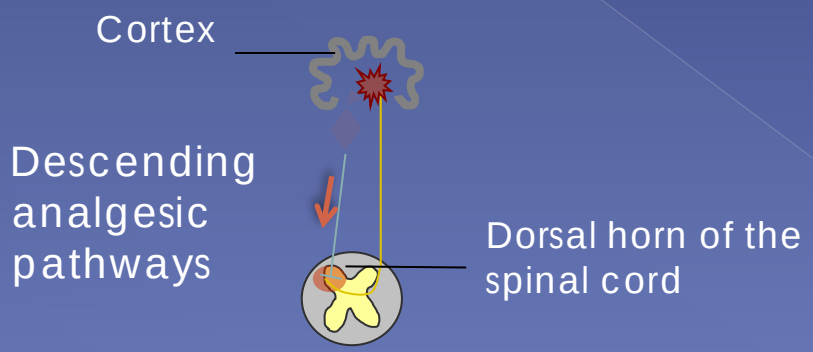
The Role of Sleep Problems in Central Pain Processing in Rheumatoid Arthritis

Yvonne C. Lee,[1] Bing Lu,[1] Robert R. Edwards,[1] Ajay D. Wasan,[1] Nicholas J. Nassikas,[1] Daniel J. Clauw,[2] Daniel H. Solomon,[1] and Elizabeth W. Karlson[1]

- Objective:
  - To examine central pain processing mechanisms among RA patients compared to healthy controls
  - To examine the role of sleep problems in mediating abnormalities in central pain processing

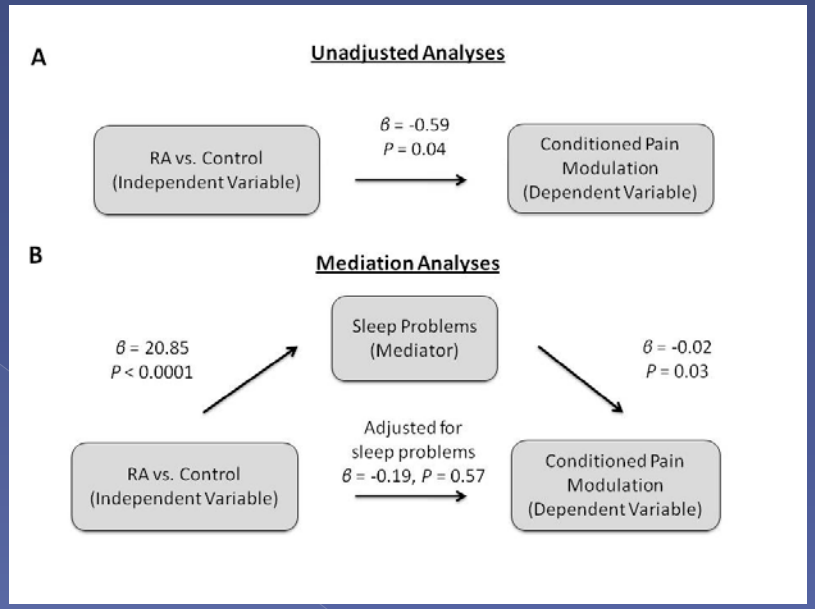
Impact of Sleep on Pain:

- 58 female RA patients and 54 healthy controls
- Completed questionnaires about pain and sleep
- Underwent experimental pain testing to assess central pain processing
  - Conditioned pain modulation (CPM): a measure of the descending analgesic pathways



Impact of Sleep on Pain: Data from BWH

- The diagnosis of RA was significantly associated with deficits in conditioned pain modulation
  - Impairments in central pain processing
- The diagnosis of RA was significantly associated with sleep problems
- Sleep problems were associated with impaired conditioned pain modulation



- Sleep problems may mediate the association between RA and impaired conditioned pain modulation → highlighting the importance of addressing sleep problems in RA

Overview

- Sleep
- Sleep Disorders in Rheumatic Diseases
  - Insomnias
  - Sleep-related breathing disorders
  - Sleep-related movement disorders
  - Circadian rhythm disorders
- Effect of Sleep on Inflammation and Pain
- Treating and Managing Sleep Problems

Effect of Disease Treatment on Sleep in RA

Effect of the first infliximab infusion on sleep and alertness in patients with active rheumatoid arthritis

C Zamarrón, F Maceiras, A Mera, J J Gómez-Reino

Ann Rheum Dis 2004;**63**:88–90. doi: 10.1136/ard.2003.007831

- Six female RA patients, starting infliximab
- Sleep studies on the night before infliximab infusion and the night after infliximab infusion
- Physical examination, questionnaires on the morning before infliximab infusion and the morning after infliximab infusion

Effect of the first infliximab infusion on sleep and alertness in patients with active rheumatoid arthritis

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Table 1 Clinical characteristics of six patients with RA before and after treatment with infliximab

		Tender joints (n)		Swollen joints (n)		Morning stiffness (min)		
Patient	Age (years)	Day 1	Day 2	Day 1	Day 2	Day 1	Day 2	ESR (mm/1st h)
1	65	21	20	19	17	60	45	30
2	42	19	21	15	11	120	90	55
3	32	16	16	14	13	120	120	34
4	62	24	21	16	16	180	180	37
5	52	23	22	13	14	240	240	43
6	71	20	20	14	13	180	180	36
Median (IR)	57 (17)	20.5 (4)	20.5 (1)	15 (2)	13.5 (4)	150 (60)	150 (90)	38.5 (9)

ESR, erythrocyte sedimentation rate.
Day 1 = morning before infliximab infusion; day 2 = morning after infliximab infusion.

Table 2 Sleep parameters of the six patients with RA before and after treatment with infliximab

	Sleep latency (min)		REM* latency (min)		Sleep efficiency (%)		Phase I+II (%)		Phase III+IV (%)		REM (%)	
Patient	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post	Pre	Post
1	97	3	186	73	36	86	83	30	7	55	10	15
2	172	36	–	134	39	70	94	37	6	52	0	11
3	197	24	–	288	32	58	84	61	16	22	0	7
4	58	38	–	106	58	68	88	58	12	30	0	12
5	32	13	113	61	55	93	80	51	4	32	16	17
6	24	27	336	85	67	80	80	88	16	6	4	6
Median IR)	77.5 (150)	25.5 (23)	–	–	44 (22)	75 (18)	83.5 (8)	54.5 (24)	9.5 (10)	31 (30)	2 (10)	11.5 (8)

Pre = the night before infliximab infusion; post = the night after the infliximab infusion.

Effect of the first infliximab infusion on sleep and alertness in patients with active rheumatoid arthritis

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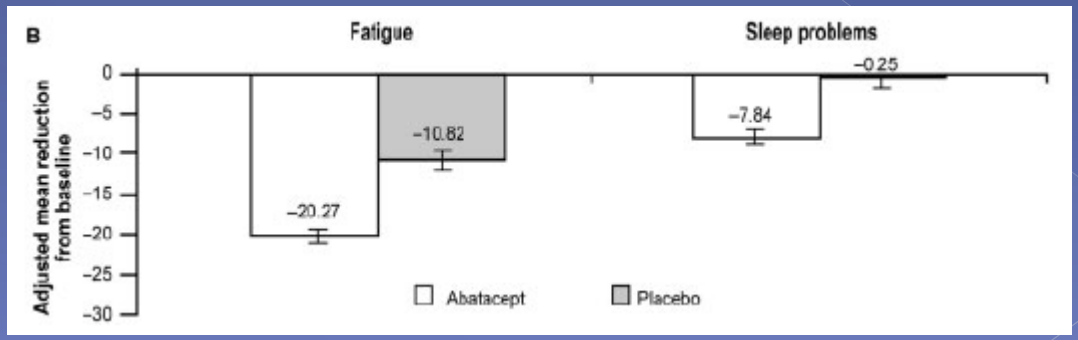
- Sleep improves soon after infliximab infusion, before measures of disease activity improve
- Sleep improvement may not solely be due to improvements in joint discomfort, but possibly through an alternative pathway
- Limitations: Very small study with limited follow-up

Effect of Disease Treatment on Sleep in Lupus

The Efficacy and Safety of Abatacept in Patients With Non–Life-Threatening Manifestations of Systemic Lupus Erythematosus

Results of a Twelve-Month, Multicenter, Exploratory, Phase IIb, Randomized, Double-Blind, Placebo-Controlled Trial

- 118 SLE patients randomized to abatacept and 57 to placebo



Merrill et al. Arthritis Rheum, 2010.

12 Tips to Improve Sleep

1. Avoid caffeine, alcohol and nicotine for 6-8 hrs before bedtime
2. Exercise early
   - Finish exercising at least 3 hrs before bed
3. Nap early (or not at all)
   - Late-day naps decrease sleep drive. If you must nap, keep it short and before 3 pm

http://healthysleep.med.harvard.edu

12 Tips to improve Sleep

4. Lighten up on evening meals
   - Finish dinner several hours before bedtime
   - Avoid foods that cause indigestion
5. Balance fluid intake
   - Drink enough to keep from waking up thirsty (but not enough to be awakened by need to go to the bathroom)
6. Keep your internal clock set with a consistent sleep schedule
   - Keep weekend schedule close to weekday schedule

http://healthysleep.med.harvard.edu

12 Tips to improve Sleep

7. Use light to strengthen your internal clock
   - Let light in first thing in the morning
   - Get out of the office for a 30-min sun break during the day
8. Turn your bedroom into a sleep-inducing environment
   - Quiet: ear plugs, “white noise”
   - Dark: heavy curtains, blackout shades, eye mask
   - Cold: 60-75°F
9. Establish a soothing pre-sleep routine
   - 1-hr before bed, take a bath, read a book, watch TV, practice relaxation exercises

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12 Tips to Improve Sleep

10. Go to sleep when you are truly tired
    - If you're not asleep after 20 min, get out of bed and do something relaxing until you are sleepy enough to go to bed

11. Don't be a nighttime clock-watcher

12. Follow through

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