

SLEEP DISORDERS IN PSYCHIATRY

György Purebl MD PhD

Associate professor



SEMMELWEIS University

Faculty of Medicine

Institute of Behavioural Sciences

<http://semmelweis.hu>

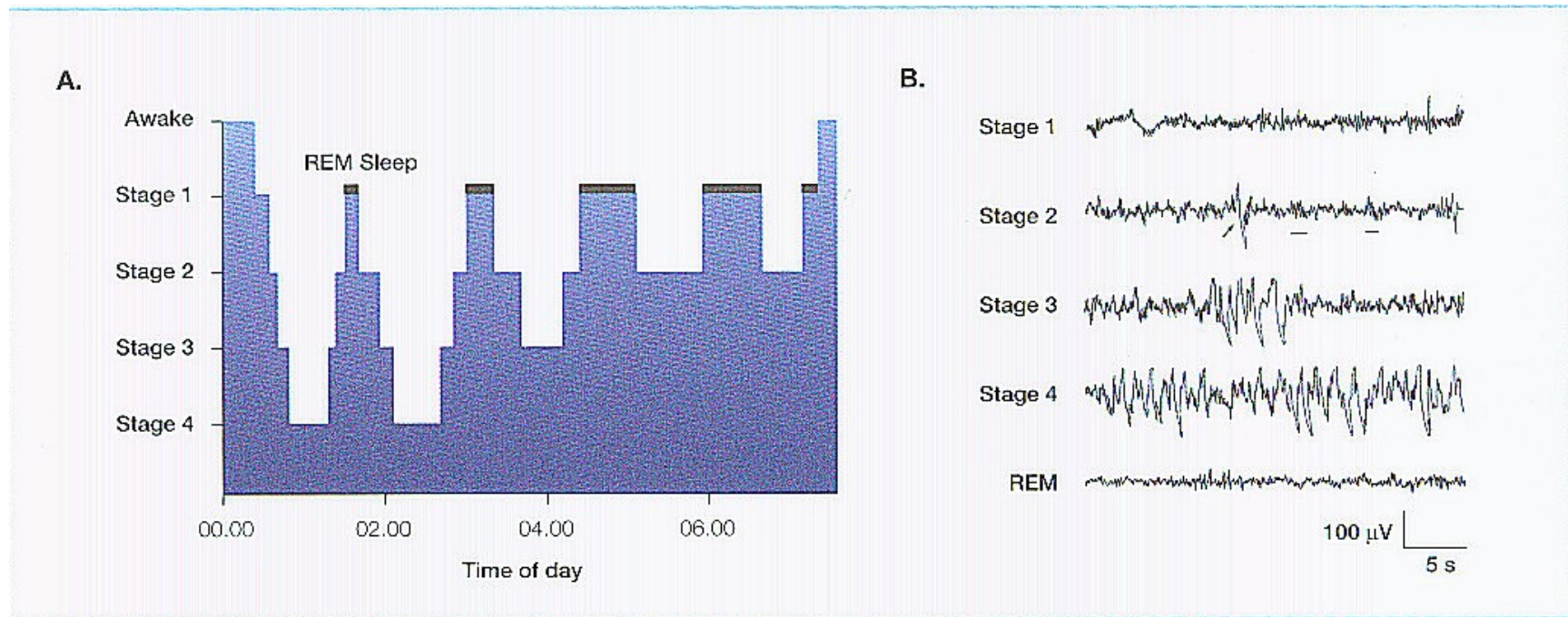


Figure 1. Sleep stages: A. Hypnogram and B. Electroencephalogram. Adapted with permission from Carskadon and Dement⁷ and Kandel et al.⁹

2017. Milestones in Sleep Medicine

- The Nobel Prize in Physiology or Medicine for the discoveries of molecular mechanisms of circadian rhythm (JC Hall, M Rosbash, MW. Young)
- New guidelines for the treatment of insomnia (AASM, ESRS)
- ICD11 preliminary version launched

ICD-11 Beta Draft (Foundation)

Search



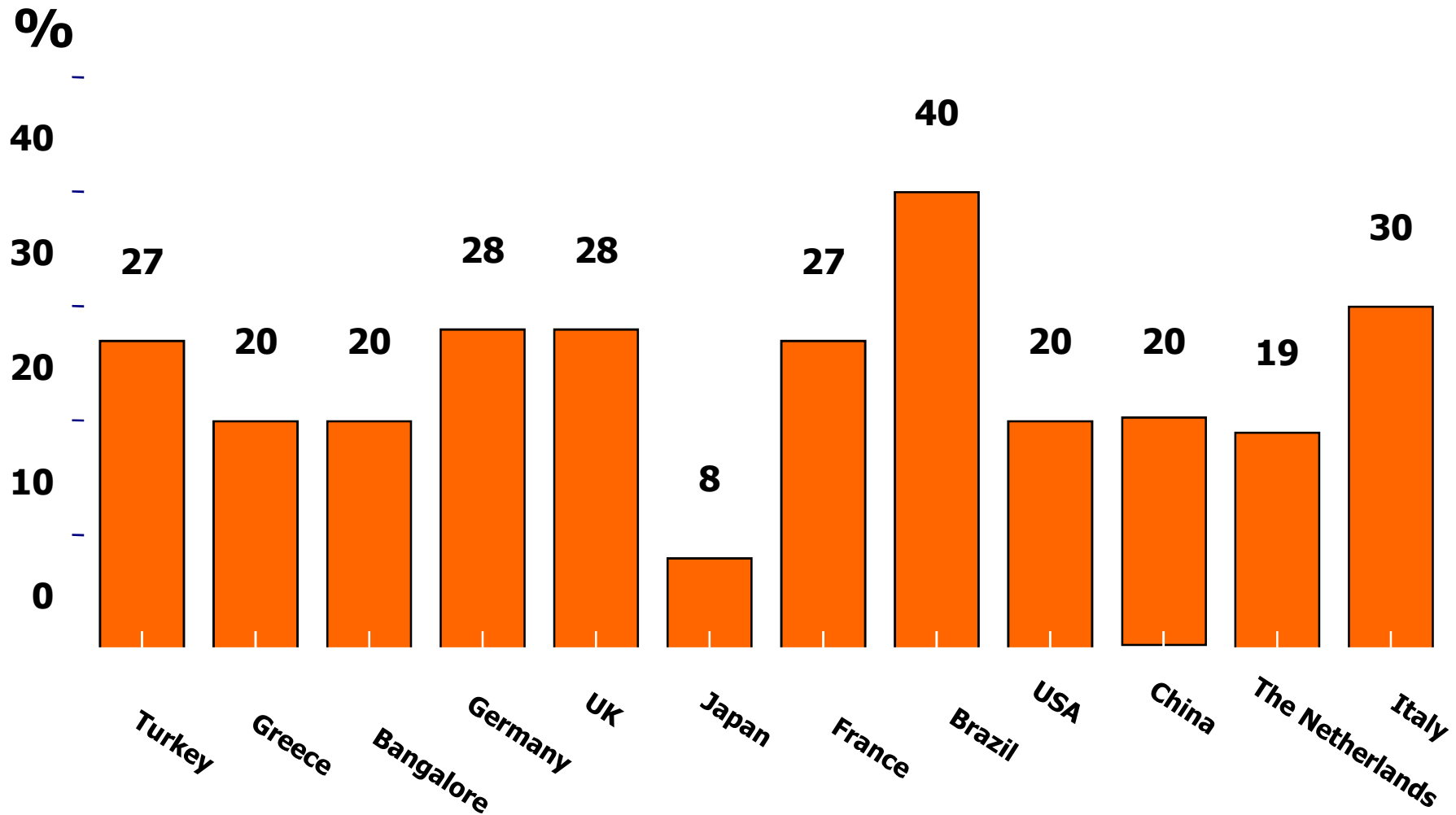
▼ ICD-11 Beta Draft



- ▶ Certain infectious or parasitic diseases
- ▶ Neoplasms
- ▶ Diseases of the blood or blood-forming organs
- ▶ Diseases of the immune system
- ▶ Endocrine, nutritional or metabolic diseases
- ▶ Mental or behavioural disorders
- ▶ Sleep-wake disorders
- ▶ Diseases of the nervous system
- ▶ Diseases of the eye or ocular adnexa
- ▶ Diseases of the ear or mastoid process
- ▶ Diseases of the circulatory system
- ▶ Diseases of the respiratory system
- ▶ Diseases of the digestive system
- ▶ Diseases of the skin
- ▶ Diseases of the musculoskeletal system or connective tissue
- ▶ Diseases of the genitourinary system
- ▶ Conditions related to sexual health
- ▶ Pregnancy, childbirth or the puerperium
- ▶ Certain conditions originating in the perinatal or neonatal period

Insomnia

WHO Collaborative Survey at Primary Care Level (Ustun es Sartorius 1995)



Sleep = passivity

Sleep = rest

Sleep= tranquillity

- ❖ Active and intensive biological process
- ❖ Different processes with different functions
- ❖ Sleep is vital

Sleep-phase functions

NREM-LHA

- ❖ Development
- ❖ Reconstruction
- ❖ Energy restoration (ATP)
- ❖ Immune regulation
- ❖ Memory-consolidation

REM

- ❖ Memory-consolidation and learning
- ❖ Pszichological well-being
- ❖ Affective learning
- ❖ Motivation
- ❖ Coping with stress
- ❖ Mood regulation

Disturbed sleep leads to psychological and physiological dysfunctions

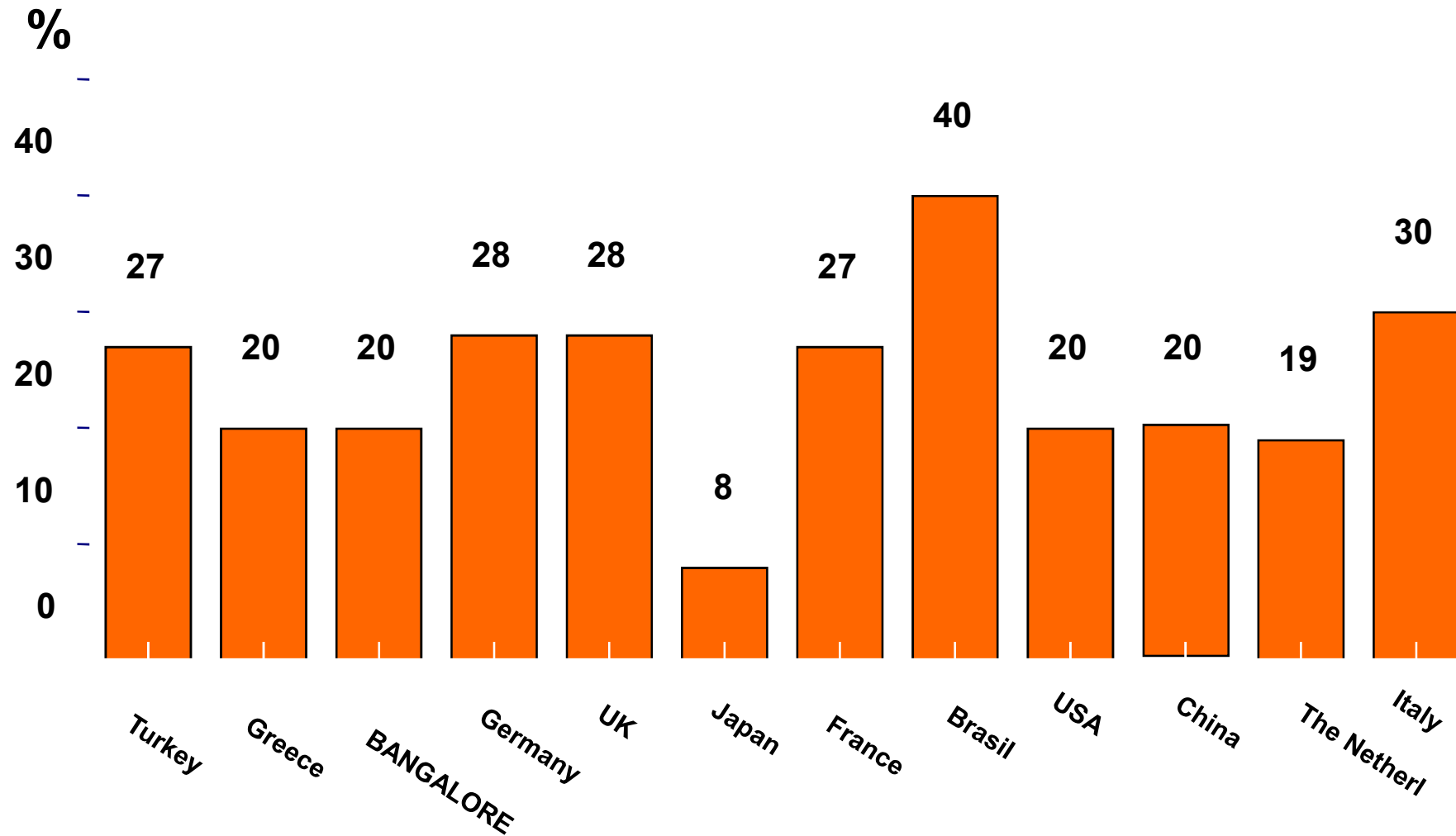
- Impaired mood regulation
- Increased stress-alertness
- ❖ 5H_{1A} attenuation
- ❖ Impaired hippocampal neurogenesis
- ❖ Severe psychopathological symptoms
 - ❖ Metabolic crisis, death
- ❖ Insulin resistance
- ❖ Impaired immunological fitness
- ❖ Increased cortisol-level
- ❖ Disturbed GH secretion

New bunch of disorders in the XXth Century

- ❖ Obesity
- ❖ Lipid and cholesterol problems
- ❖ Type 2 diabetes
- ❖ CHD
- ❖ Depression
- ❖ Anxiety and stress-related disorders
- ❖ Insomnia and circadian rhythm disorders

Insomnia amongst top 10 health complaint in XX. Century WHO Collaborative

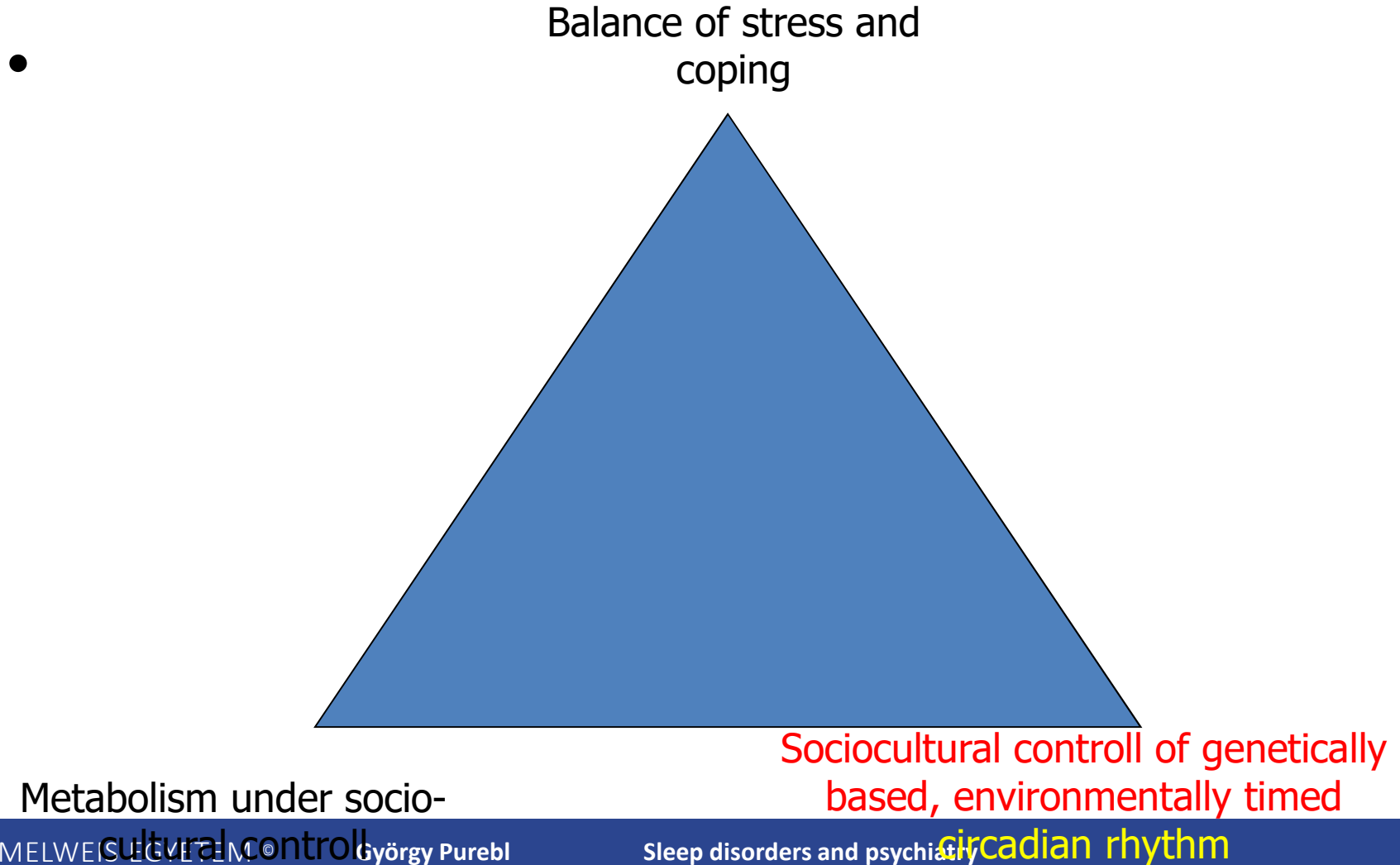
Survey at Primary Care Level (Ustun es Sartorius 1995)



No change in

- Chronotype
- Circadian rhythm
- Ultradian rhythms (pl. sleep-wake cycle, sleep architect)

Civilisational challenges



Sleep, circadian rhythms and biological clocks

- ❖ Daily oscillation of metabolic, physiological processes and behaviour
- ❖ Thermoregulation independent
- ❖ Under genetic control, but
- ❖ Timed by environmental stimuli (**zeitgebers**)
- ❖ SCN as „master clock”

Circadian rhythm

- Little more than 24 hrs (individual differences!)
 - Genetically encoded (CLOCK, Bmal, per, cry etc. genes)
 - Suprachiasmatic nucleus (SCN) as „master clock”
 - ❖ Controls many homeostatic processes (sleep, metabolism, activity etc)
- The internal clock is losing track (more than 24 hrs) therefore needs **resynchronisation**
- ❖ Specific stimuli act as resynchronizing **zeitgebers**
- ❖ Stimuli with non-appropriate timing could disturb the rhythm - **desynchronisation**

Zeitgebers

❖ Light/darkness

❖ Exercise

❖ Social activity

❖ Eating

Cultural effects on the Zeitgebers

- ❖ Light pollution/shortage of light
- ❖ „Conquest of night”
- Irregular work
- ❖ Lack of exercise
- ❖ Psychoactives

Sleep disorders

- Insomnia
- Circadian rhythm disorders*
- Sleep and movement related sleep disorders
- Parasomnias
- Hypersomnia
- Narcolepsia
- Etc



Hypersomnia

Depression

OSAS/UARS

Infections

Etc

Narcolepsia

Kataplexy

Seep attacks

Sleep paralysis

hypnagogic hallucinations

Th: stimulants (modafinil)

orexinergic agents

Breathing related sleep disorders

OSAS (Obstructive
Sleep Apnea
Syndrome)

- Obstruction
- Hypoxia
- Apnea

CSAS

- Lack of SWS – severe sleep deficit

UARS (Upper Airway
Resistance
Syndrome)

- Sympathetic hyperactivity

Risk factors

- Obesity
- Hypertension
- Diabetes
- Mandible anatomy
- Chr. adenoiditis

Consequences

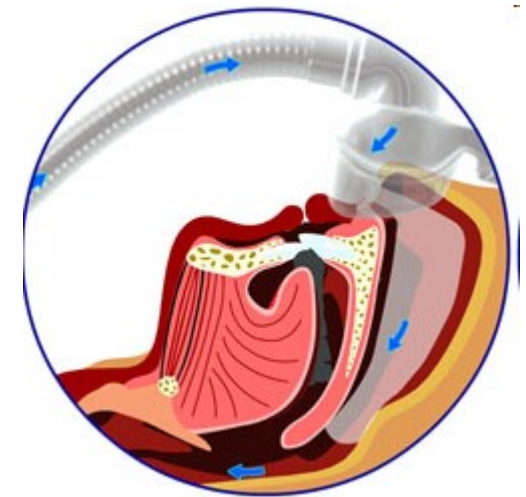
- Arrhythmias
- Hypertension
- **Dementia**
- **Depression**
- Diabetes
- Sudden death

Therapy

Lifestyle

Surgical

CPAP



Movement related sleep disorders

- Restless leg syndrome (RLS)
- Th:
 - ❖ Dopamin agonists (pergolid, pramipexol)
 - ❖ Pain management agents (gabapentin, opioids*)
- Periodic Limb Movement Disorder (PLMD) Th:
 - ❖ Dopamin agonists (pergolid, pramipexol)
 - ❖ Muscle-relaxants (clonazepam, baclofen)
 - ❖ Anti-seizure drugs (gabapentin)

Parasomnias

- Sleepwalking
 - Sleep terror
 - Nightmare disorder
 - **REM behaviour disorder** – the exception!
- Mainly in childhood frequency decreasing with age
 - No adverse consequences in most of the cases
 - Possible genetic background
 - Diff. Dg.: Epilepsy!
 - Th: Sleep hygiene, chorotherapy, supportive psychotherapy

REM Behaviour Disorder

- Later ages
- Frequently violent behaviour
- In REM-phase

- Early sign of degenerative CNS disorders!

- **Th**: REM suppression, underlying condition

Insomnia one of the top health complaint

- ❖ 1/3 of the adult population has transient/chronic sleep complaints
- ❖ 9-10% has chronic insomnia
- ❖ Frequency increasing with age

Nau és mtsai (2005). In: Carney PR, Berry RB, Geyxer JD (eds): Clinical sleep disorders.
Ohayon M. (1996). Sleep. 19:S7–S15
Novak és mtsai (2004). J Psychosom Res. 56(5):527-36.

The insomnia syndrome

- ❖ Difficulty of falling asleep
- ❖ Difficulty in the maintenance of sleep/early morning awakening
- ❖ Non restorative sleep
- ❖ Consecutive daytime consequences

The International Classification of Sleep Disorders. Diagnostic and coding manual. Second Edition. 2005.

American Academy of Sleep Medicine. Westchester IL

SEMMELWEIS EGYETEM ©

György Purebl

Sleep disorders and psychiatry

<http://semmelweis.hu>

The severity of insomnia is determined by daily symptoms **only**

❖ Irritability

❖ Fatigue

❖ Low mood

❖ Anxiety

❖ Memory/learning difficulties

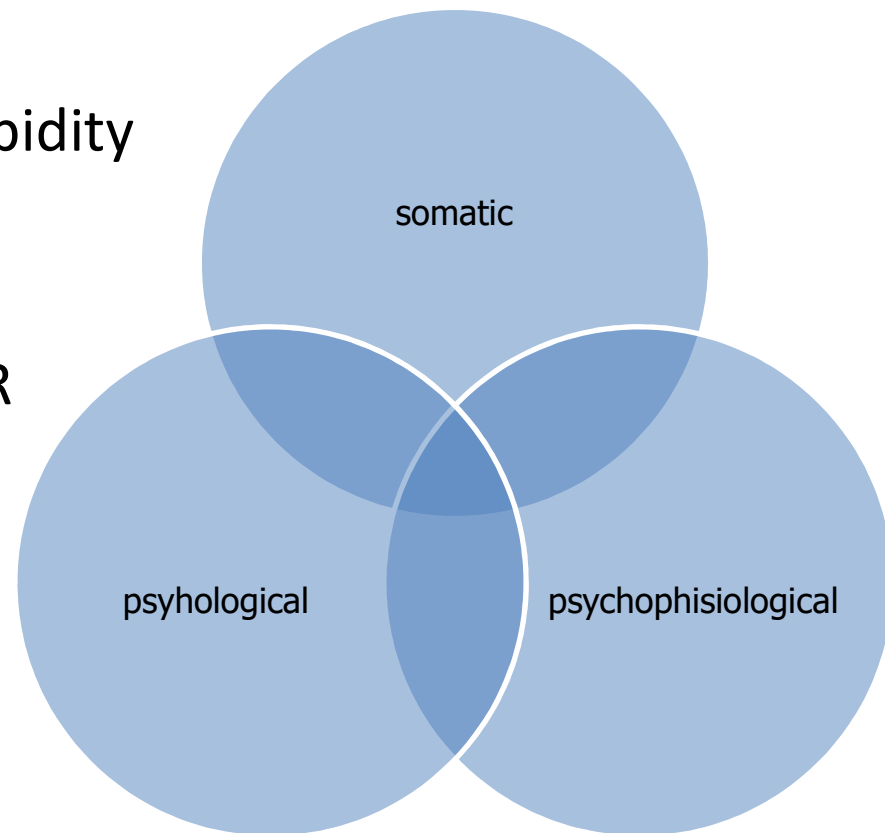
Decreased concentration and reaction time

Risk of home/workplace/traffic accidents

The International Classification of Sleep Disorders. Diagnostic and coding manual. Third Edition. 2013.
American Academy of Sleep Medicine. Westchester IL

Primary (psychophysiological) or comorbid insomnia?

- cc. 50% psychiatric comorbidity
- Cc. 50% other medical comorbidity
- Kb 25% psychophysiological
 - Irregular lifestyle, disturbed CR
 - Stress

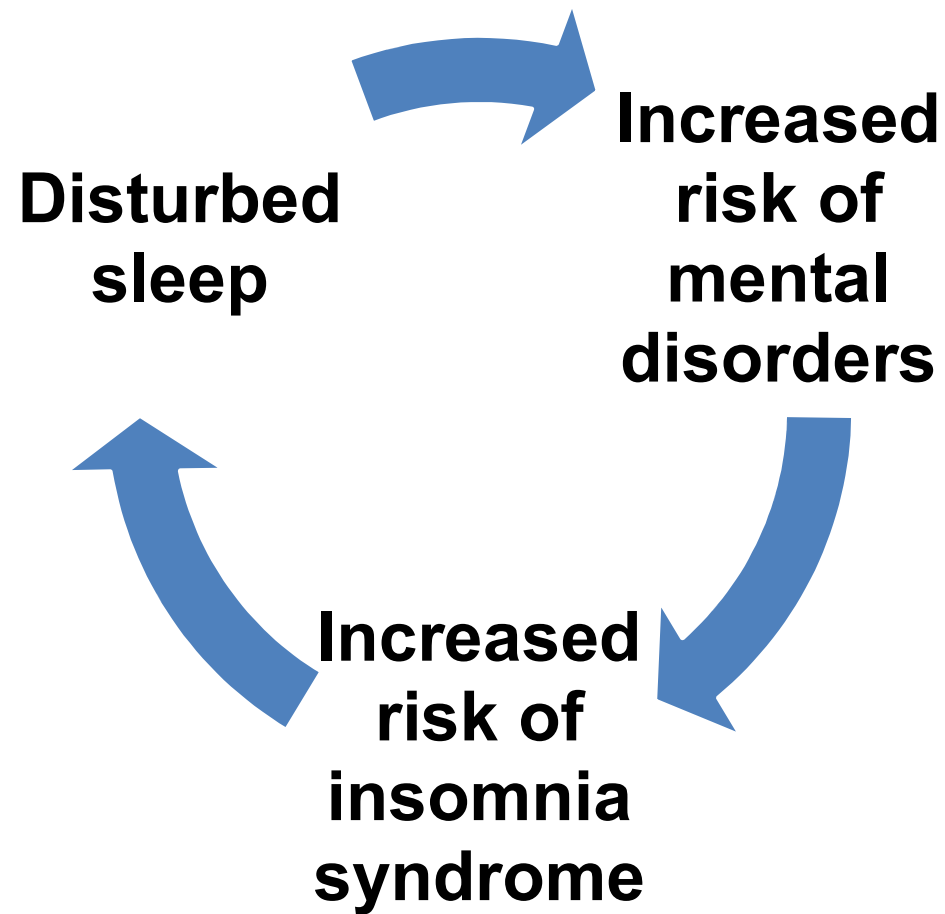


Psychiatric comorbidity cause or consequence?

Few psychiatric disorders has no insomnia symptom

Insomnia pose a risk for the majority of the psychiatric disorders

- Mood disorders
 - Anxiety disorders
 - Delusional/psychotic states
 - Pszichoactive abuse/withdrawal
 - Dementia
-
- Pharmacological treatment

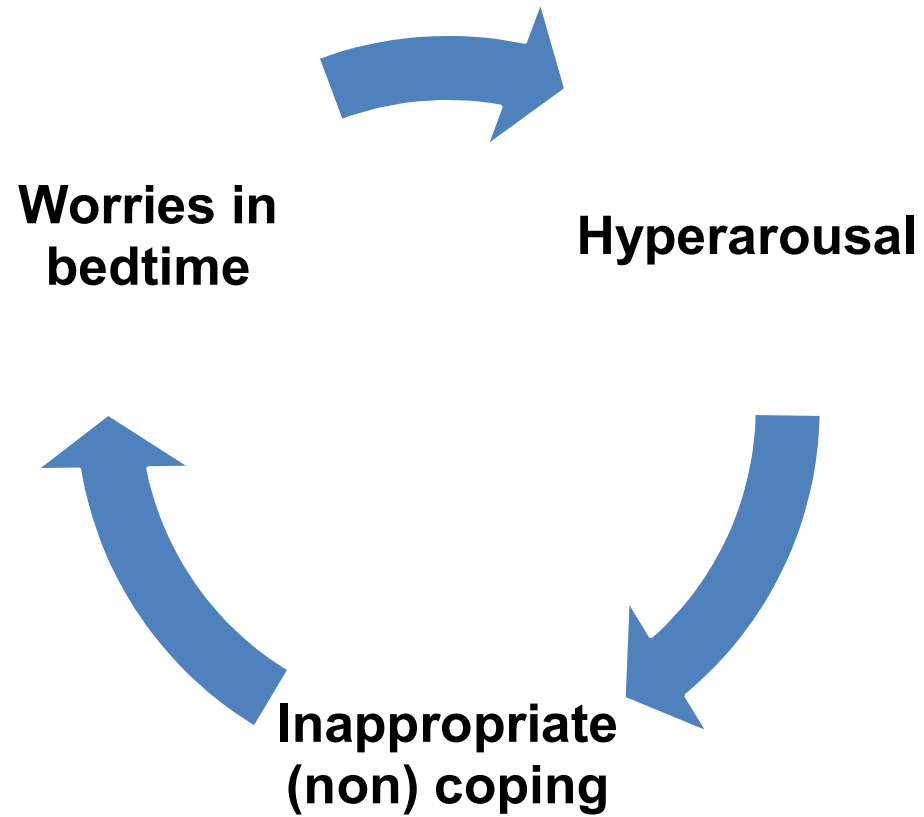


General medical comorbidities

- Difficulty of breathing (ec. COPD, severe asthma bronchiale, etc.)
- Arteriosclerosis (CHD, Brain vessel damage, cardiomyopáthy)
- Hypertension
- Diabetes
- Hepatic diseases
- Hyper- és hypothyreoidism
- Autoimmun diseases
- GERD, peptic/duodenal ulcers
- Bone-joint diseases (rheumatoid arthritis, etc.)
- Urological diseases
- Other

Lifestyle factors

- Irregular lifestyle
 - Psychoactives
 - Lack of exercise
 - Daily stress
 - Sleep related worries and dysfunctional thinking
- Remove the cause but not the symptom
 - The sleep related worry became the dominant insomnia maintaining factor in chronic insomnia



Treatment

- Treat the sleep-wake rhythm, not the sleep only
- Preference on sleep quality (REM, SWS), not the duration of sleep
- Lifestyle changes are crucial – just like in diabetes, cardiovascular disorders etc.

Four target of therapy

Lifestyle and sleep hygiene counselling

Treatment of underlying medical condition (if any)

- ❖ Somatic
- ❖ Psychological
- ❖ Other sleep disorder

Non pharmacological treatment

- ❖ Cognitive behaviour therapy
- ❖ Chronotherapies (sleep restriction, light therapy)

Pharmacotherapy only for adjunctive treatment not longer than 4 weeks

Lifestyle and sleep hygiene counselling

- ❖ Regularity
- ❖ Exercise
- ❖ Restriction of psychoactive agents
- ❖ Stimulus-control
- ❖ Coping with stress

Management of underlying medical condition

❖ Somatic

❖ Psychological

❖ Other sleep disorder

Non pharmacological treatment

❖ Cognitive Behaviour
Therapy (CBT)

❖ Sleep restriction

❖ Relaxation

❖ Light therapy

Pharmacotherapy

Maximum 4 weeks

Should not be the only
intervention (never in
monotherapy)

The least effective
approach

- ❖ GABA-erg (preferable nonBZD) hyperarousal – zolpidem, zopiclon etc
- ❖ MT-erg (MLT-PR, tasimelteon*) CRZ type
- ❖ Orexin antagonist (suvorexant*, Belsomra) hit the market in Japan, about to be launched in US and Canada in early 2015
- ❖ Mirtazapin, trazodon, myanserin (off label in Europe)

Avoid

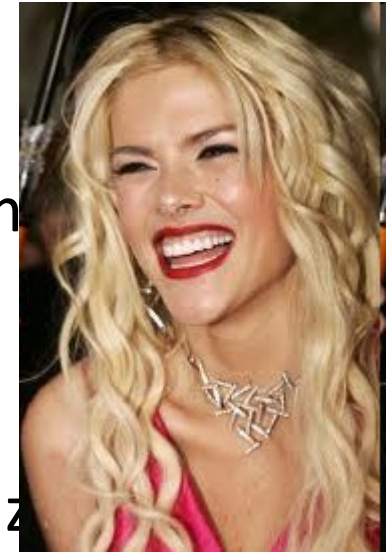
- Barbiturates
- Glutehtimid
- Clomethiazol
- Meprobamat
- Antipsychotics
- Antihistamines
- Ultra-short acting or long-acting BZD-s!

Heath Ledger (†28) Anne Nicole Smiths (†39)

- Diazepam
- Alprazolam
- Temazepam
- Doxilamin
- Oxikodin
- Hydrocodin



- Diazepam
- Clonazepam
- Lorazepam
- Oxazepam
- Difenilhidraz
- Chloralhidrate
- Topiramate



All in appropriate doses

Michael Jackson (†50) Whitney Houston (†48)

- propofol
- lorazepam
- midazolam

- alprazolam
- alcohol



(other) circadian rhythm disorder

- Jet lag
- Shift work related
- Advanced or delayed sleep-phase syndrome

Th: chronotherapies: light/darkness, activity/rest resetting, pharmacotherapy

❖ The significance of sleep are increased in medicine

❖ Sleep quality is a major determinant of health and well-being

❖ Disturbed sleep is a health risk factor (ec. depression, diabetes)

- ❖ The treatment of sleep complaints is **prevention** decrease the somatic/psychological health risk
- ❖ Inappropriate treatment otherwise may lead to more medical problems