

# Sleep disorders in psychiatry

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Sleep = passivity

Sleep = rest

Sleep = tranquillity



The background is a dark blue field with a light blue topographic map overlay. The map features various contour lines and a compass rose in the lower-left quadrant. The compass rose includes a stylized arrow pointing towards the top-left, with the letters 'NW' and 'SE' visible. The text 'Sleep is vital' is positioned over the compass rose area.

❖ 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
- ❖ Psychological well-being
- ❖ Affective learning
- ❖ Motivation
- ❖ Coping with stress
- ❖ Mood regulation

Siegel Science (2001) 294: 5544

# Disturbed sleep leads to psychological and physiological dysfunctions

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

# New bunch of disorders in the XXth Century

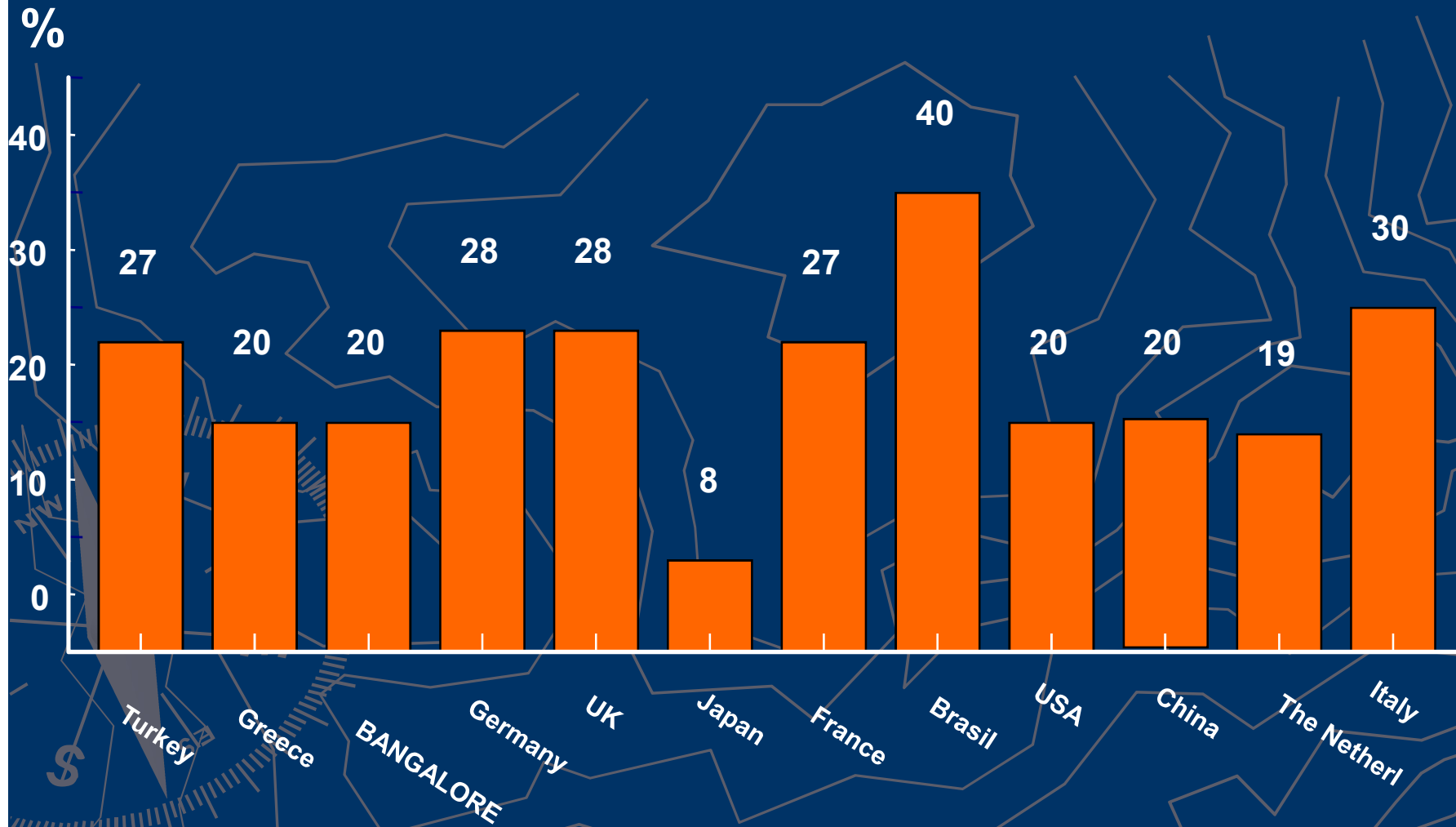
- ❖ Obesity
- ❖ Lipid and cholesterol problems
- ❖ Type 2 diabetes

❖ 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)



# Does the relationship of humans to time change?

- ▶ Life expectations increasing
- ▶ Somatic development accelerates
- ▶ Psychosocial development slows down
- ▶ Duration of marriages increased(?)
- ▶ Changing in chronobiological rhythms:
- ▶ Rhythm and timing of reproduction
- ▶ Annual rhythms (?)

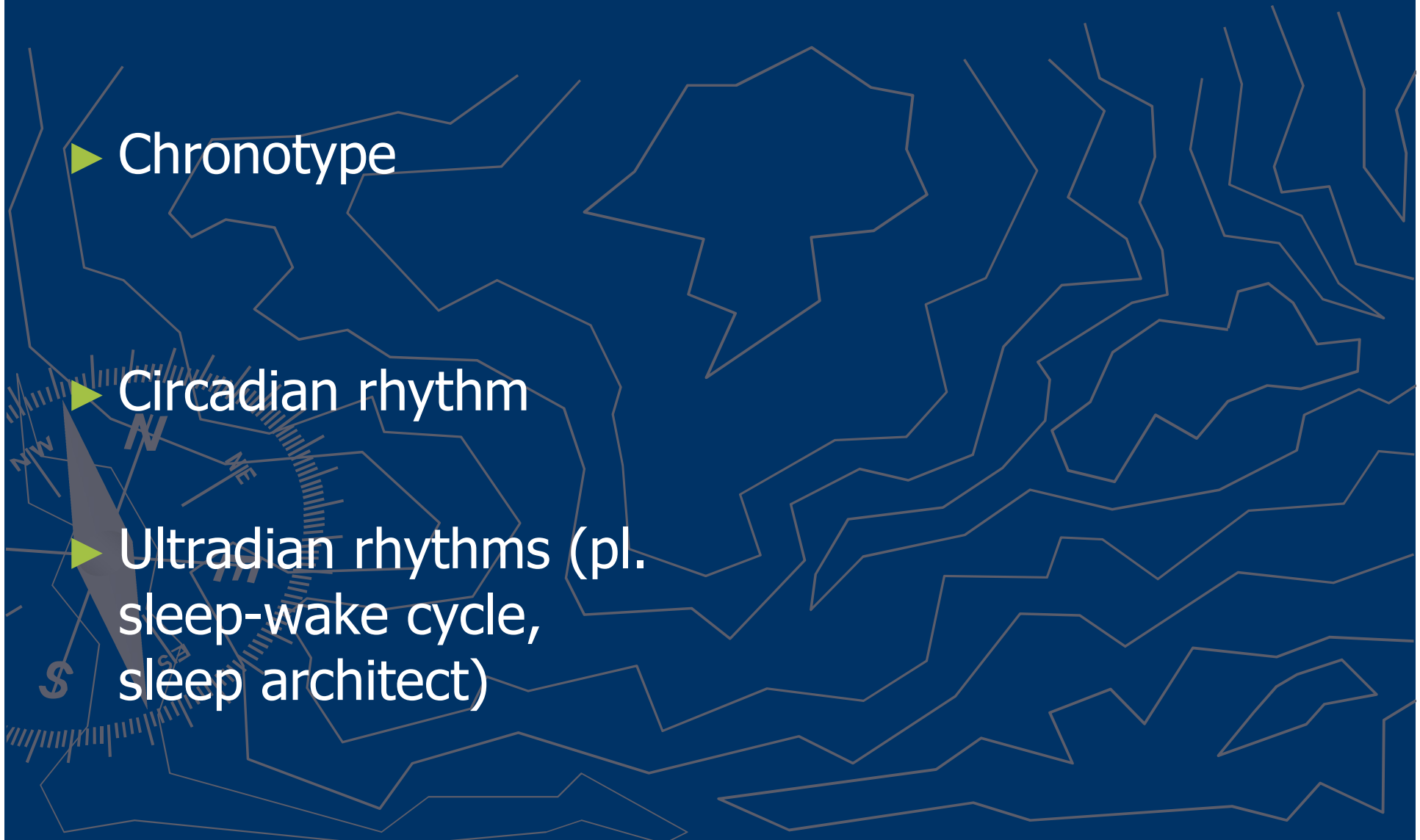


# No change in

▶ Chronotype

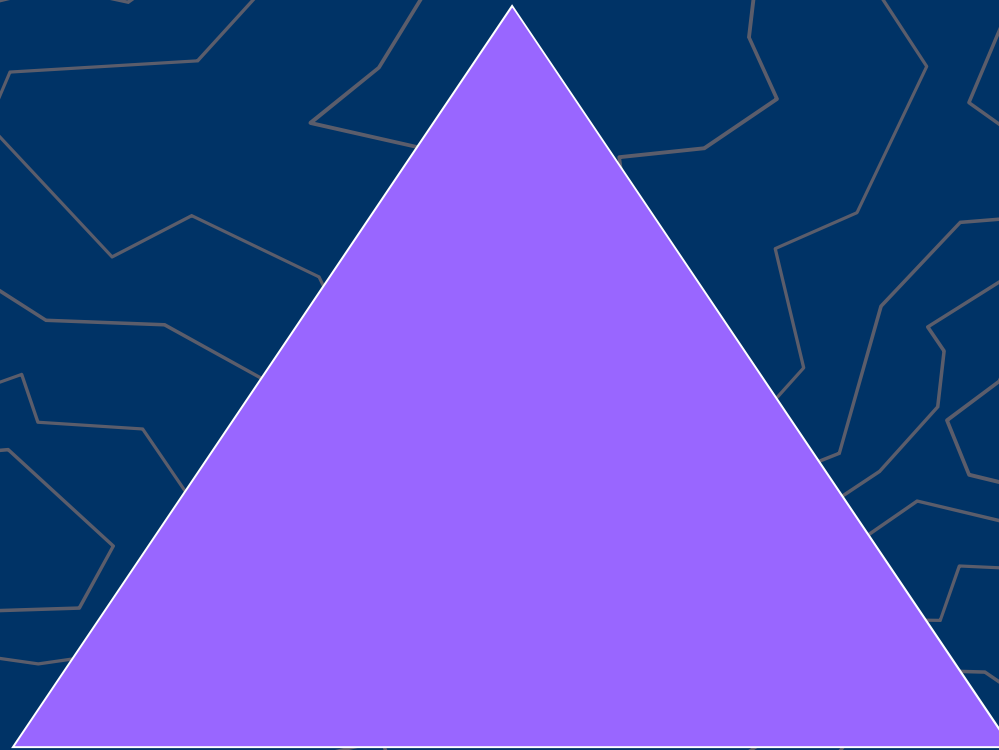
▶ Circadian rhythm

▶ Ultradian rhythms (pl.  
sleep-wake cycle,  
sleep architect)



# Civilisational challenges

Balance of stress and coping



Metabolism under socio-cultural control

Sociocultural control of genetically based, environmentally timed circadian rhythm

# 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 késik (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



## 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

# Sleep disorders

▶ Insomnia

▶ Circadian rhythm disorders\*

▶ Sleep and movement related sleep disorders

▶ Parasomnias

▶ Hypersomnia

▶ Narcolepsia

▶ Etc



# Narcolepsia

Kataplexy

Seep attacks

Sleep paralysis

hypnagogic hallucinations

## Hypersomnia

Depression

OSAS/UARS

Infections

Etc

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 pills, 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



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

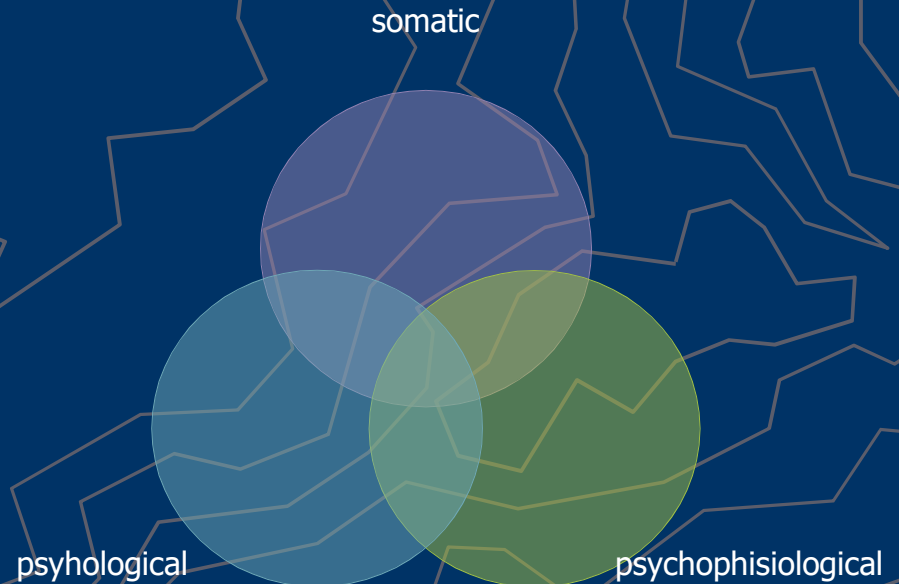
- ❖ Irritability
- ❖ Fatigue
- ❖ Low mood
- ❖ Anxiety
- ❖ Memory/learning difficulties

Decreased concentration  
and reaction time

Risk of  
home/workplace/traffic  
accidents

# 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
- ▶ Psychoactive abuse/withdrawal
- ▶ Dementia
- ▶ Pharmacological treatment

**Disturbed  
sleep**

**Increased  
risk of  
mental  
disorders**

**Increased  
risk of  
insomnia  
syndrome**

# 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

**Worries in bedtime**

**Hyperarousal**

**Inappropriate (non) coping**

# 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

- ❖ GABA-erg (nonBZD) hyperarousal
- ❖ MT-erg (MLT-PR, tasimelteon\*) CRZ-type
- ❖ Orexinerg (suvorexant\*) – prior to US and CAN launch
- ❖ 5HT-erg (eplivanserin\* - discontinued prior to market authorisation)
- ❖ Certain antidepressives (off label in Europe)

# 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

Should not be the only  
intervention (never in  
monotherapy)

The least effective  
approach in chronic  
insomnia

## Arousal-promoting agents:

- ❖ Catecholamines,
- ❖ Orexines
- ❖ Histamine
- ❖ Acetylcholin
- ❖ 5HT
- ❖ CRH!

## Sleep-promoting agents:

- ❖ 5HT
- ❖ GABA-galanin
- ❖ Adenozin
- ❖ Melatonin



- ❖ 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
- ▶ Meprobumat
- ▶ Antipsychotics
- ▶ Antihistamines
- ▶ Ultra-short acting or long-acting BZD-s!



# (other) circadian rhythm disorder

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

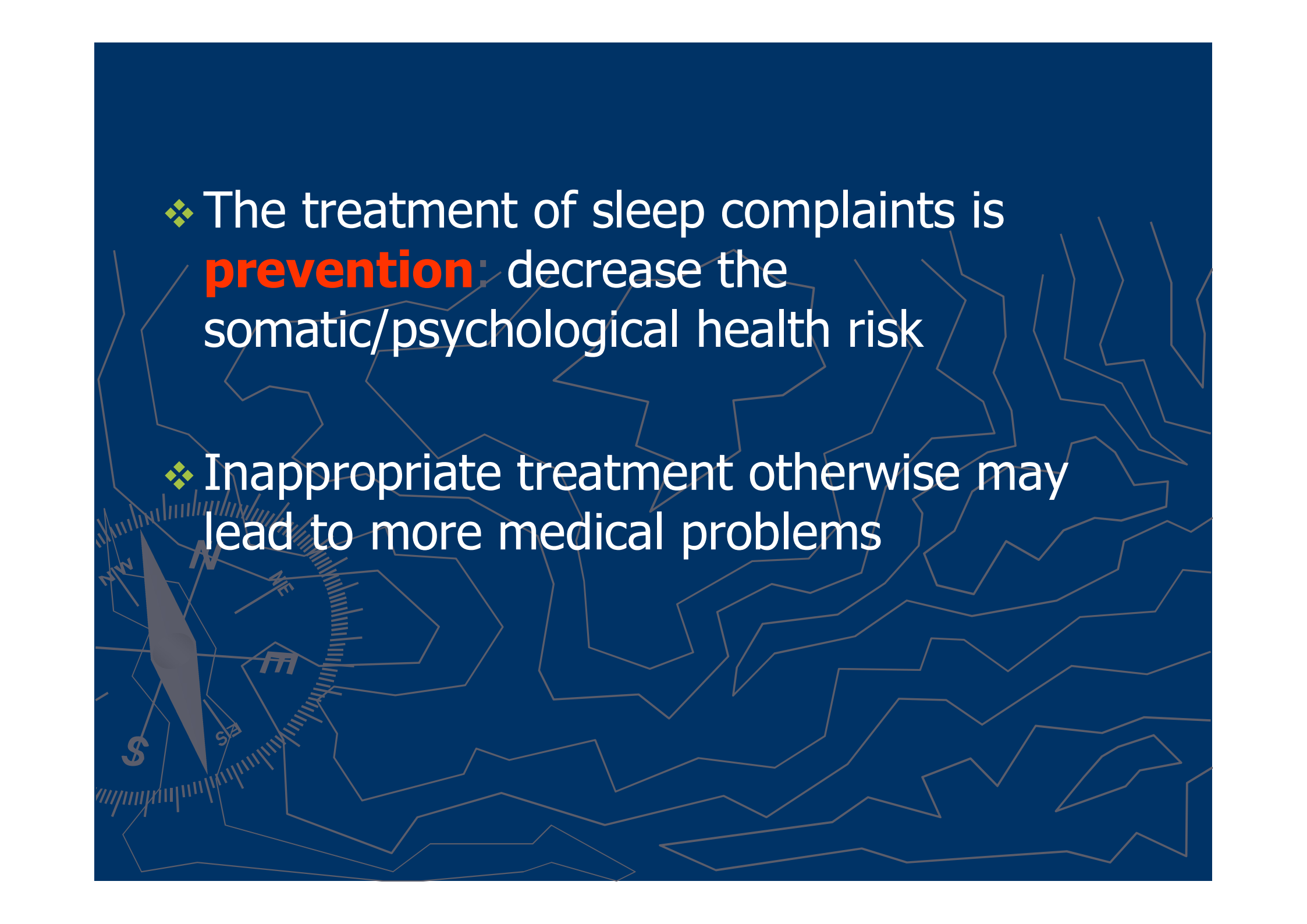
Th: chronotherapies: light/darkness, activity/rest resetting, pharmacotherapy

The background is a dark blue color with a complex, abstract pattern of light-colored lines. In the lower-left corner, there is a stylized compass rose with a needle pointing towards the top-left. The compass rose includes directional labels: 'NW' (Northwest), 'N' (North), 'NE' (Northeast), 'E' (East), 'SE' (Southeast), and 'S' (South). A dollar sign (\$) is also visible near the compass. The rest of the background is filled with irregular, jagged lines that resemble topographic contour lines or a network of paths.

❖ 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