

Sleep disorders in psychiatry

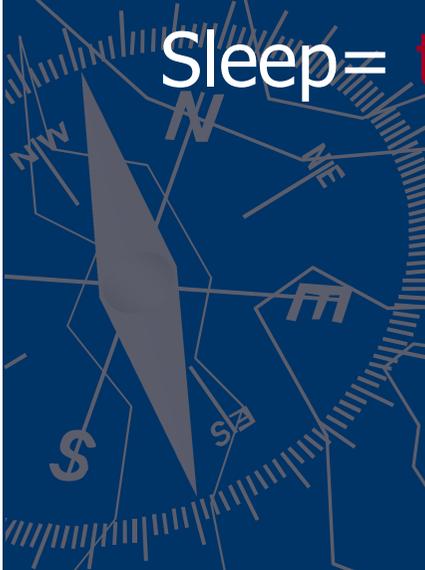
György Purebl MD PhD

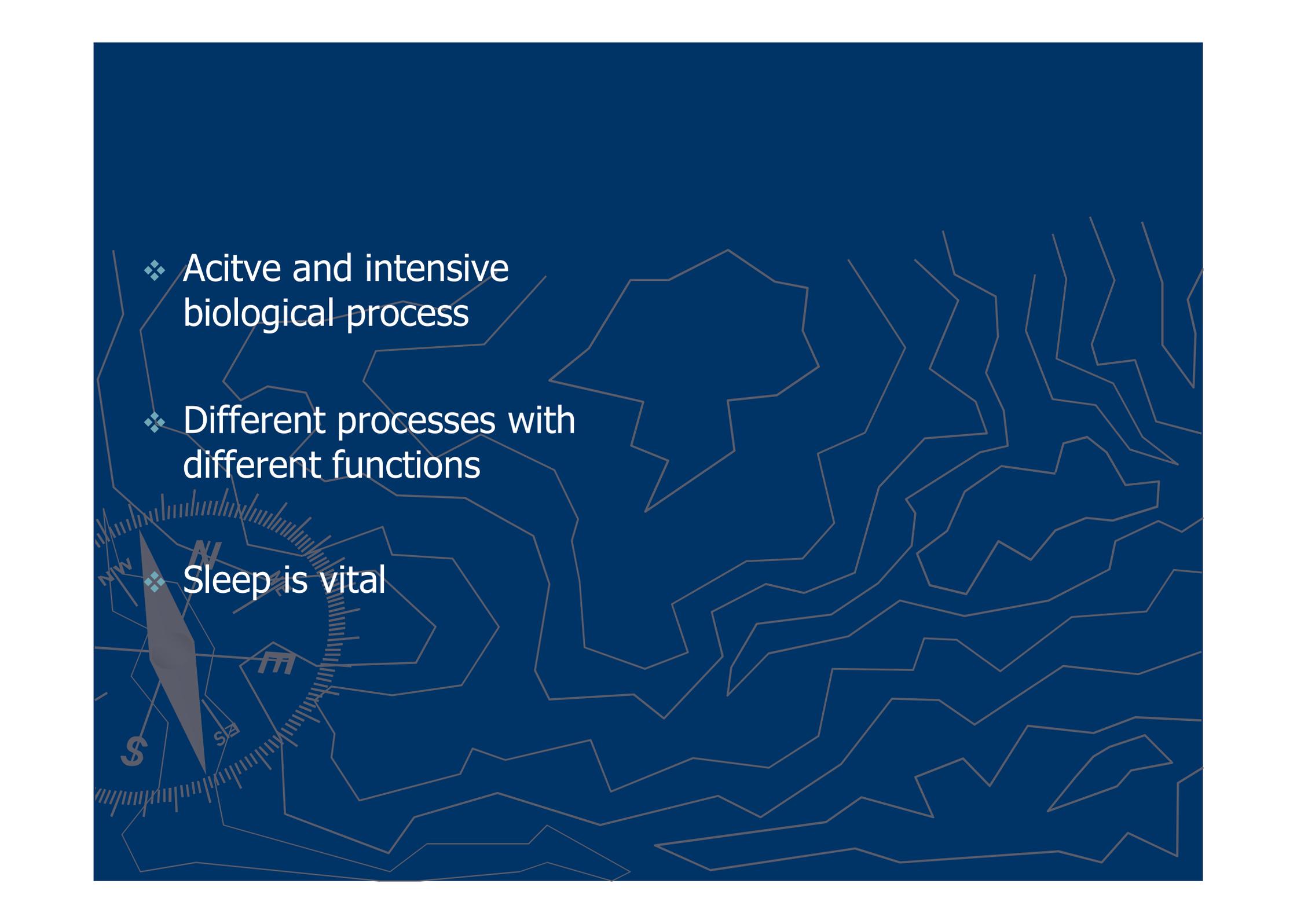


Sleep = passivity

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
- ❖ 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

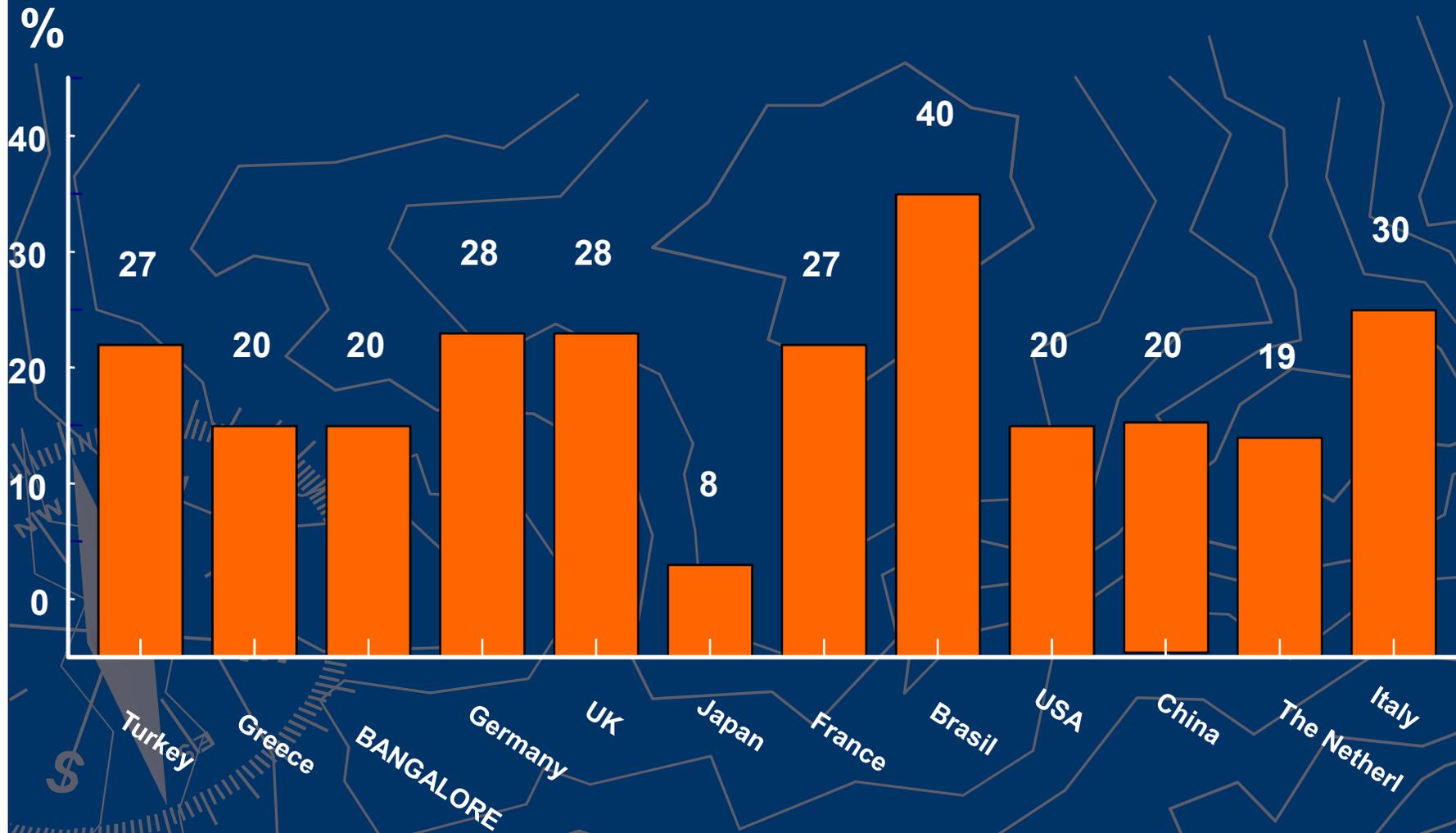
- ❖ Obesity
- ❖ Lipid and cholesterol problems
- ❖ Type 2 diabetes

❖ 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?

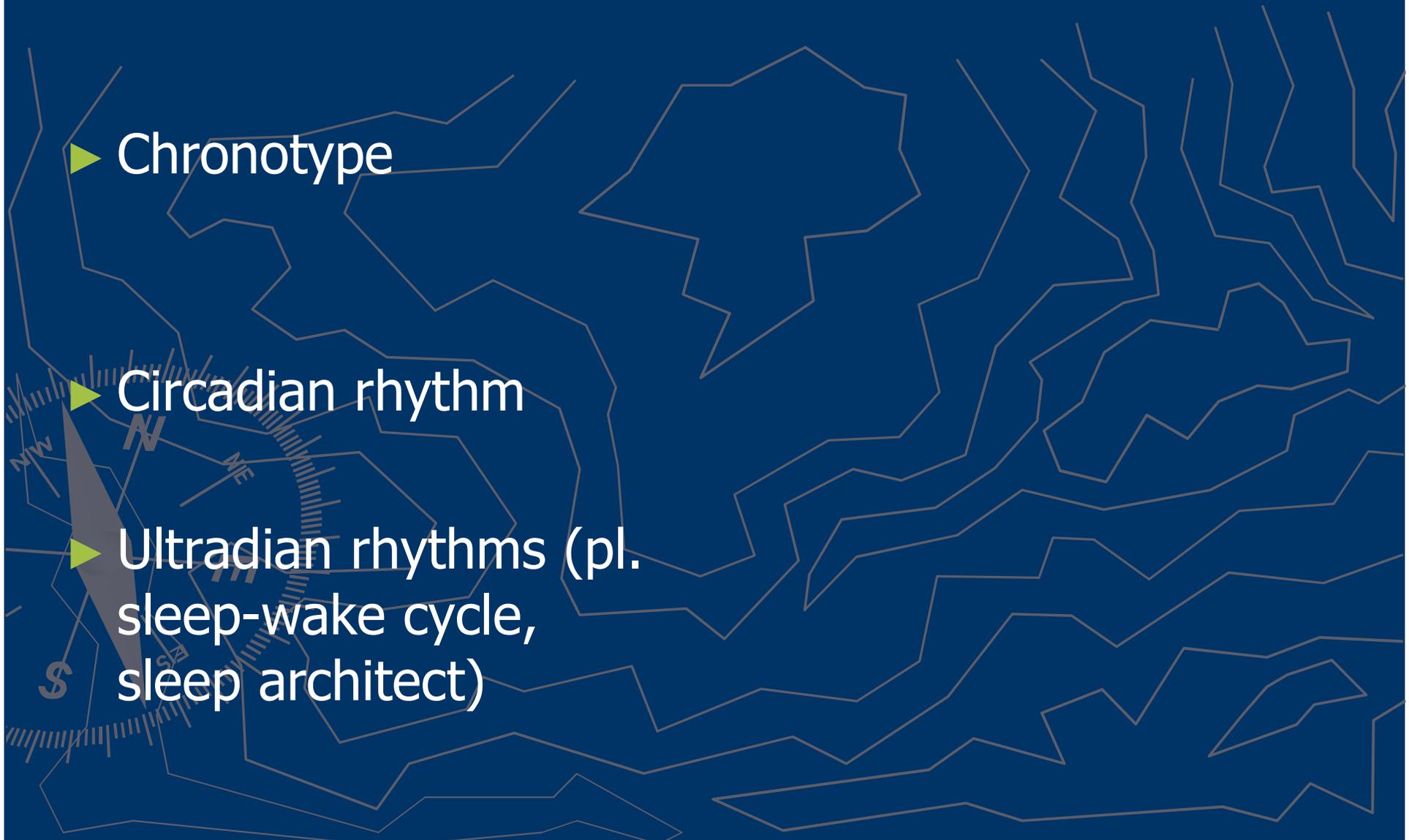
- ▶ Life expectations increasing
- ▶ Somatic development accelerates
- ▶ Psychosocial development slows down
- ▶ Duration of marriages increased(?)
- ▶ Changing in chronobiological rhythms:
- ▶ Rhythm and timing of reproduction
- ▶ Annual rhythms (?)

No change in

▶ Chronotype

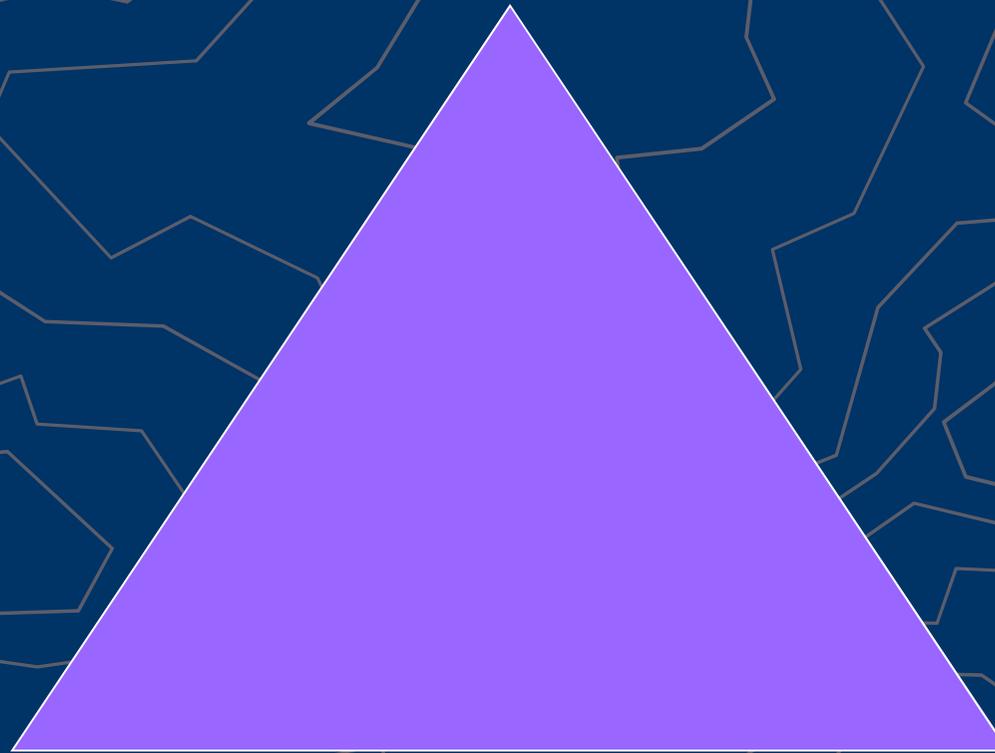
▶ Circadian rhythm

▶ 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

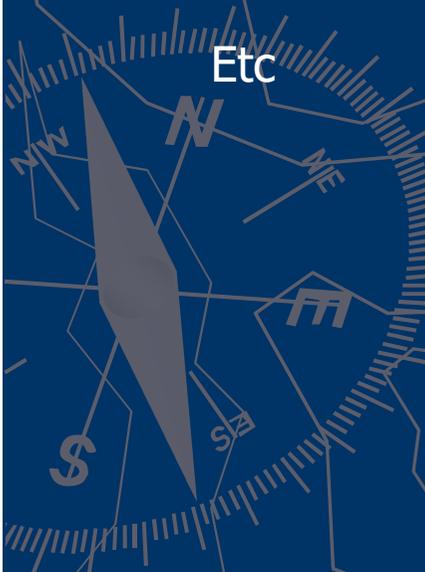
OSAS/UARS

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**

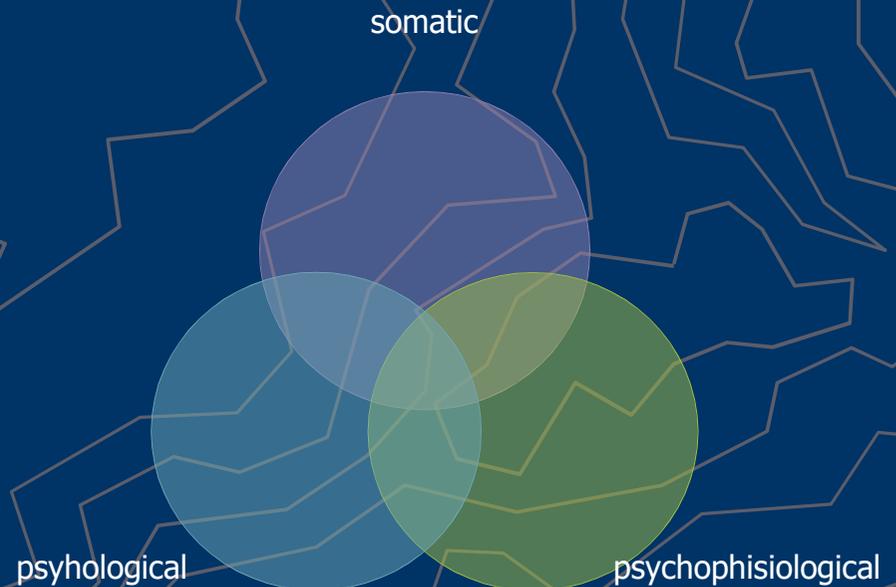
- ❖ Irritability
- ❖ Fatigue
- ❖ Low mood
- ❖ Anxiety
- ❖ Memory/learning difficulties

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**

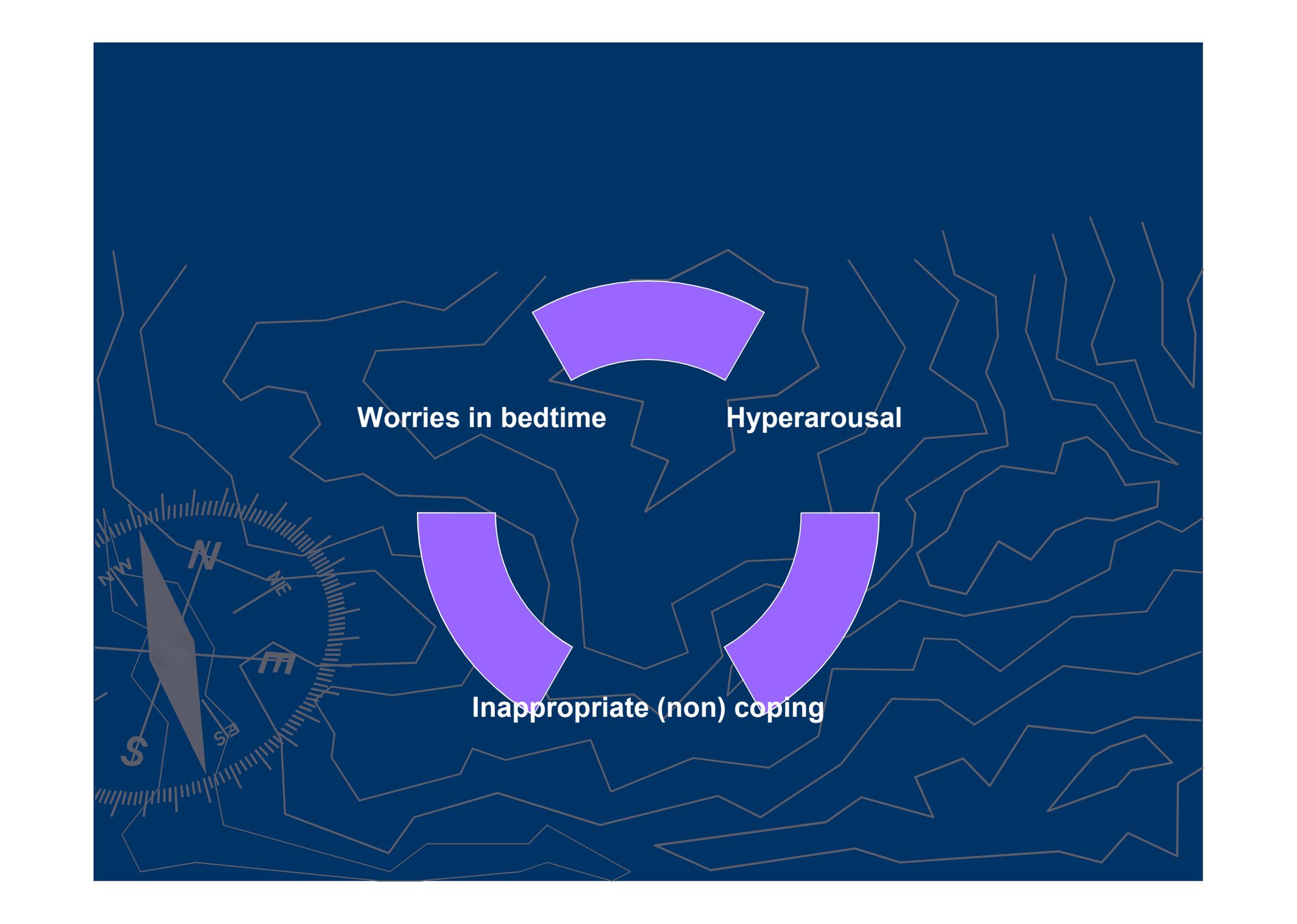
General medical comorbidities

- 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)

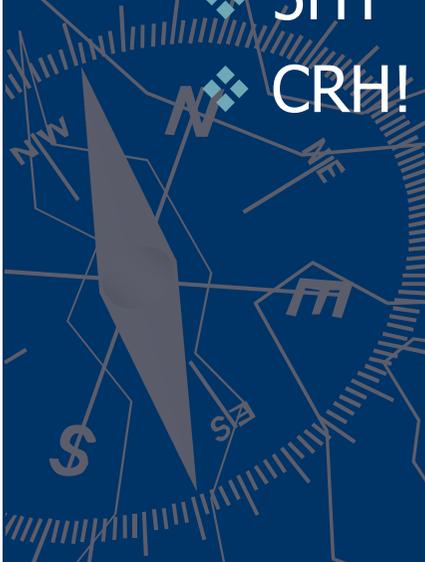
The least effective
approach in chronic
insomnia

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)

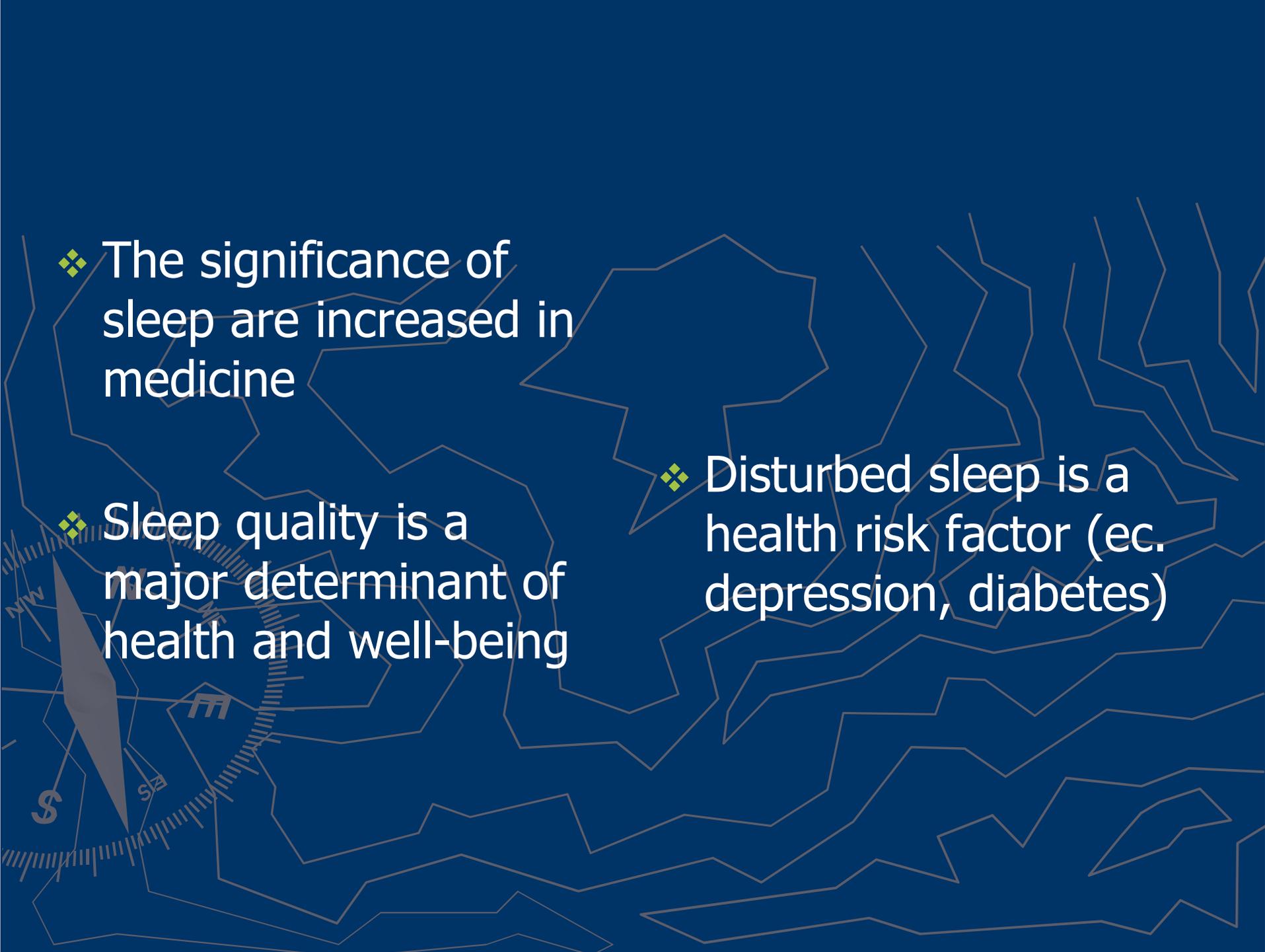
Avoid

- ▶ Barbiturates
- ▶ Glutehtimid
- ▶ Clomethiazol
- ▶ Meprobammat
- ▶ 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

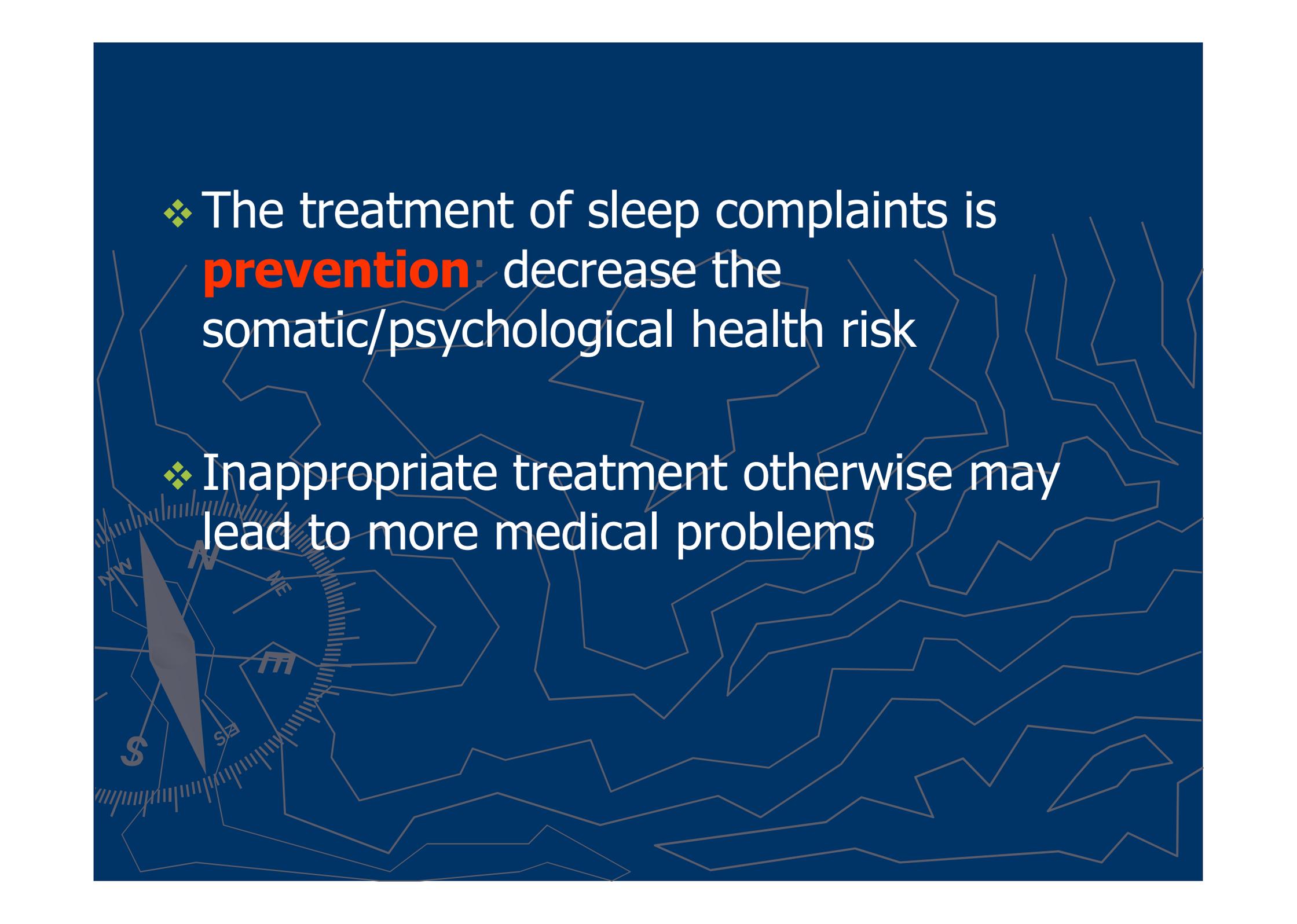
Th: chronotherapies: light/darkness, activity/rest resetting,
pharmacotherapy



❖ The 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