

Sleep disorders in psychiatry

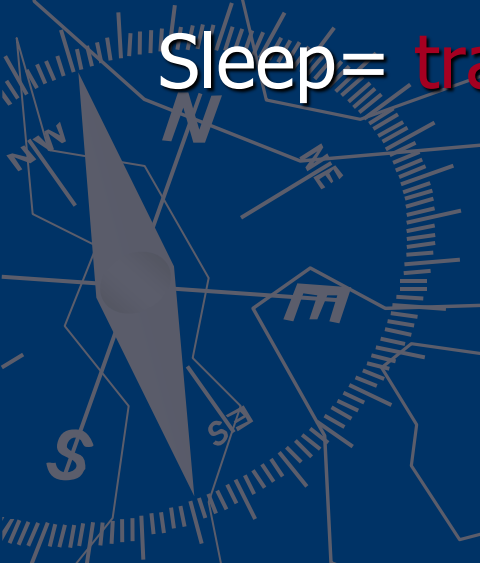
György Purebl MD PhD



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
- ❖ Rekonstruction
- ❖ 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

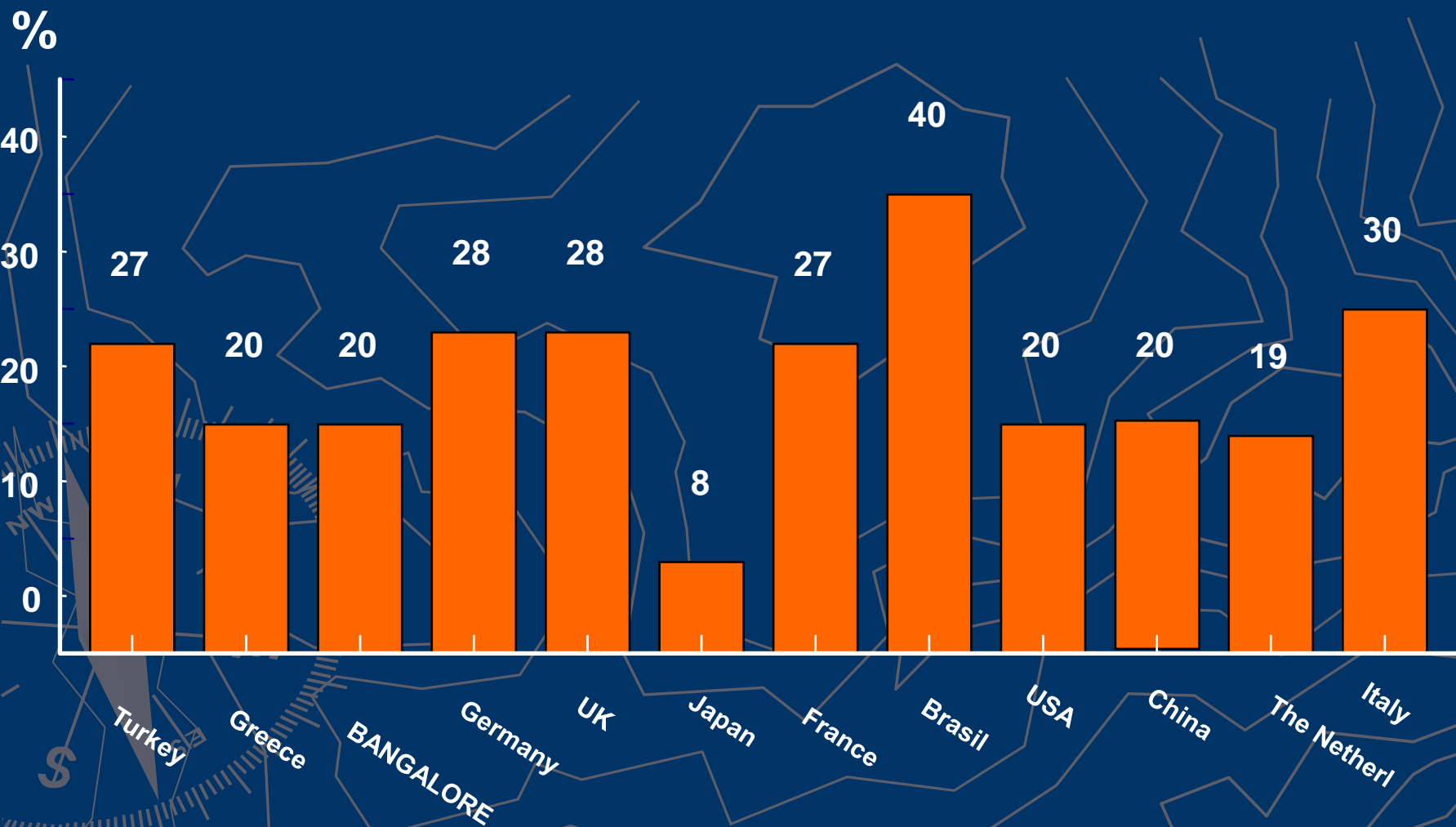
- ▶ Impaired mood regulation
- ▶ Increased stress-alertness
- ❖ 5H_{1A} attenuation
- ❖ Impaired hippocampal neurogenesis
- ❖ Severe psychopathological symptoms
- ❖ Insulin resistance
- ❖ Impaired immunological fitness
- ❖ Increased cortisol-level
- ❖ Disturbed GH secretion
- ❖ Metabolic crisis, death

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)

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



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
- ▶ Diabetes
- ▶ Sudden death

Th

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, chorootherapy, 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 severity of insomnia is determined by daily symptoms **only**

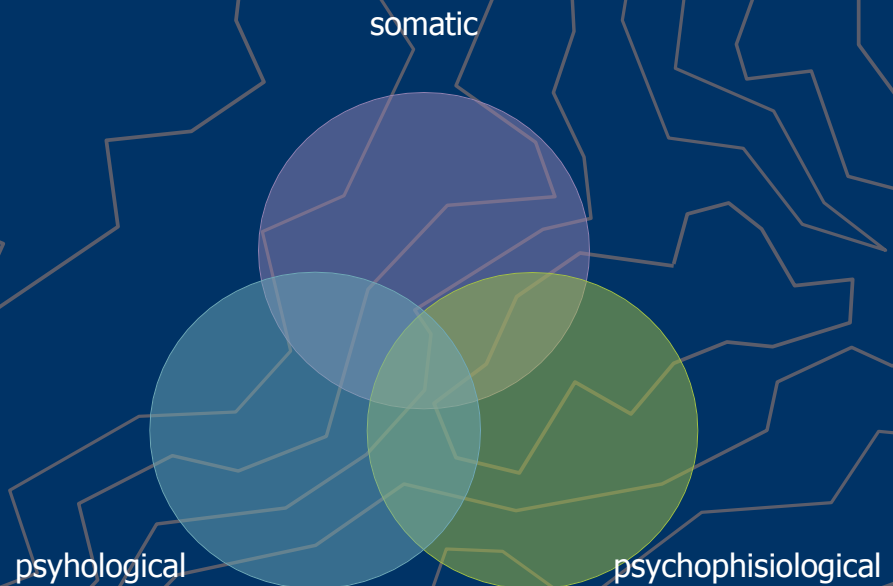
- ❖ Irritability
- ❖ Fatigue
- ❖ Low mood
- ❖ Anxiety
- ❖ Memory/learning difficulties

Decreased concentration and reaction time

Risk of home/workplace/traffic accidents

Primary (psychophysiological) or secondary 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 disorder has no
insomnia symptom

Few psychiatric disorder has no
insomnia risk factor

- ▶ Mood disorders
- ▶ Anxiety disorders
- ▶ Delusional/psychotic states
- ▶ Psychoactive abususus/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



Worries in bedtime

Hyperarousal

Inappropriate (non) coping

Treatment

- ▶ We 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

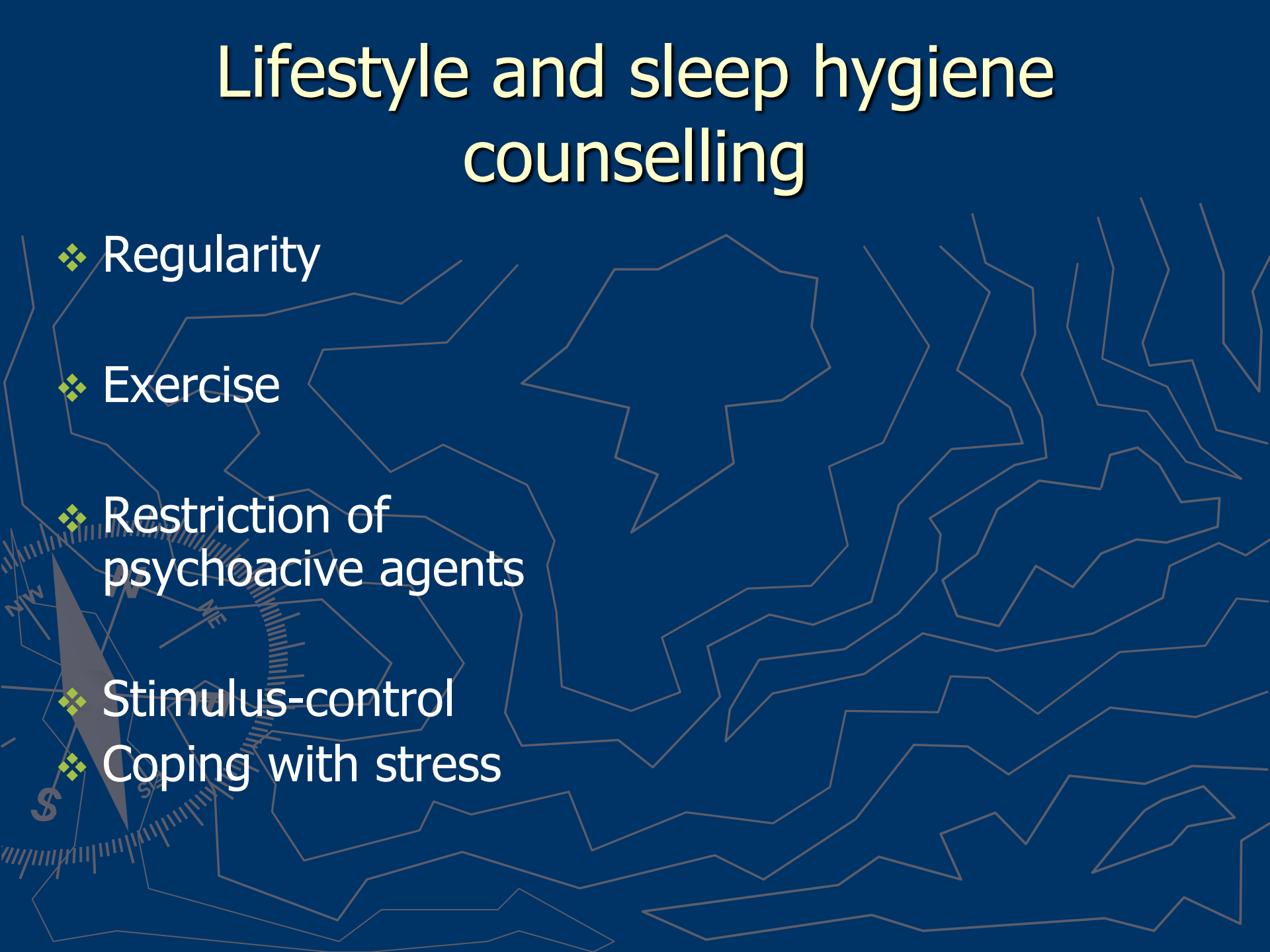
Non pharmacological treatment

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

Pharmacotherapy

- ❖ GABA-erg (nonBZD) hyperarousal
- ❖ MT-erg (MLT-PR, tasimelteon*) CRZ-type
- ❖ Orexinerg (almorexant*)
- ❖ Certain antidepressives (off label in Europe)

Lifestyle and sleep hygiene counselling


- ❖ Regularity
 - ❖ Exercise
 - ❖ Restriction of psychoactive agents
 - ❖ Stimulus-control
 - ❖ Coping with stress
- 
- The background of the slide is a dark blue color. On the left side, there is a faint, stylized map of the United Kingdom. Overlaid on the map is a compass rose with a dollar sign (\$) positioned near the bottom left. The map and compass are rendered in a light, golden-brown color.

Management of underlying medical condition

- ❖ Somatic
- ❖ Psychological
- ❖ Other sleep disorder



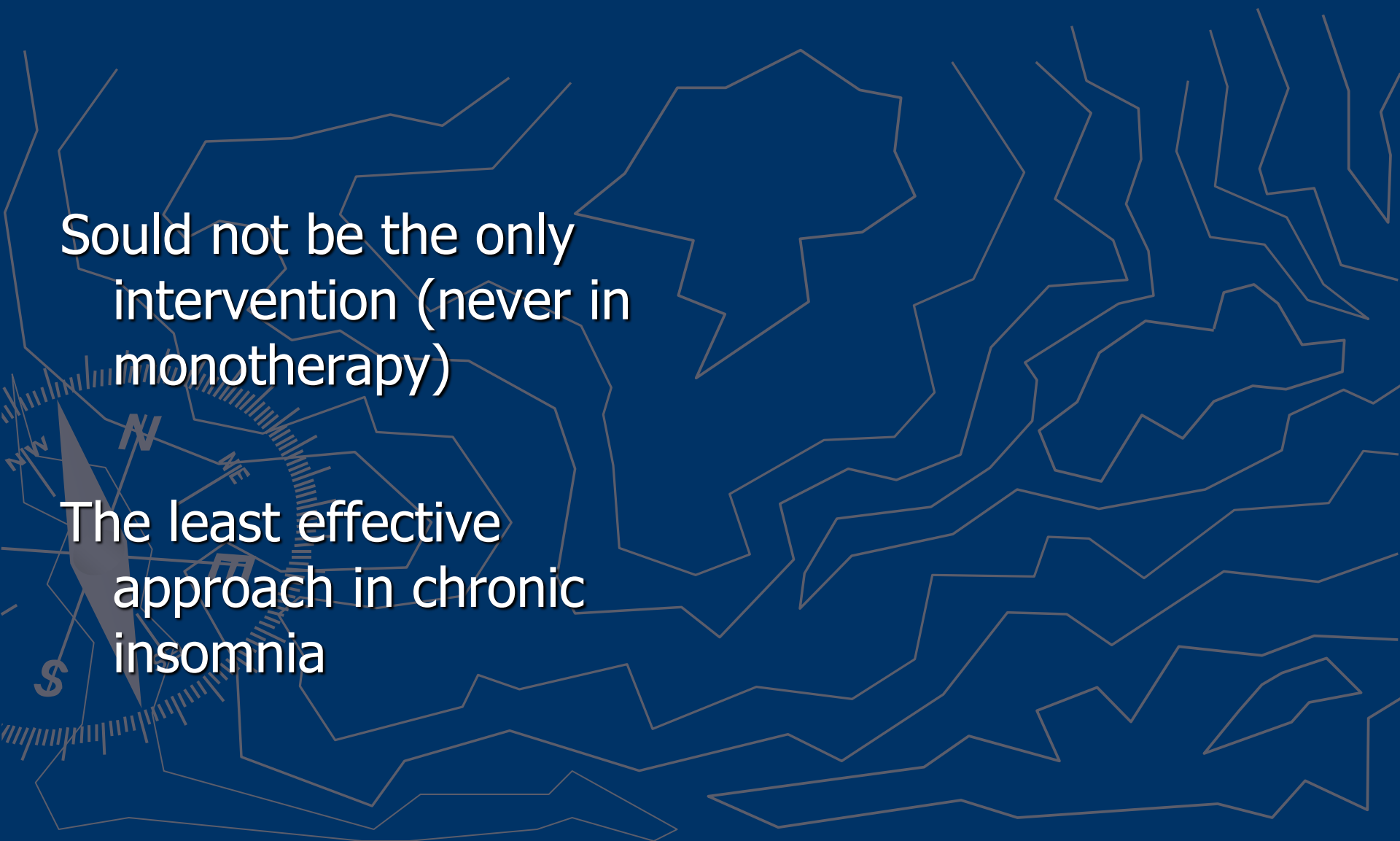
Non pharmacological treatment

- ❖ Cognitive Behaviour Therapy (CBT)
 - ❖ Sleep restriction
 - ❖ Relaxation
 - ❖ Light therapy
- 
- The background of the slide is a dark blue color. It features a faint, light-colored topographic map with contour lines. In the lower-left corner, there is a compass rose with a needle pointing towards the top-left. The compass rose includes directional labels: 'NW' (Northwest), 'N' (North), 'E' (East), and 'S' (South). The needle is a dark grey shape with a white tip.

Pharmacotherapy

Should not be the only
intervention (never in
monotherapy)

The least effective
approach in chronic
insomnia

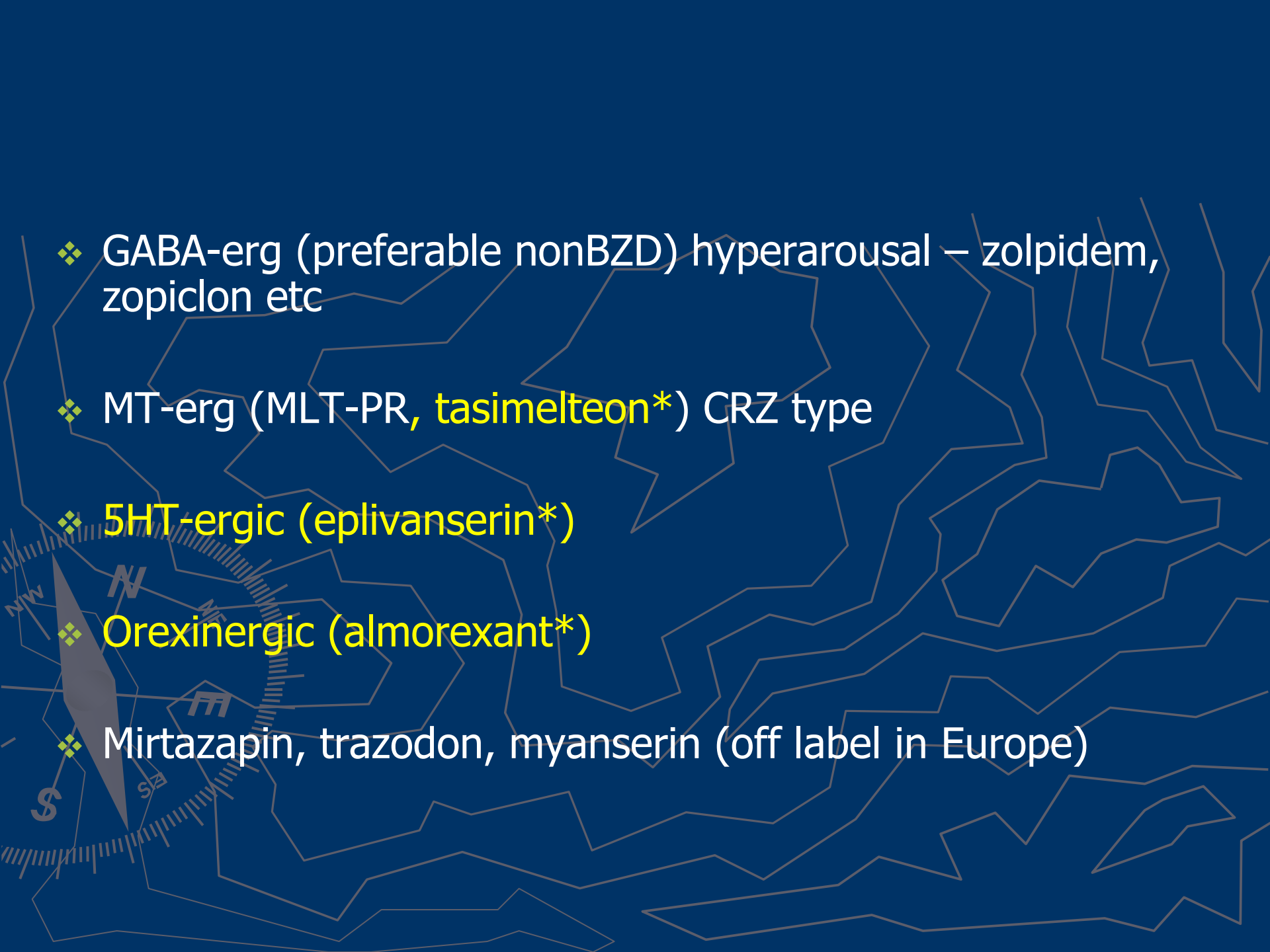


Arousal-promoting agents:

- ❖ Catecholamines,
- ❖ Orexines
- ❖ Histamin
- ❖ 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
 - ❖ **5HT-ergic (eplivanserin*)**
 - ❖ **Orexinergic (almorexant*)**
 - ❖ Mirtazapin, trazodon, myanserin (off label in Europe)

Avoid

- ▶ Barbiturates
- ▶ Glutehtimid
- ▶ Clomethiazol
- ▶ Meprobumat
- ▶ Antipsychotics
- ▶ Antihisztamines
- ▶ 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
- ▶ Difenilhidrazin
- ▶ Chloralhydrate
- ▶ Topiramate

All in appropriate dose

(other) circadian rhythm disorder

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

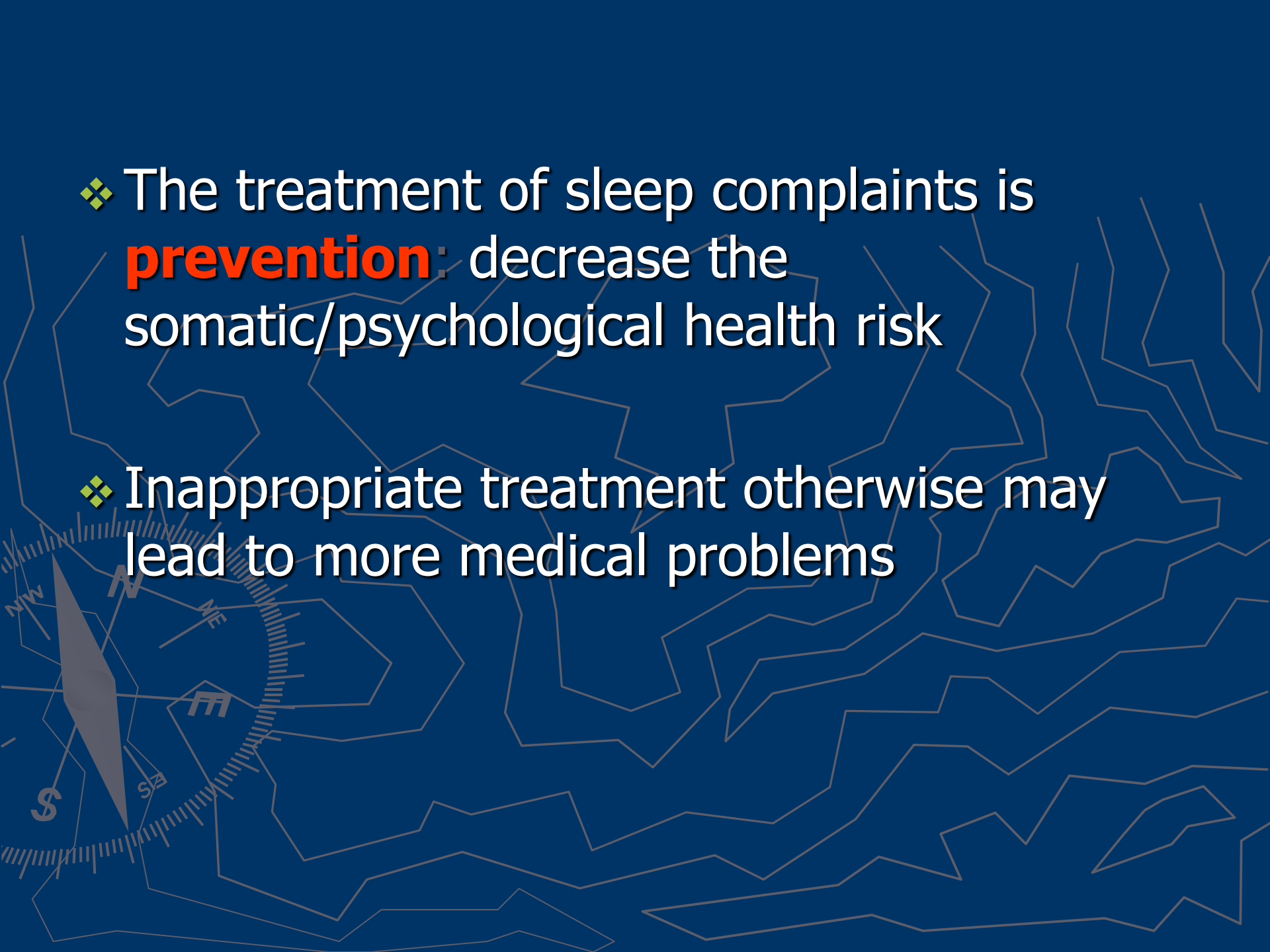
Th: chronotherapies: light/darkness, activity/rest resetting, pharmacotherapy



❖ 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