The Roadmap Series

Mapping Sleep & Insomnia

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amrita education

Sleep- Facts

- Almost 23% of people in UK only get between 5 and 6 hours of sleep per night.
- This means that many of us miss out on the recommended amount of sleep by at least 114 minutes.
- 3 times more likely in women
- Sleep occurs in 90-110 minute cycles divided into non-REM and REM(brain/memory) sleep

REM sleep every three to four days! and they only sleep for about three hours day!

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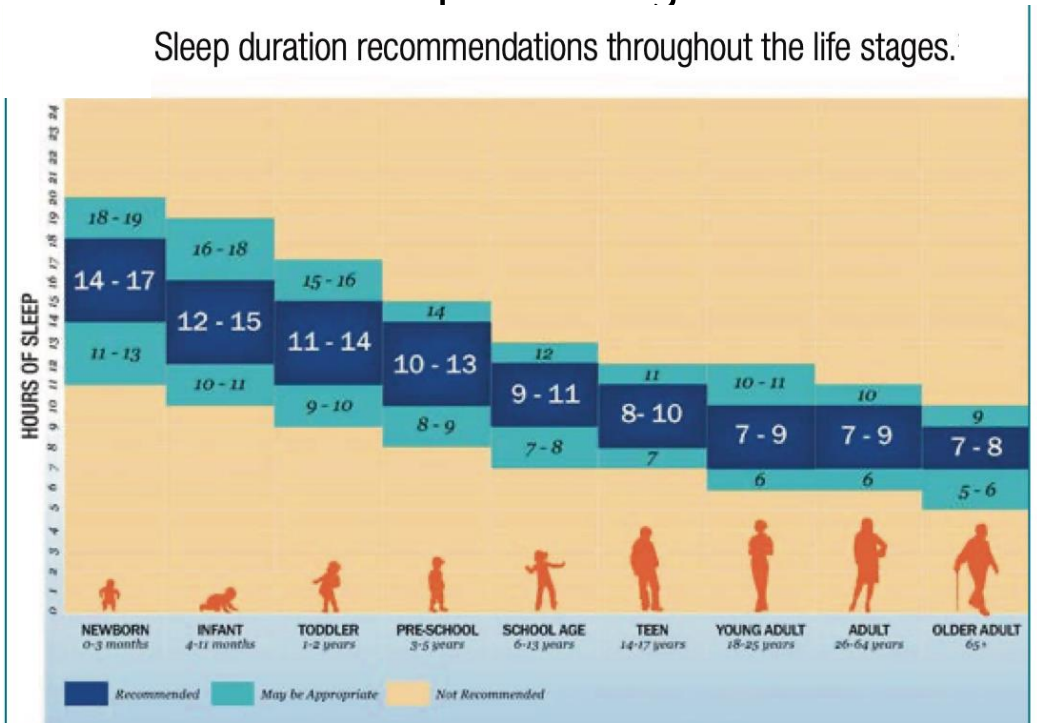
Sleep

- Humans spend approximately one-third of their lives sleeping, with healthy sleep required for immune system function, restoring physical and mental function, and supporting energy and vitality

- Sleep requirements change throughout life stages - To garner optimal health benefits from sleep, an adult aged between 24-64 years requires **7-9 hours' sleep each night**

Insomnia is related to significant, long- term health <u>consequences;</u> early mortality, more likely to develop **depression, hypertension, obesity, impaired fasting glucose and type 2 diabetes; reduced immune function and infections**



Clinical Presentations of acute sleep deprivation

Figure 3: Clinical presentations of acute sleep deprivation

Insomnia statistics

- 40-50% of the population are affected by insomnia at any time[8]
- According to Australian population surveys, 13-33% of the adult population regularly experience difficulty staying asleep or getting to sleep[3]
- Chronic insomnia doubles the risk of developing depression[3]
- Insomnia is associated with the development of hypertension and cardiovascular disease[3,9]
- Insomnia affects twice as many women compared to men[1,8]
- Insomnia occurs more frequently with ageing[1]
- Insomnia is the third most common reason for visits to a General Practitioner[3]
- 26% of adults' report using the internet most or every night of the week just before bed, and experience frequent sleep difficulties or daytime impairments[7]
- Benzodiazepine medications are frequently prescribed for sleep disturbances but come with several side-effects, including: day time sedation, respiratory depression and withdrawal symptoms[5]
- Rebound insomnia may occur with benzodiazepines after just 1 night of use; tolerance can occur after 1-2 weeks[5]

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What is insomnia?

In the Diagnostic and Statistical Manual of Mental Disorders (DSM-V), insomnia is defined as **difficulty initiating or maintaining sleep**, or having **non-restorative sleep despite having adequate opportunity for sleep,** together with associated impairment of daytime functioning, with symptoms being present for **at least 4 weeks**

Other scientific literature has defined insomnia as

Sleep Latency (time taken to fall asleep)	> 30 minutes
Sleep Efficiency (time asleep vs time in bed)	< 85%
Sleep disturbance frequency	> 3 times/week

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What is insomnia

- Sleep disorders can be classified as primary or secondary, as well as acute or chronic in nature.
- These classifications relate strongly to cause and contributing factors and may guide the clinical approach for individual patients

Table 1: Classifications of insomnia and clinical considerations

Primary	Secondary	Acute	Chronic
Not attributable to a medical, psychiatric or environmental cause. Typically caused by general issues of sleep hygiene, stress and substance abuse.	Presents as a comorbidity with other physical (e.g. restless leg syndrome, obstructive sleep apnoea), physiological (e.g. hormonal changes in perimenopause), or psychiatric (e.g. anxiety, depression and panic disorders) disorders.	Typically lasts 24-48 hours. Associated with stressful life events such as: family, relationship, and financial stress; jetlag; consumption of caffeine, alcohol, nicotine; changing or starting certain medications such as steroids, beta-blockers and antidepressants.	Symptoms occur at least 3 times per week; lasting more than 3 months.
• Educate on sleep hygiene • Develop sleep hygiene plan • Address stress • Address substance abuse • Counsel on diet and lifestyle	• Address underlying condition/ comorbidity • Establish a mental health plan • Develop sleep hygiene plan	• Where possible, remove source of insomnia • Stress/grief management where required	• Long-term treatment approach required

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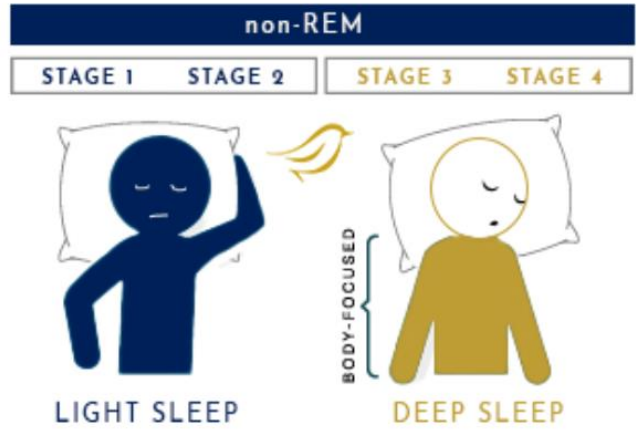
Sleep architecture

generally **four to five different sleep cycles** during a given night and each of one lasts for about **90 to 120 minutes**, shifting from lighter stages to deepest ones.

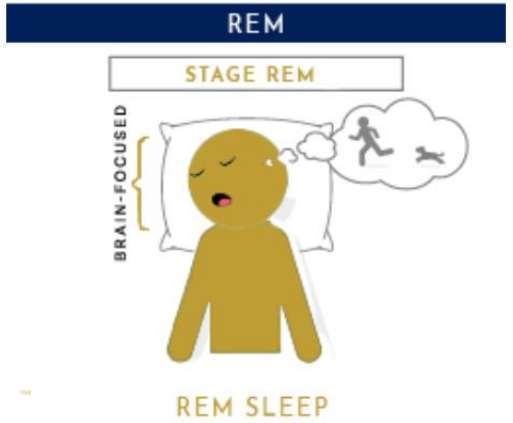
A complete sleep cycle progress between 5 different phases:

•non-REM phase

- Stage 1: the lightest stage of sleep
- Preparing for deep sleep: Stage 2 and Stage 3:
- Stage 4: the deep sleep *(body focused)*



•REM Phase: the deepest sleep, where dreams occur



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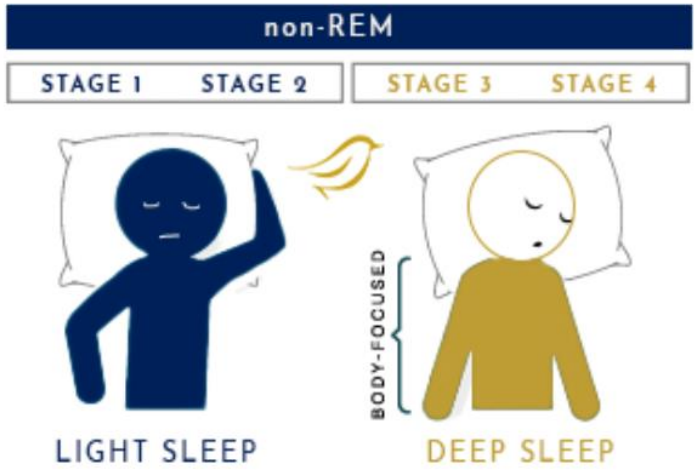
Sleep architecture

non-REM phase

- Stage 1: the lightest stage of sleep, during this short period (lasting several minutes) brain wave activity begins to slow from that of wake. Sensation of falling, hypnic jerks.

- Stage 2 :heartbeat and breathing slow, and muscles relax further, body temperature drops.

- Stage 3 & 4: the deep sleep *(body focused*)- Brain wave activity slows but is marked by brief bursts of electrical activity.

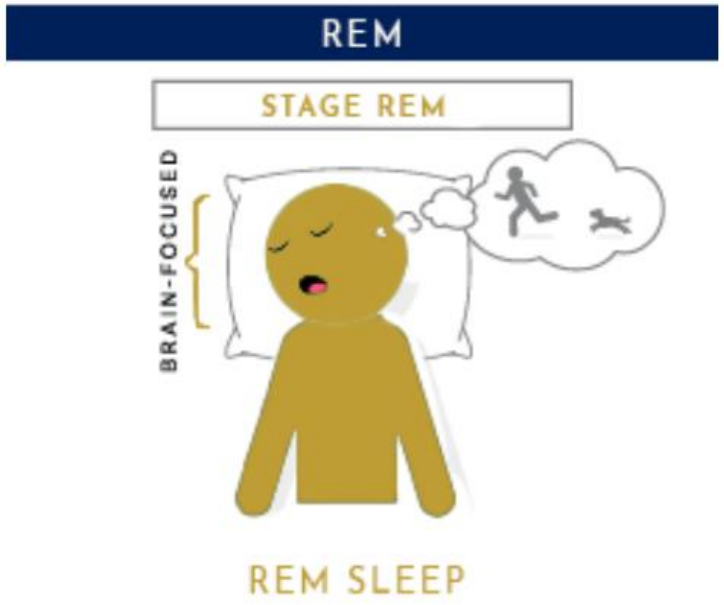


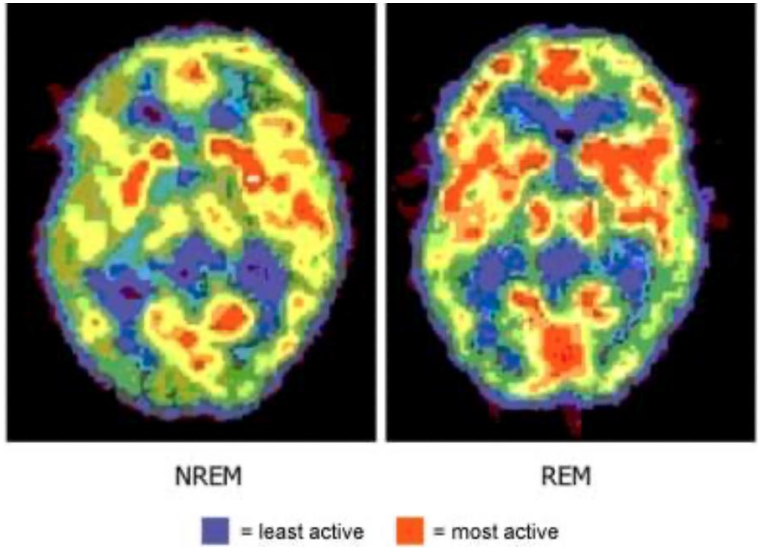
It is the most rejuvenating and restorative sleep stage, promoting human growth hormone and restores body and muscles from the stresses of the day. immune system also restores itself.

Sleep architecture

REM Phase: the deepest sleep, where dreams occur

- REM begins 70-90mins after we fall asleep
- Ideally achieve 3-5 REM episodes each night
- Brain activity heightened leading to dream state
- Breathing rate and blood pressure rise slightly but skeletal muscle activity lowest





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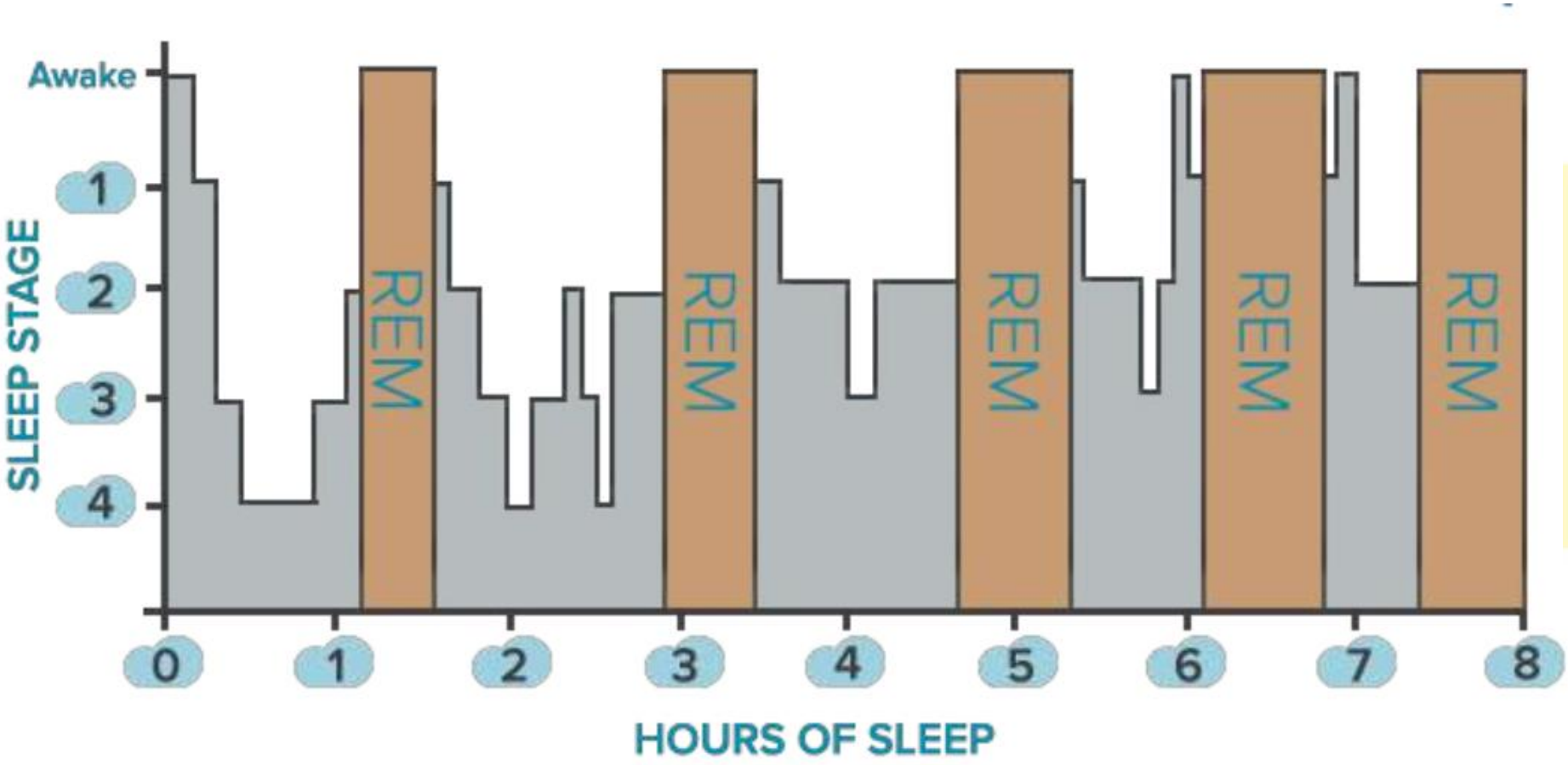
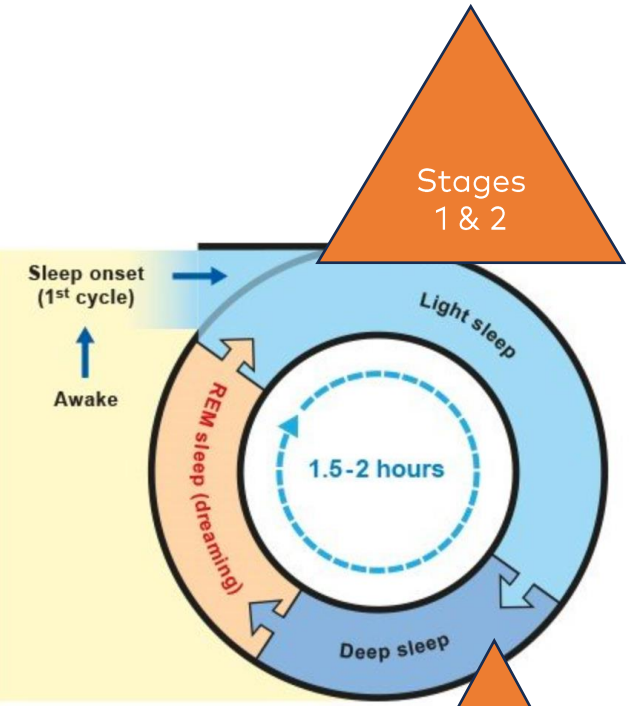
Sleep architecture- stages health sleep





Stages
1 & 2

Stage
s
3 & 4

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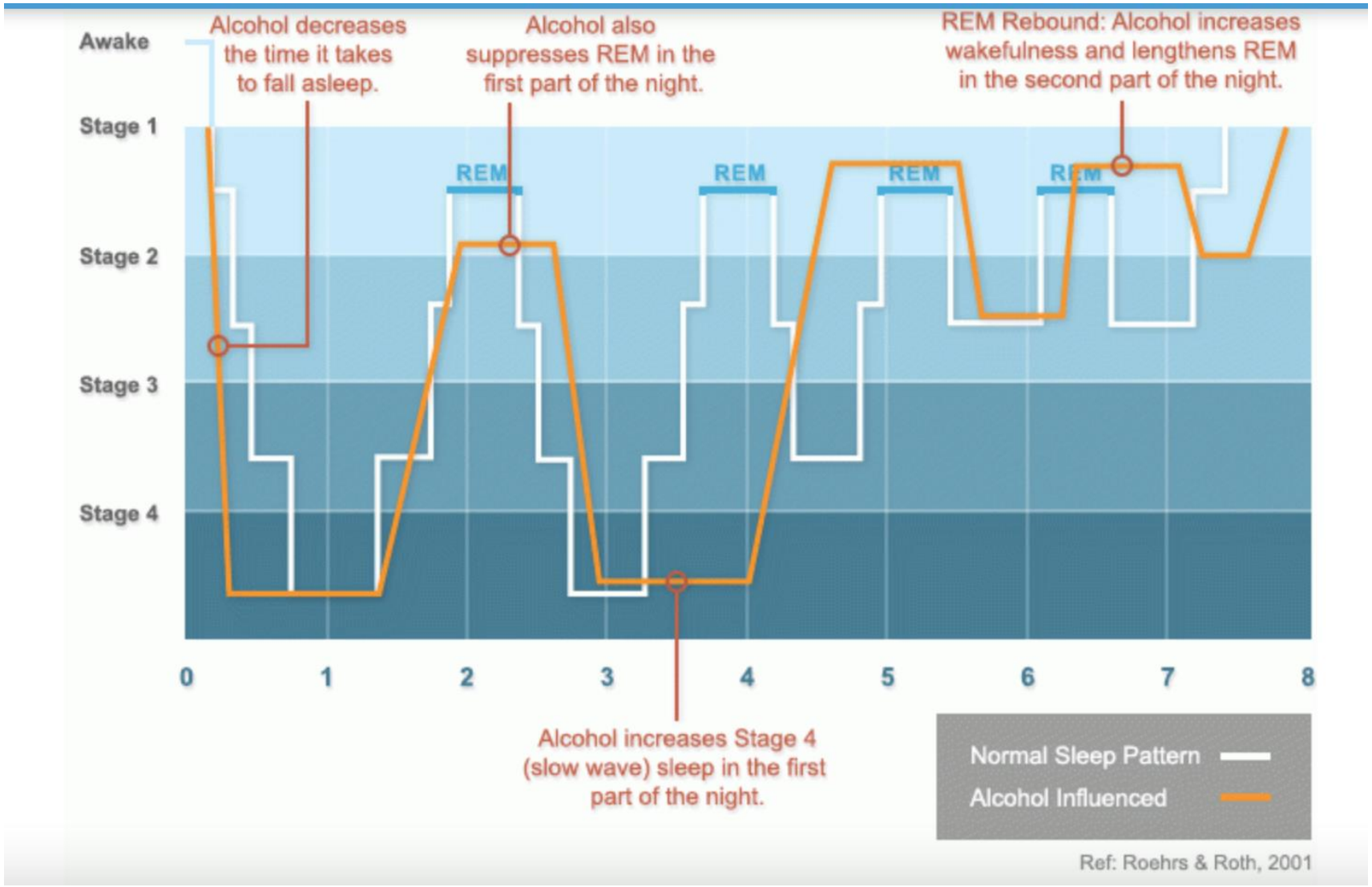
Sleep architecture- alcohol



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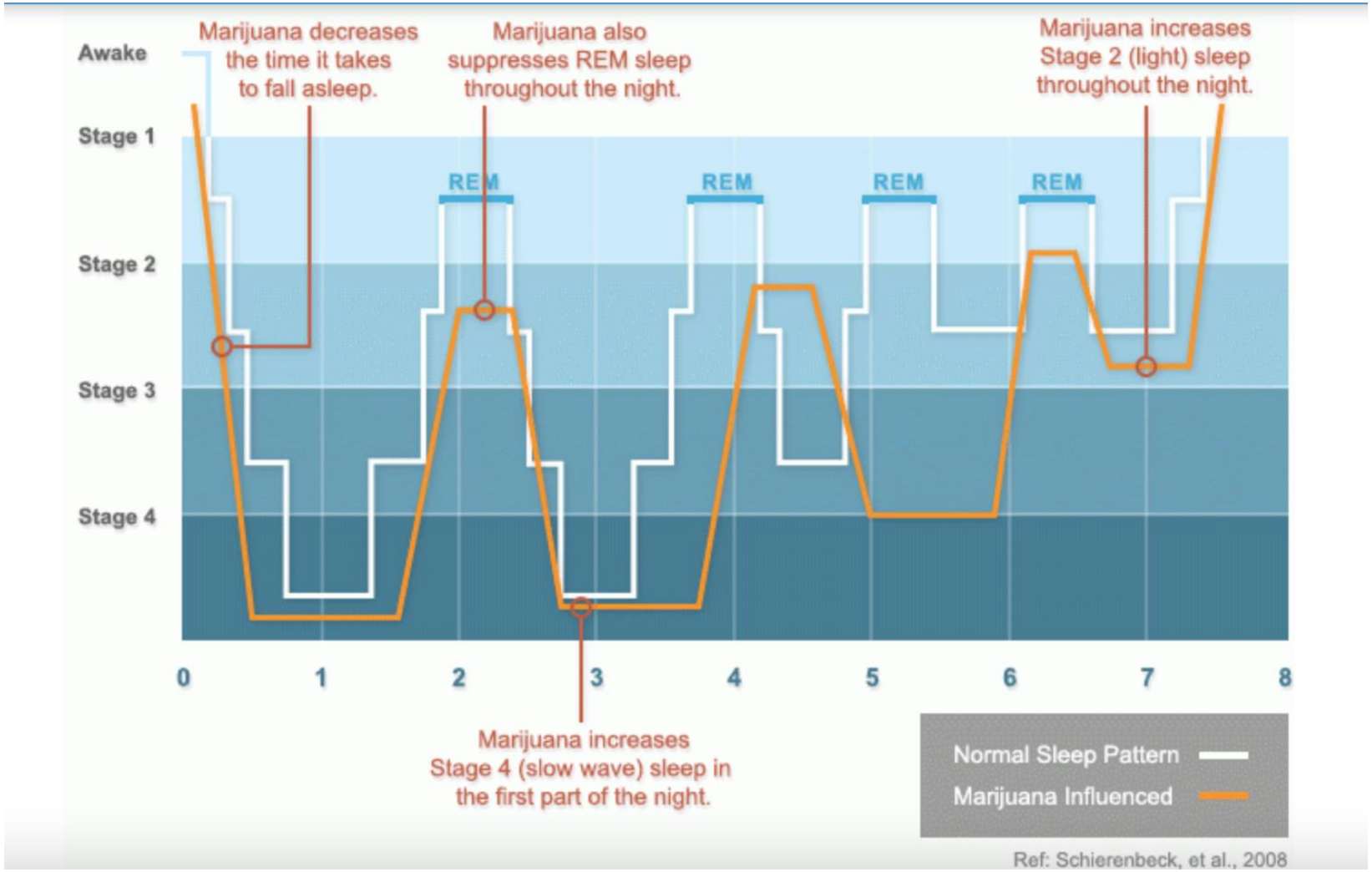
Sleep architecture- marijuana



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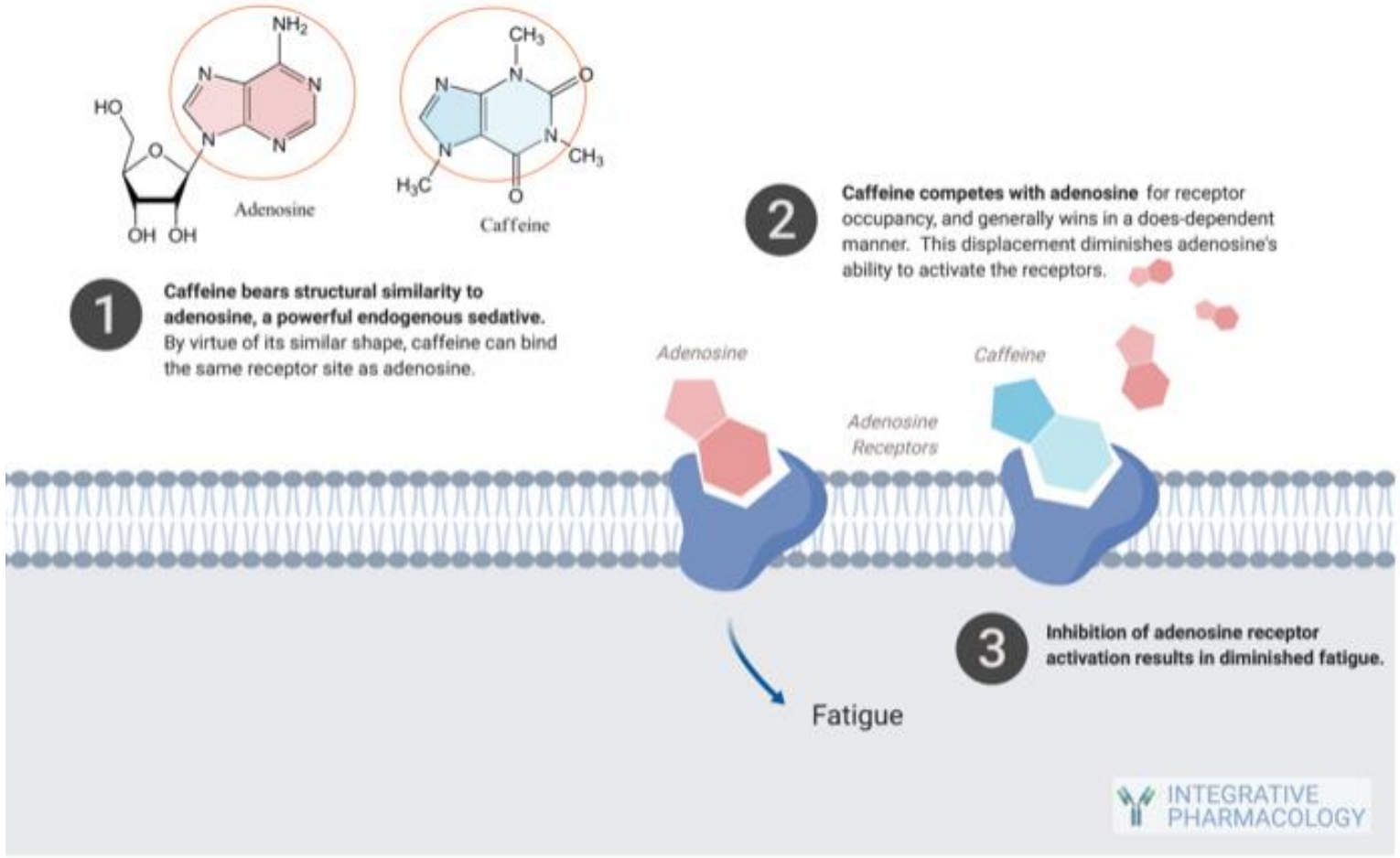
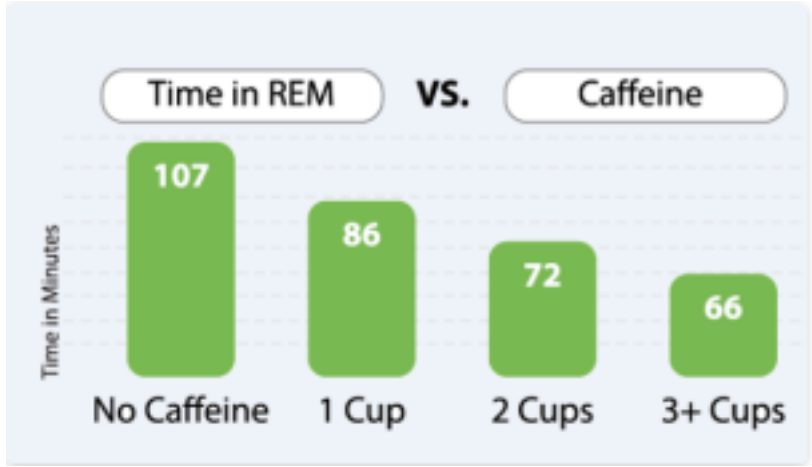
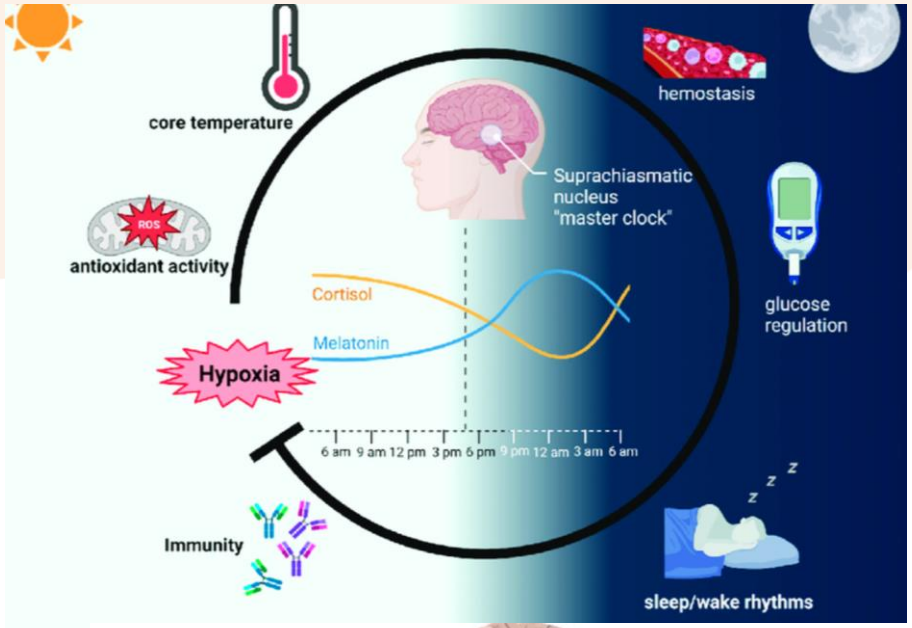
Sleep architecture- Caffeine

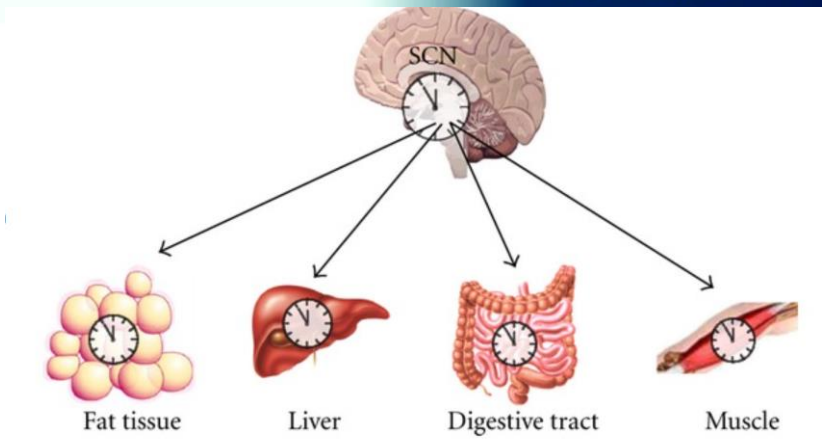




https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3381939/

Sleep Wake Cycle & Clocks





- The sleep-wake state is a circadian rhythm—denoting a roughly 24-h cycle. It is governed by the suprachiasmatic nucleus (SCN) in the anterior hypothalamus—also known as our central circadian clock
- The SCN is aligned with light-dark cues from our external environment, whereby light detected via our optic retina regulates melatonin production by the pineal gland ***to initiate and maintain sleep.***
- Yet circadian rhythms are intrinsic to nearly every aspect of our physiology—from cells to organs, and manifest as peripheral circadian clocks. The SCN communicates with peripheral clocks via neural and hormonal pathways such that all our biological functions operate roughly on a 24-h cycle.

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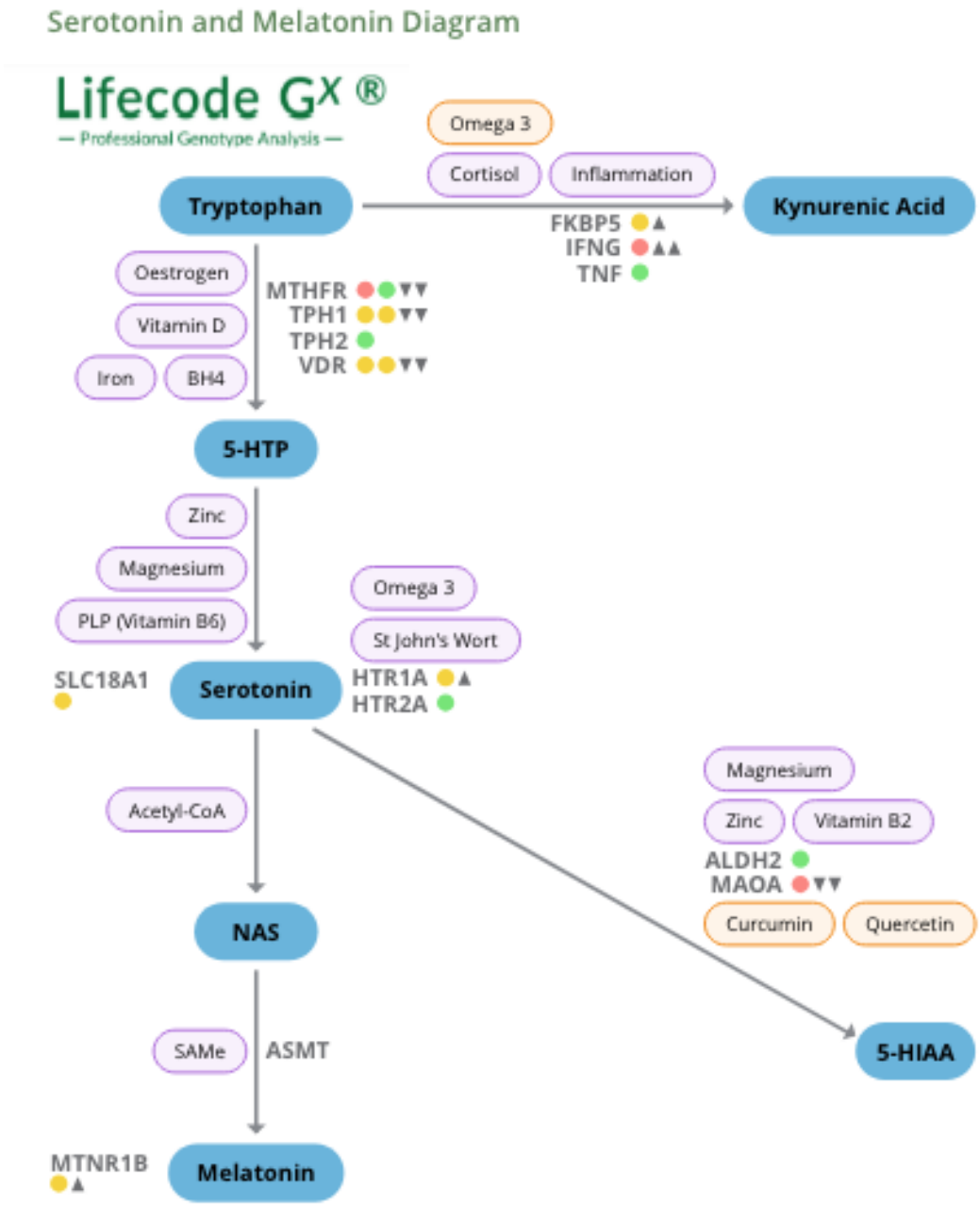
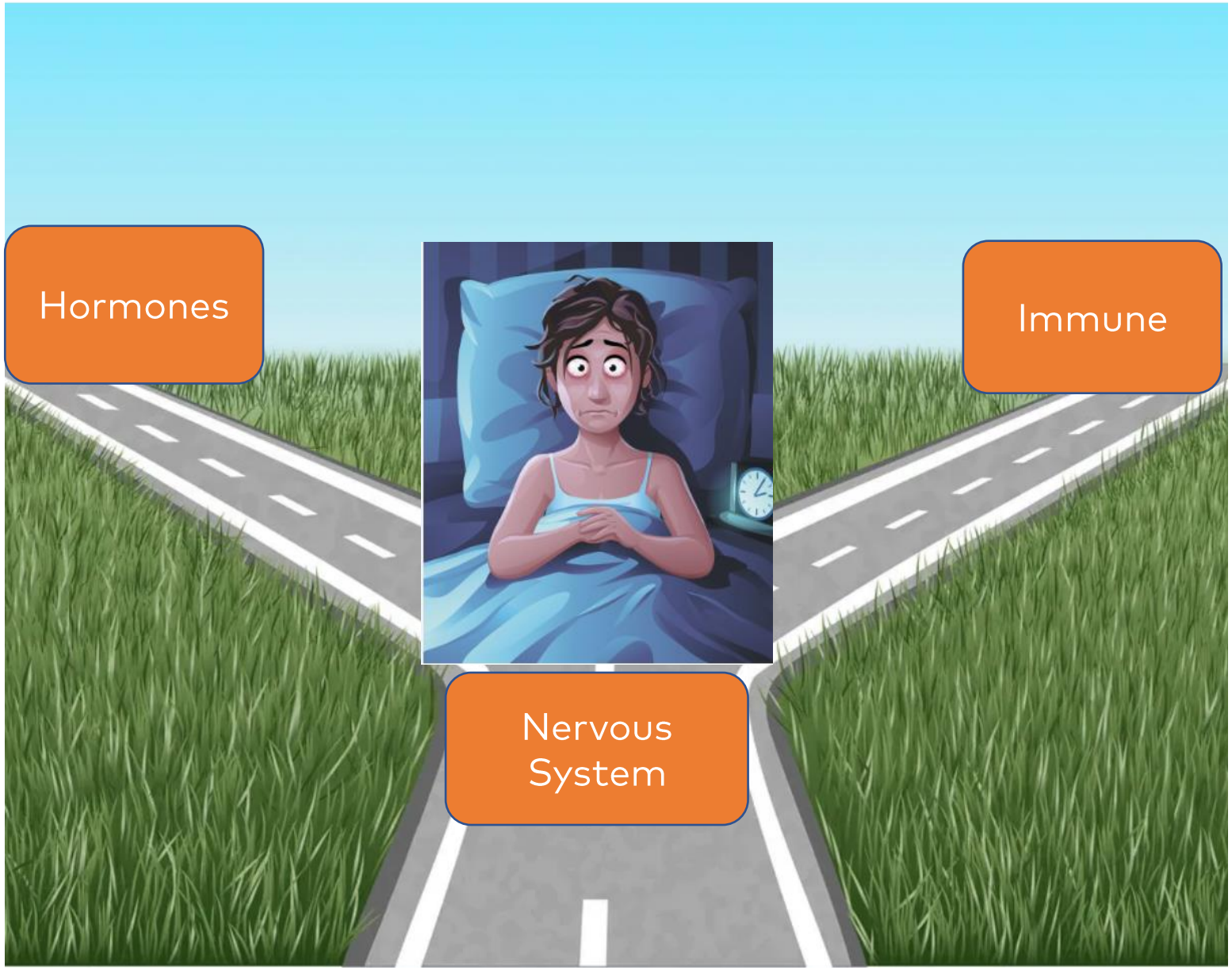
Melatonin

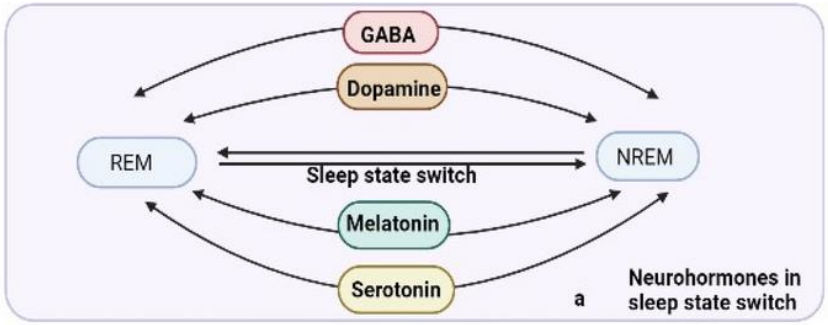
Can they make it?
How do they receive it ?
What is the biotransformation activity?

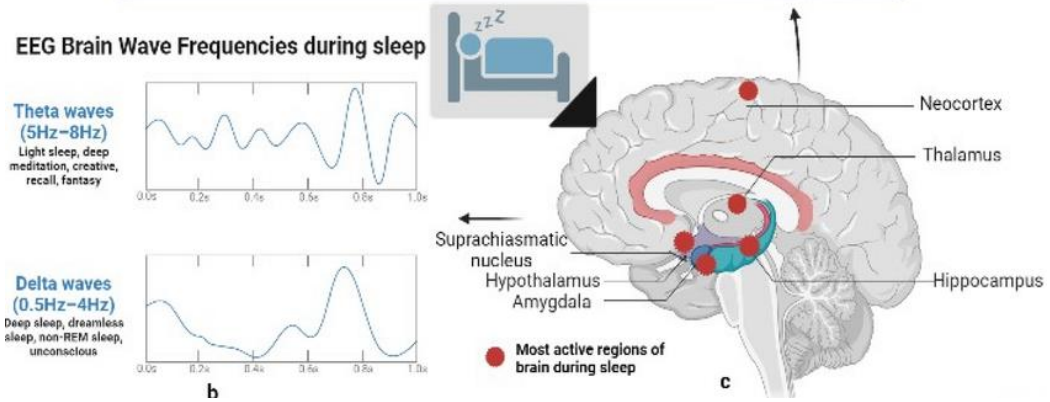


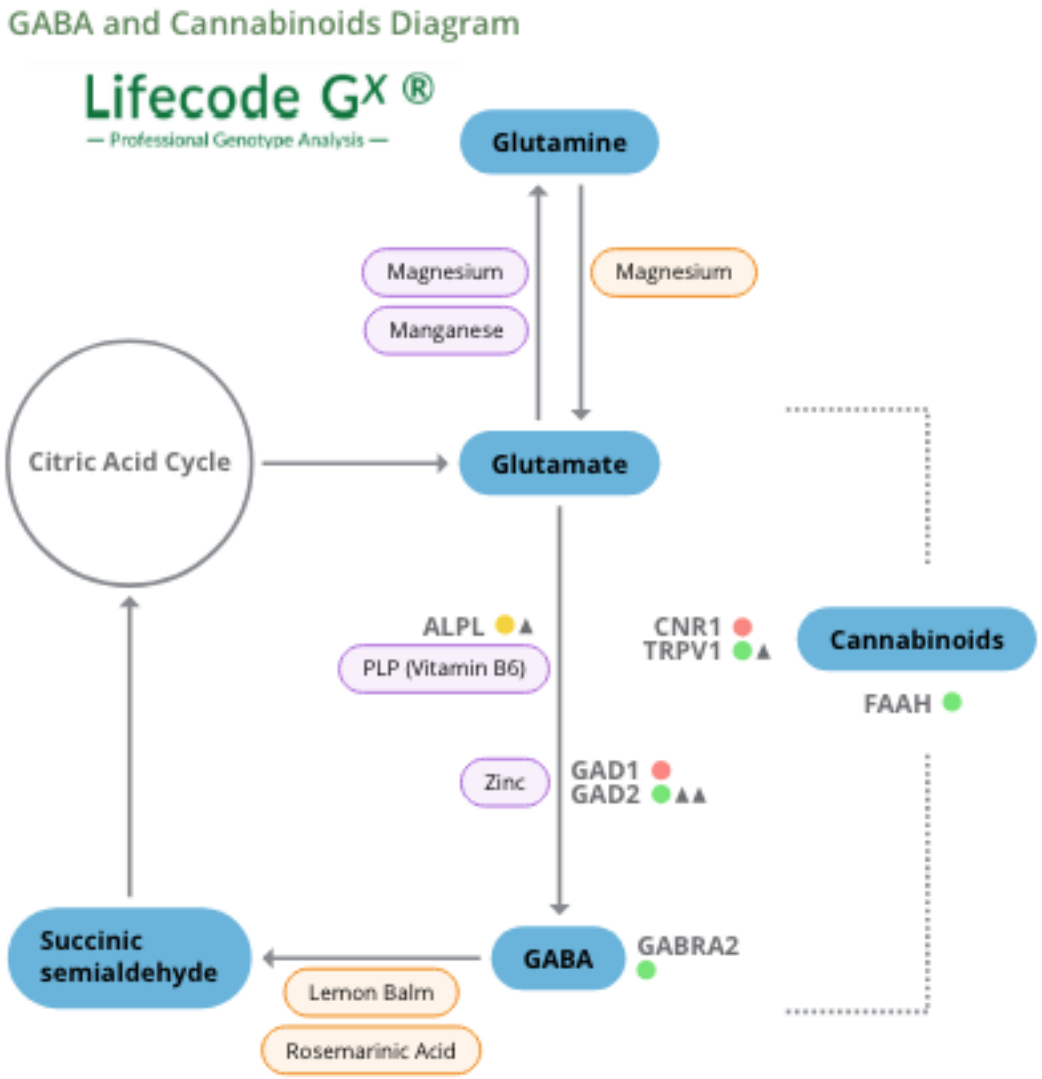
Insomnia Crossroads



Nervous System
GABA





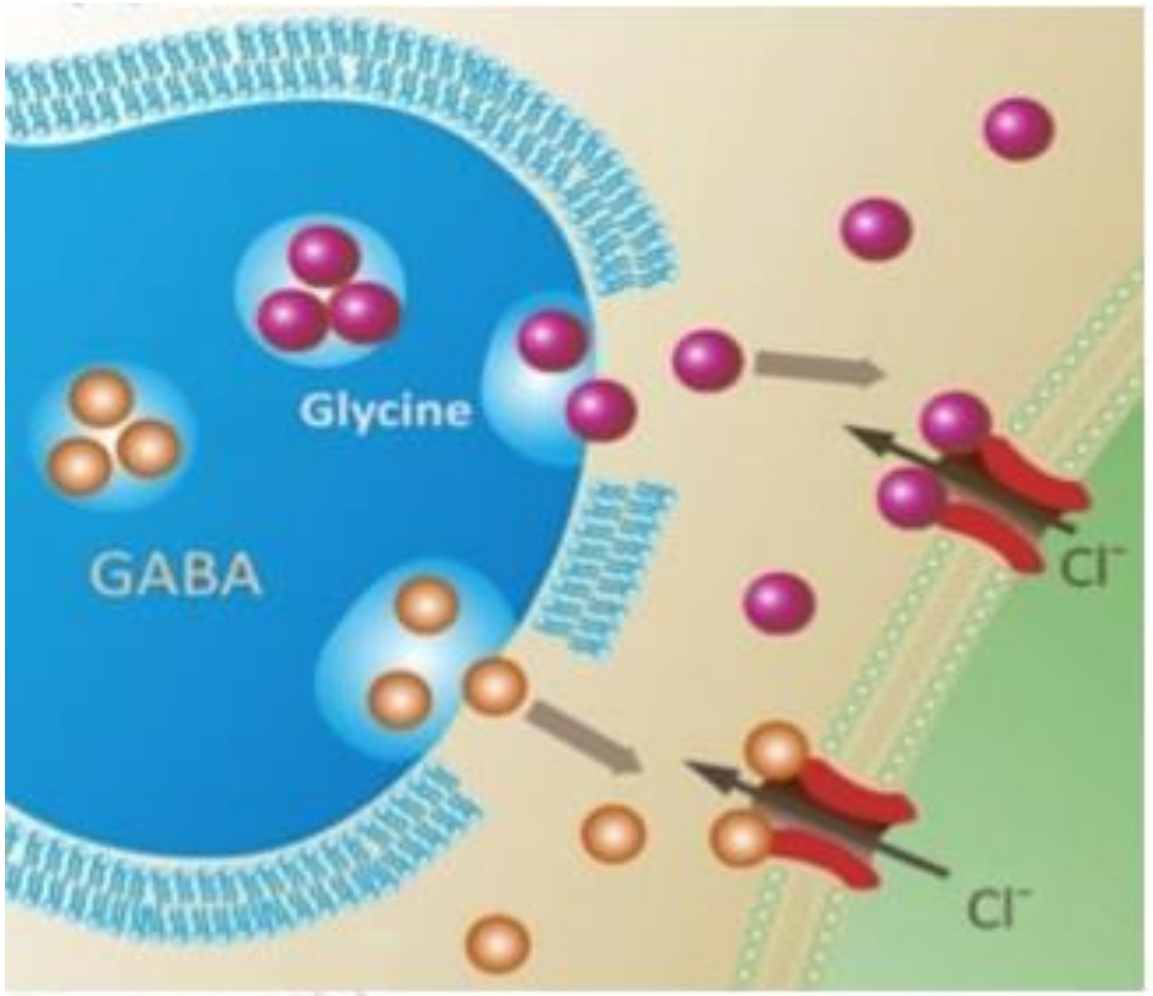


Nervous System GABA- Glycine

GABA is the principal inhibitory NT in CNS

Binding to GABA receptors in the membranes of neuronal junctions, or synapses

Once bound, the receptor opens to allow negatively charged chloride ions to flow into the cell. The negative charge on the inside of the membrane and the positive charge on the outside limits the neuron's ability to respond to further stimulatio

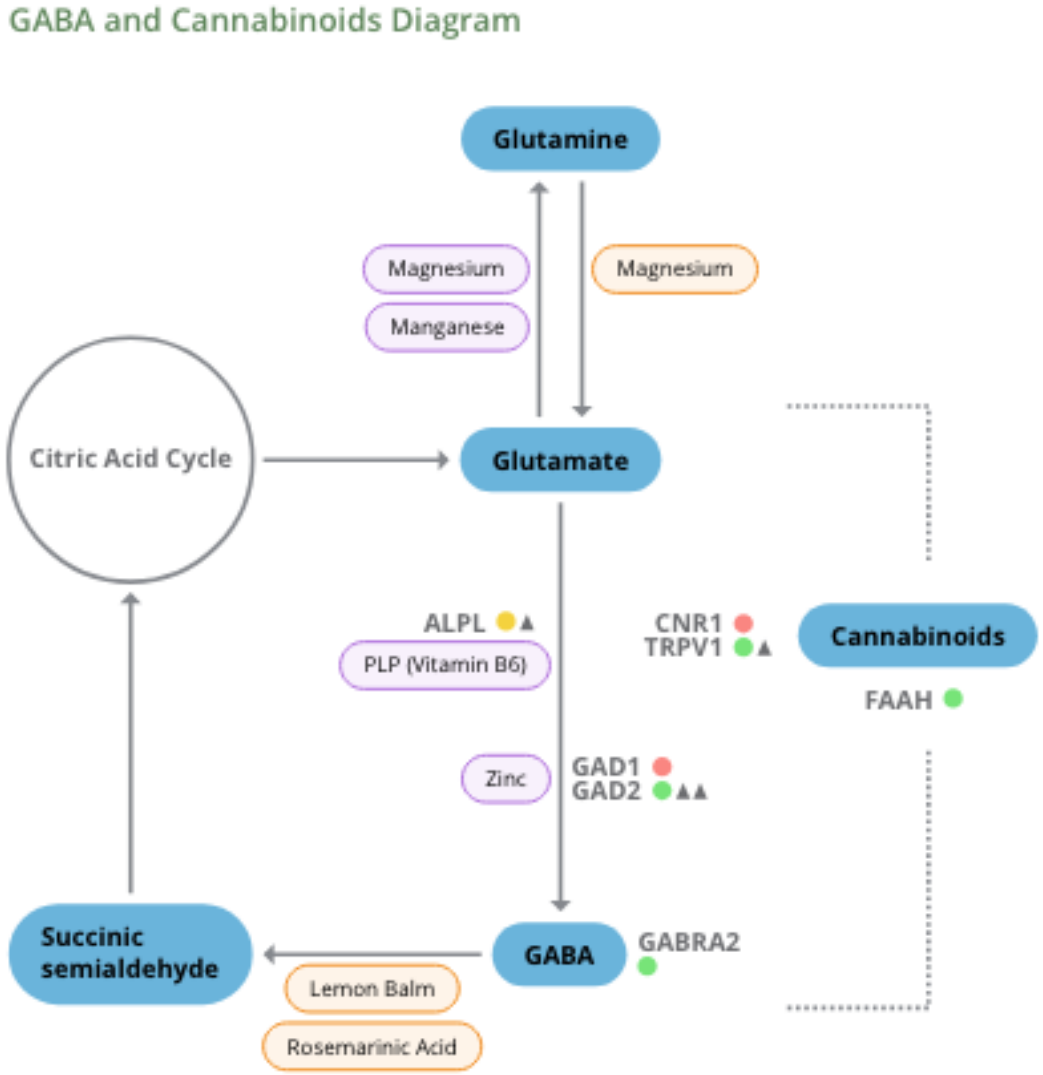


Glycine "ALSO inhibitory amino acid neurotransmitter that binds to chloride ion channels to relax CNS neurons. Oral administration of glycine prior to sleep has been shown to support general subjective and objective indices of sleep quality

Nervous System
L –theanine

Has molecular structure nearly identical to glutamate (excitatory).

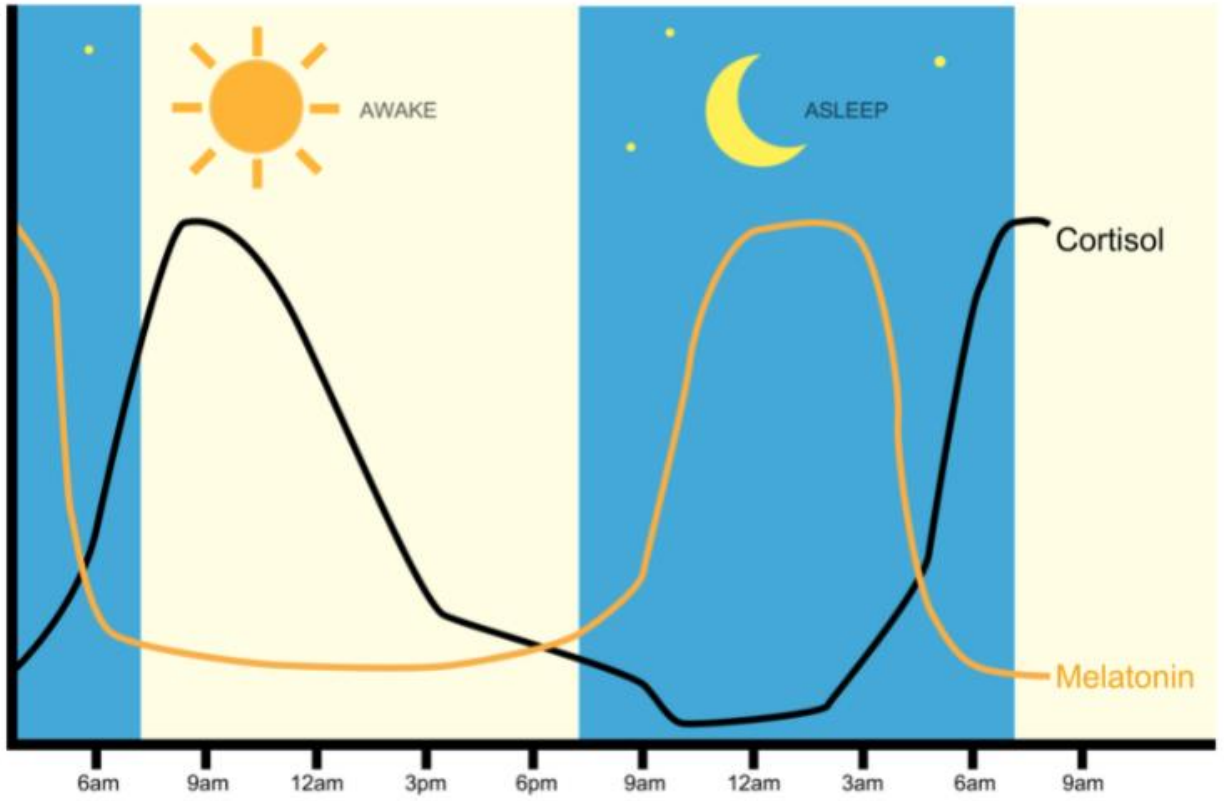
scientists believe L-theanine's structural nuance allows it to act as a "Trojan horse" at receptors. As such, it may compete with glutamate to balance its excitatory effects. Preclinical studies indicate that L-theanine also supports healthy levels of serotonin, dopamine, and GABA in the brain.



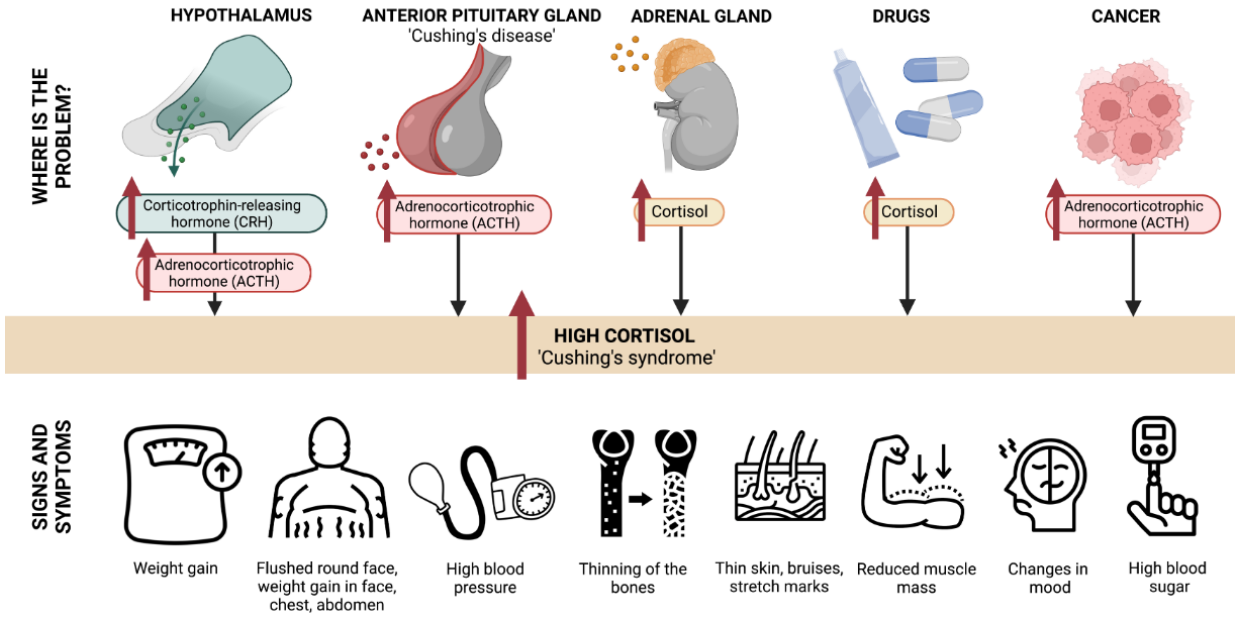
Abdou AM, Higashiguchi S, Horie K, et al. Relaxation and immunity enhancement effects of gamma-aminobutyric acid (GABA) administration in humans. Biofactors. 2006;26(3):201-208.

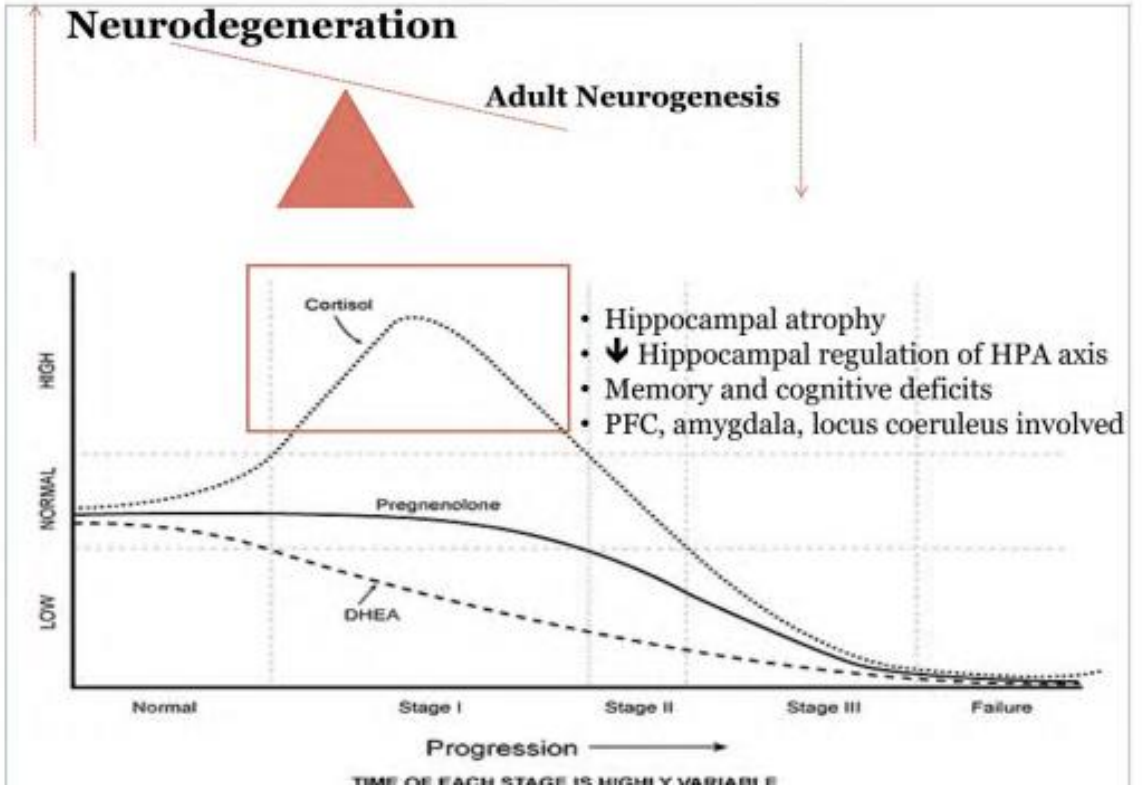
Nervous System- Cortisol

Almost every cell contains receptors for cortisol and so cortisol can have lots of different actions depending on which sort of cells it is acting upon. These effects include; controlling the body's blood sugar ,acting as an anti-inflammatory, influencing memory formation, controlling salt and water balance & influencing blood pressure

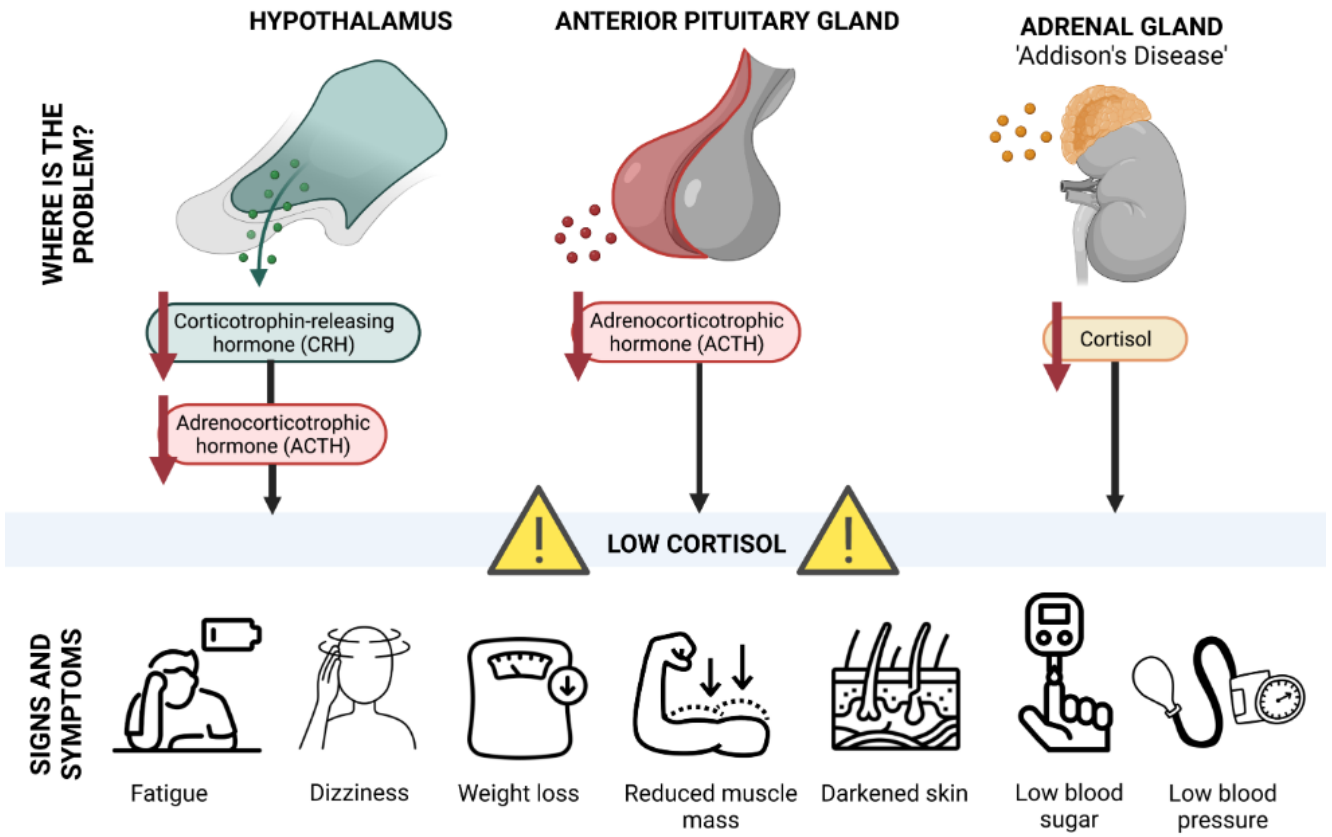


Nervous System- Cortisol (high)

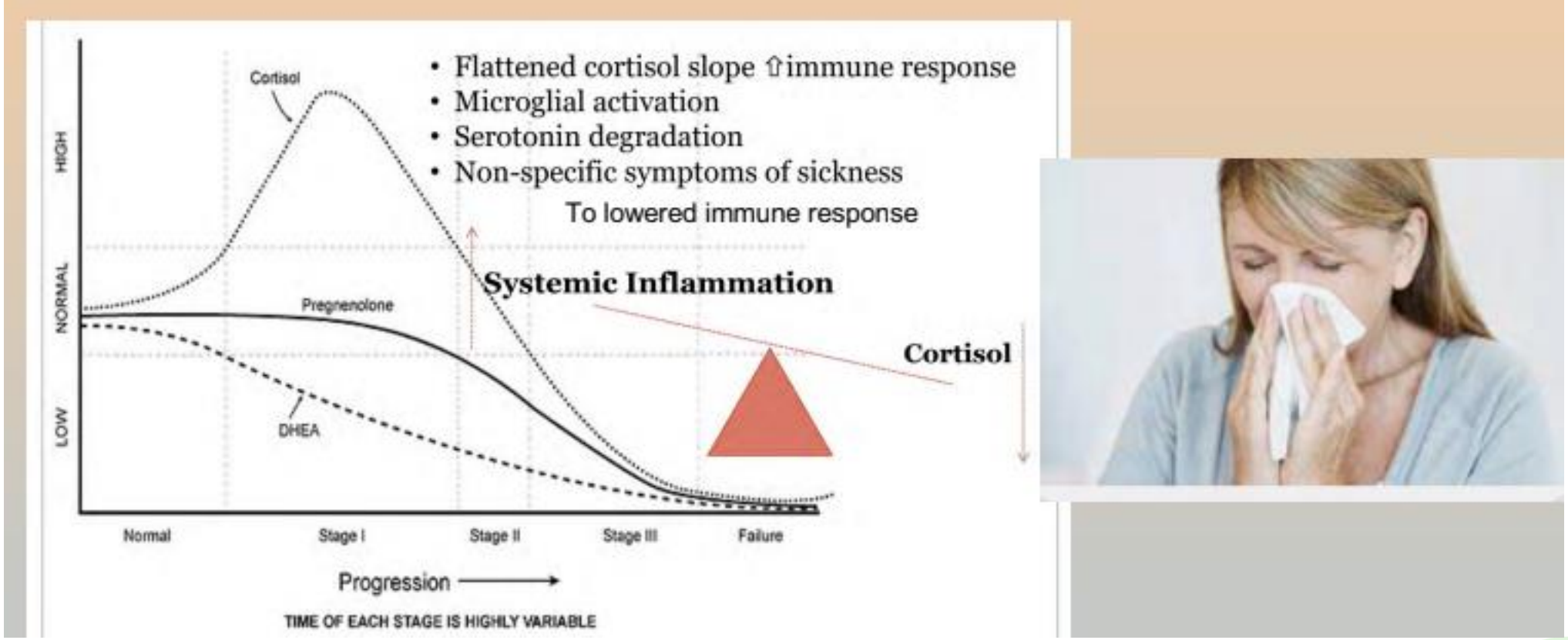


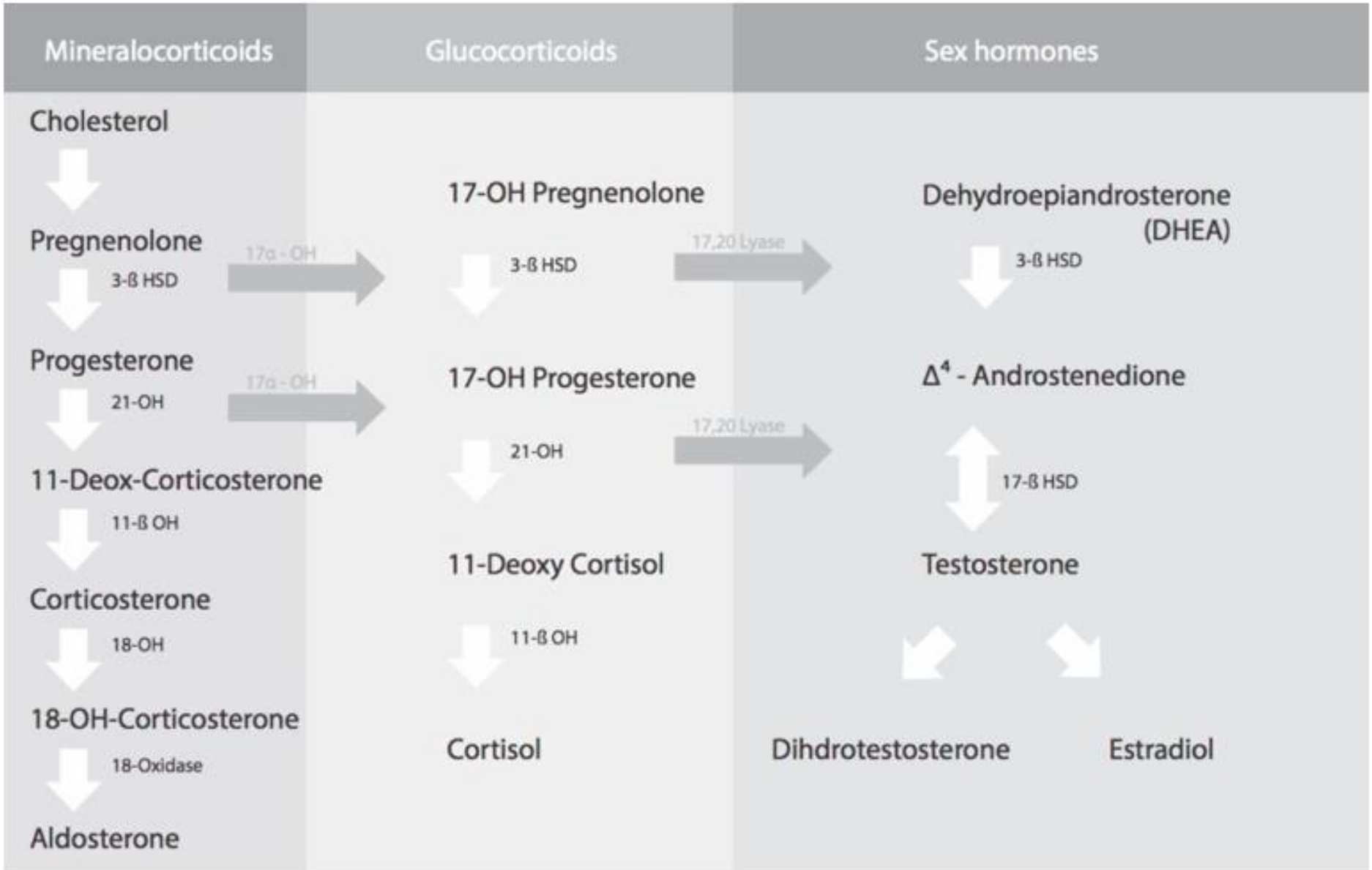


Nervous System- Cortisol (low)



Nervous System- Cortisol (low CAR & flatline)




Mineralocorticoids
Glucocorticoids
Sex hormones
Cholesterol
Pregnenolone
3-ß HSD
Progesterone
21-OH
11-Deox-Corticosterone
11-ß OH
Corticosterone
18-OH
18-OH-Corticosterone
18-Oxidase
Aldosterone
17α - OH
17-OH Pregnenolone
3-ß HSD
17-OH Progesterone
21-OH
11-Deoxy Cortisol
11-ß OH
Cortisol
17,20 Lyase
Dehydroepiandrosterone (DHEA)
3-ß HSD
Δ4 - Androstenedione
17-ß HSD
Testosterone
Dihdrotestosterone
Estradiol

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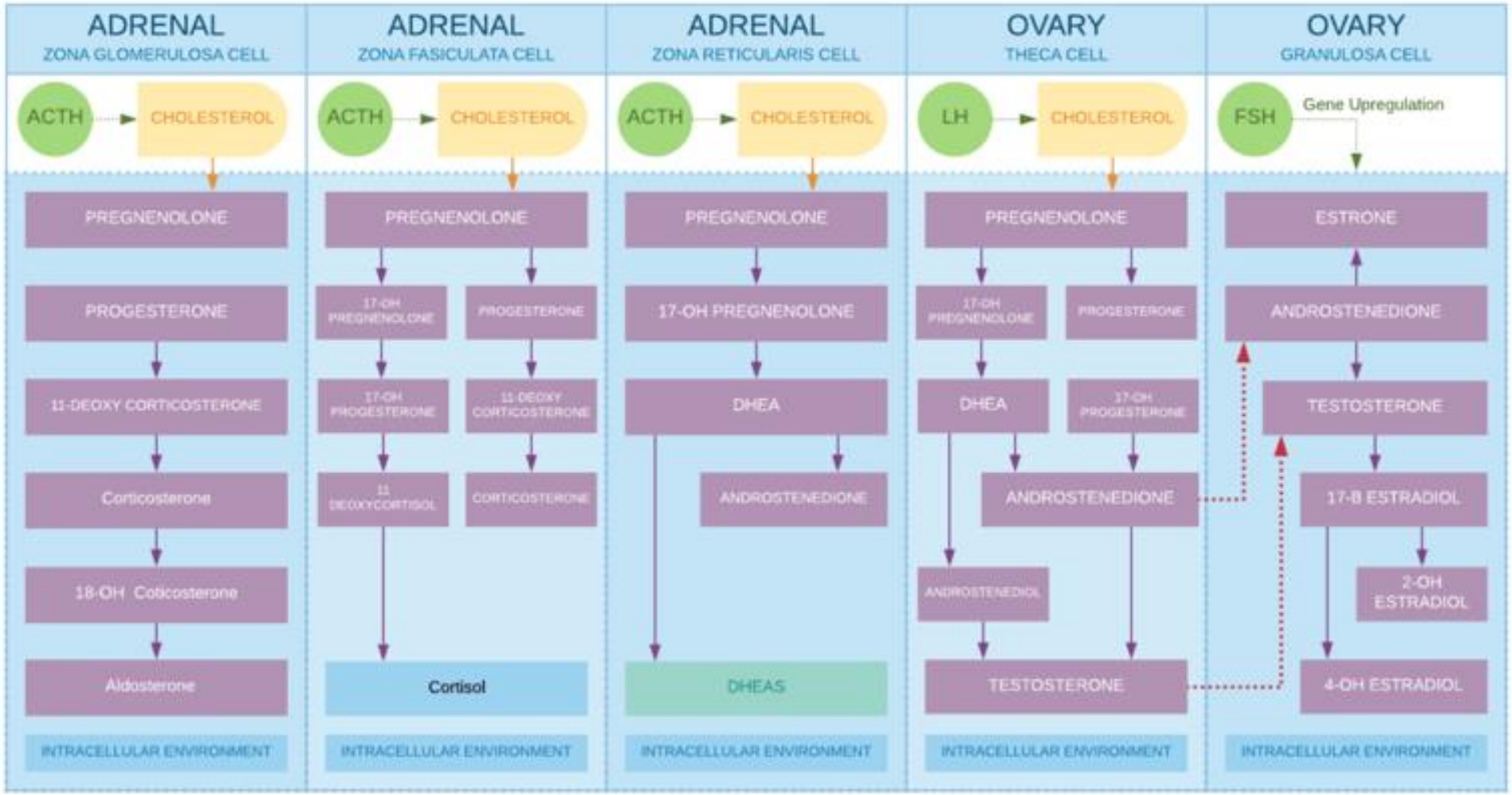

The conversion of pregnenolone into other hormones is determined by the type of endocrine gland itself, as well as enzymes, cellular signals, regulatory hormones and gene activity.

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Hormones – O &P

•Studies show that patients have more slow wave sleep, and deep sleep during the luteal phase of the menstrual cycle
•It has also been found that low levels of progesterone and lack of ovulation (common in PCOS) are associated with significantly more wake time during the night.

During the late luteal phase, when progesterone levels drop (basically, PMS) there is a decrease in sleep quality with more frequent waking during the night.

•Micronized progesterone has been found to improve a variety of sleep parameters in a recent systematic review and meta-analysis.
•Studies have also found an increase in the amount of REM sleep with the luteal rise of progesterone.
•It's thought that many of these effects reflect the actions of metabolites of progesterone like allopregnanolone on the calming GABA receptors in the brain.

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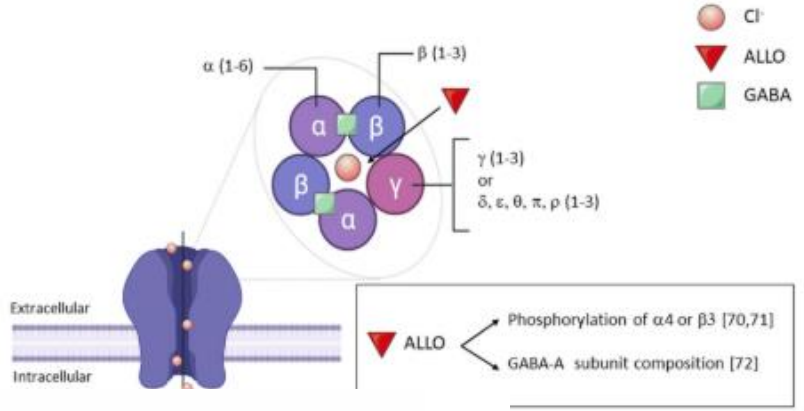
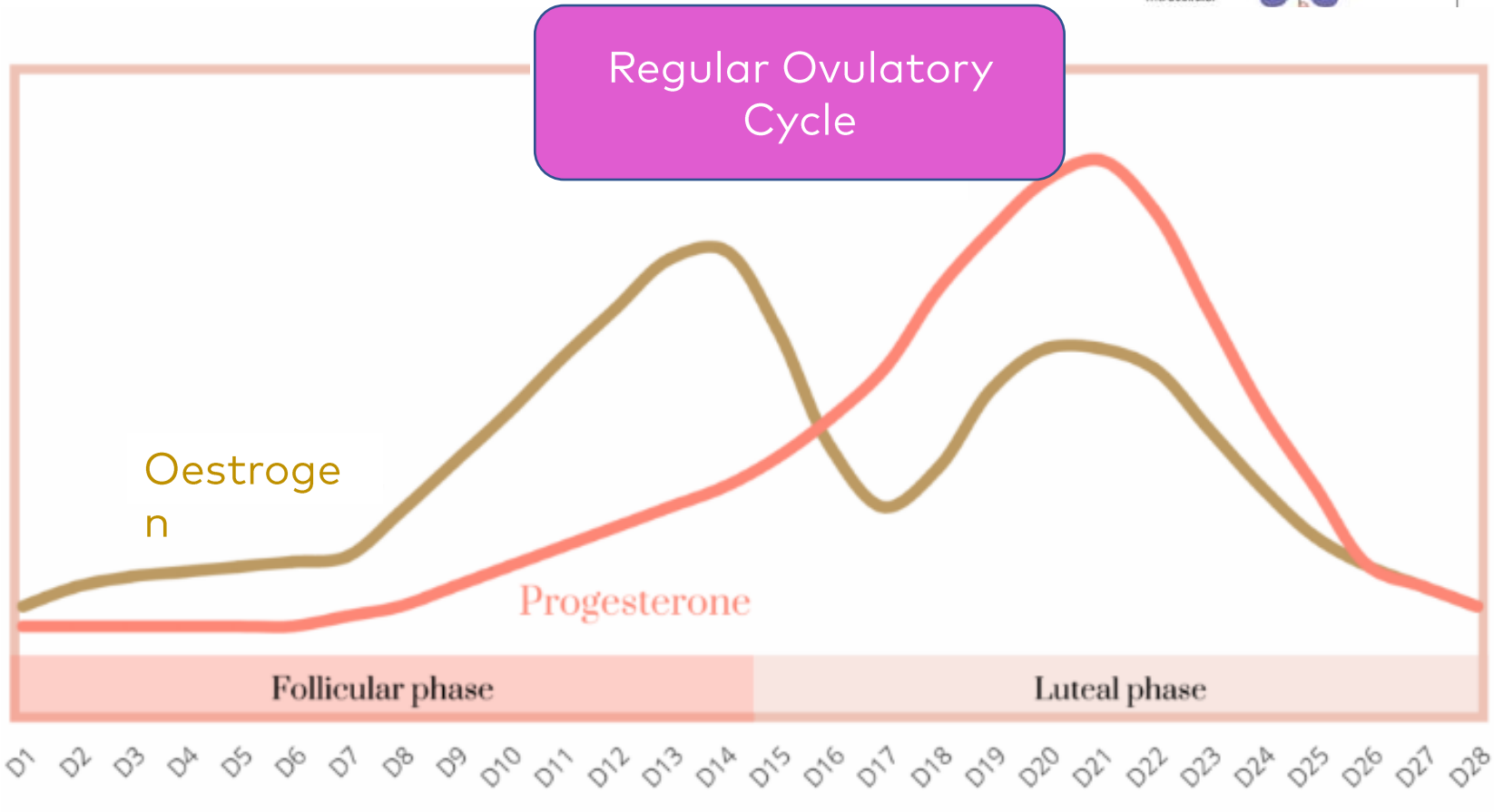
PMID 37091307, 7973319, 11083596, 10607105, 10607105, 33245776



Regular Ovulatory Cycle



Insomnia & The “pauses”

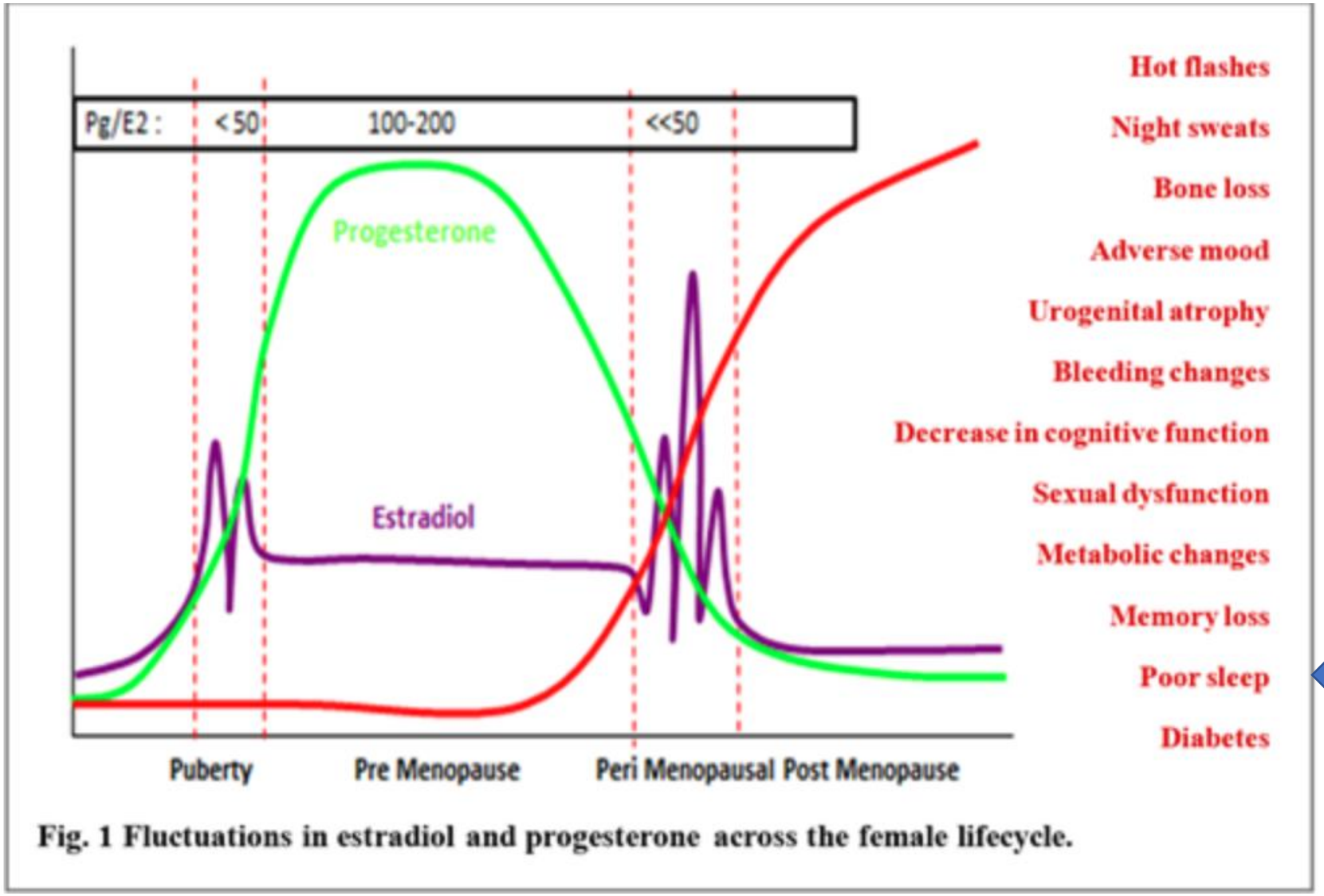


Fig. 1 Fluctuations in estradiol and progesterone across the female lifecycle.

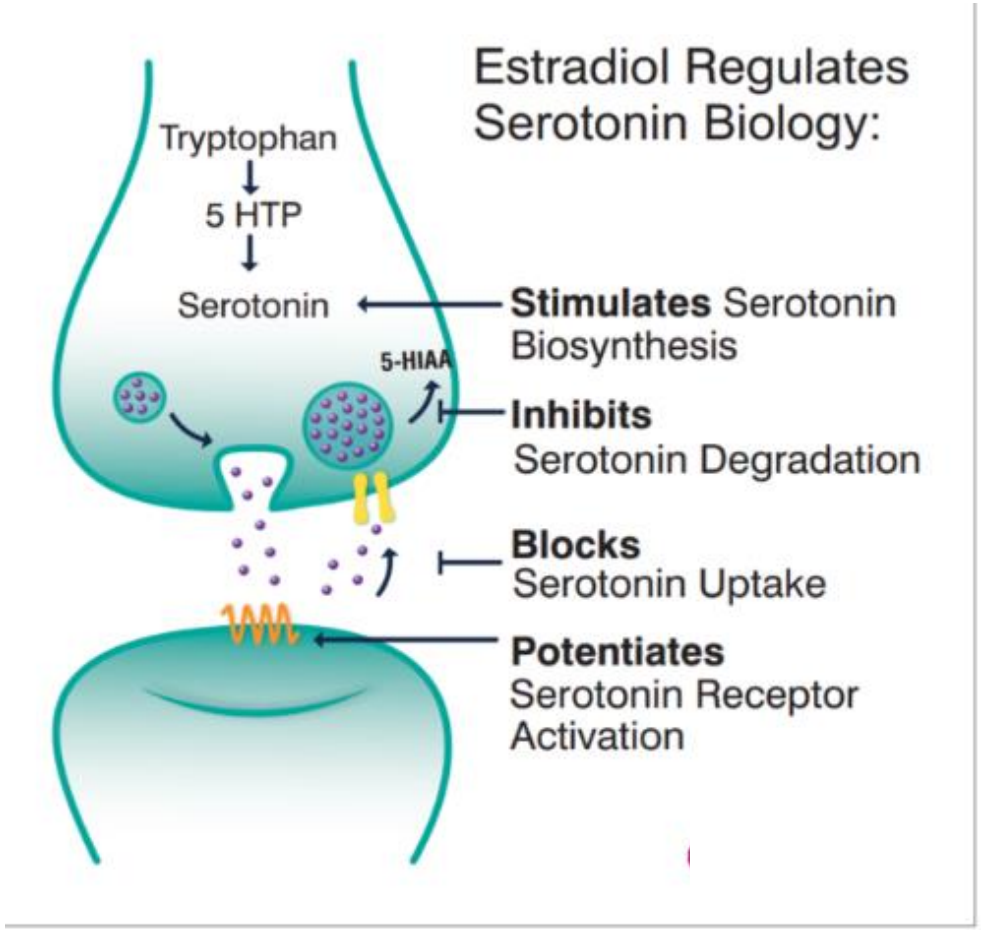
Insomnia & pauses

Oestradiol

- Upregulates the expression of tryptophan hydroxylase, the rate-limiting step in the serotonin biosynthesis pathway;
- Helps augment serotonin receptor activation and subtype expression;
- Blocks re-uptake; slows down degradation by suppressing monoamine oxidase

In other words, in order to have enough serotonin around, you need adequate oestradiol levels.

A newly acquired low serotonin tone perpetuates the tenacity of unremitting sleepless nights, hot flashes, mood swings, and brain fog.



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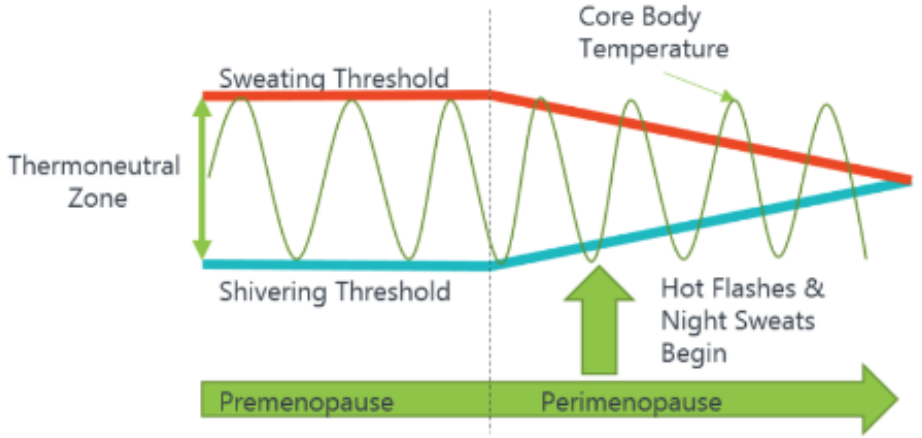
Insomnia & pauses

Oestradiol & NE

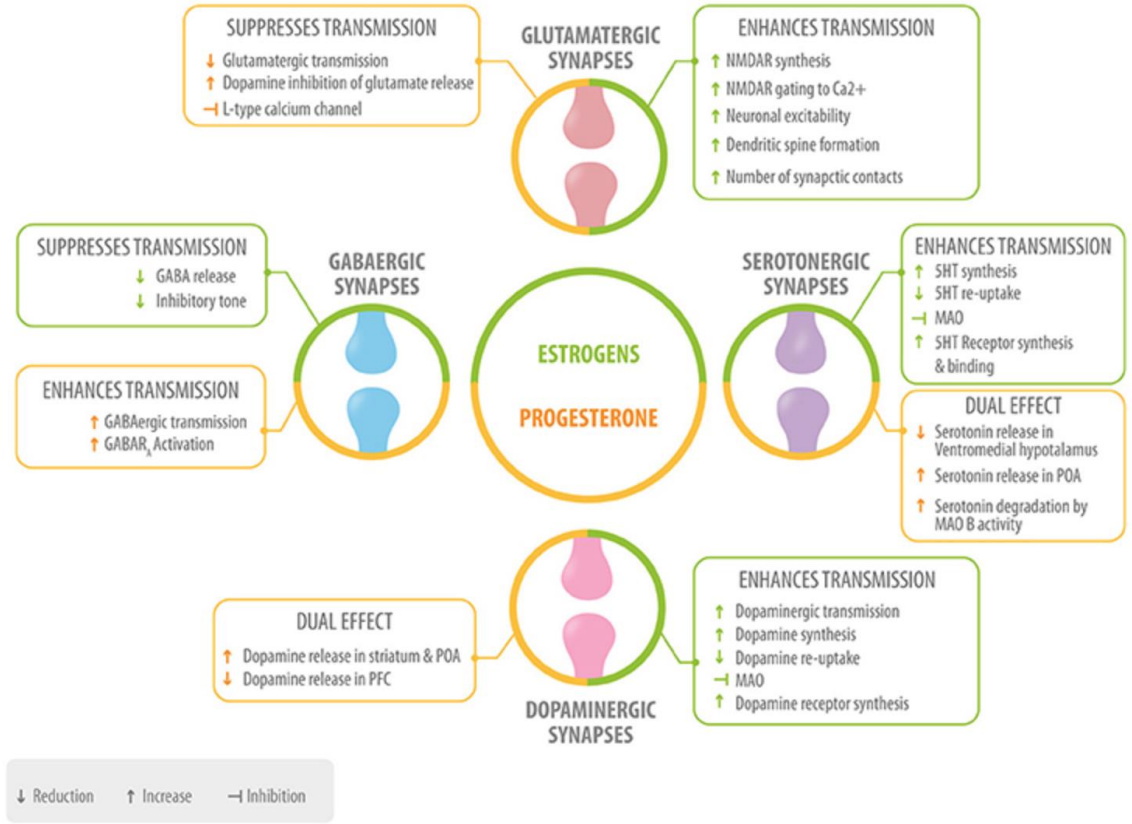
- Decreases in serotonin and oestrogen cause narrowing of the thermoneutral zone

- While decreases in serotonin may lead to hot flushes, the opposite is true of NE. Increases in central NE cause narrowing of the thermoneutral zone



Insomnia & Menopause

Oestrogen and Progesterone in Balance for synthesis, activation and biotransformation NT'S



Gut Brain

There are three main ways the microbiome and brain can affect each other:

•One way is through interacting with the immune system.

•Another is by regulating the production of essential neurotransmitters, like serotonin . Dopamine & melatonin

•A final way is through the vagus nerve, substances produced by your gut microbiome can affect brain functions including sleep.

In one study, researchers analysed samples of the participants' gut bacteria and then used activity watches to record their sleep behaviour over a 30-day period.
The study found that increased microbiome diversity correlated with longer sleep times and better sleep efficiency,

PMID: 31589627

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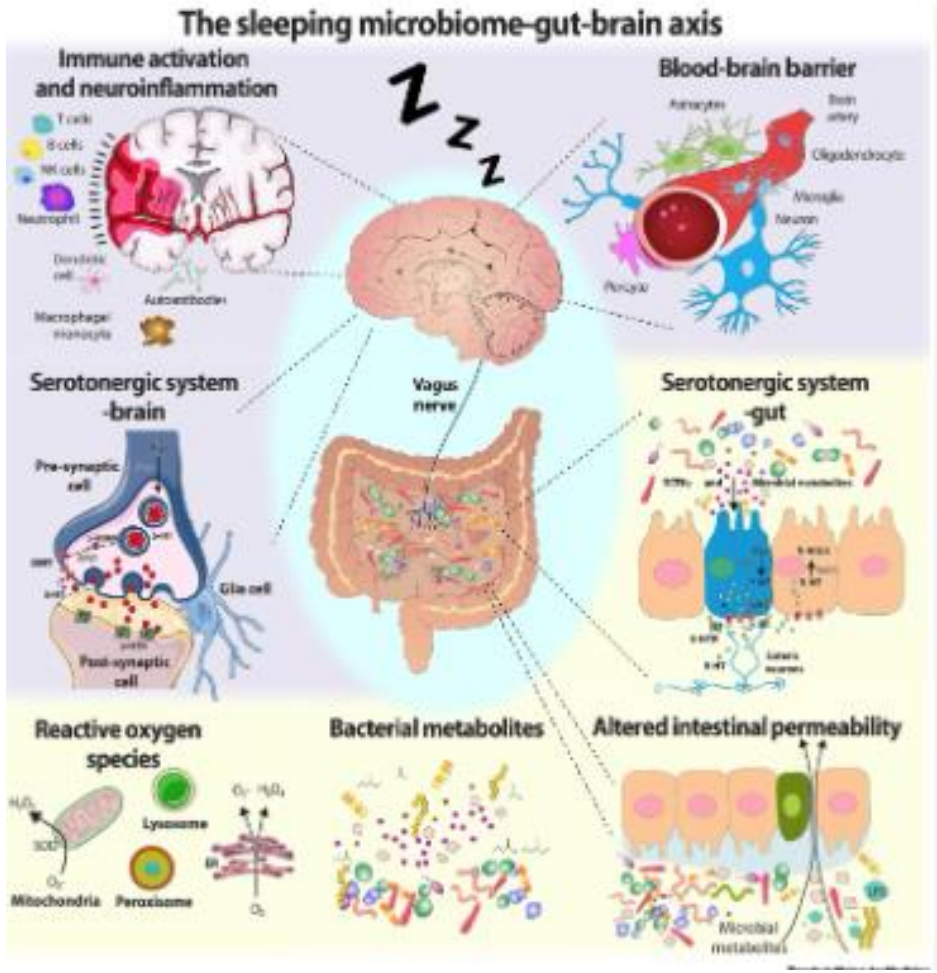
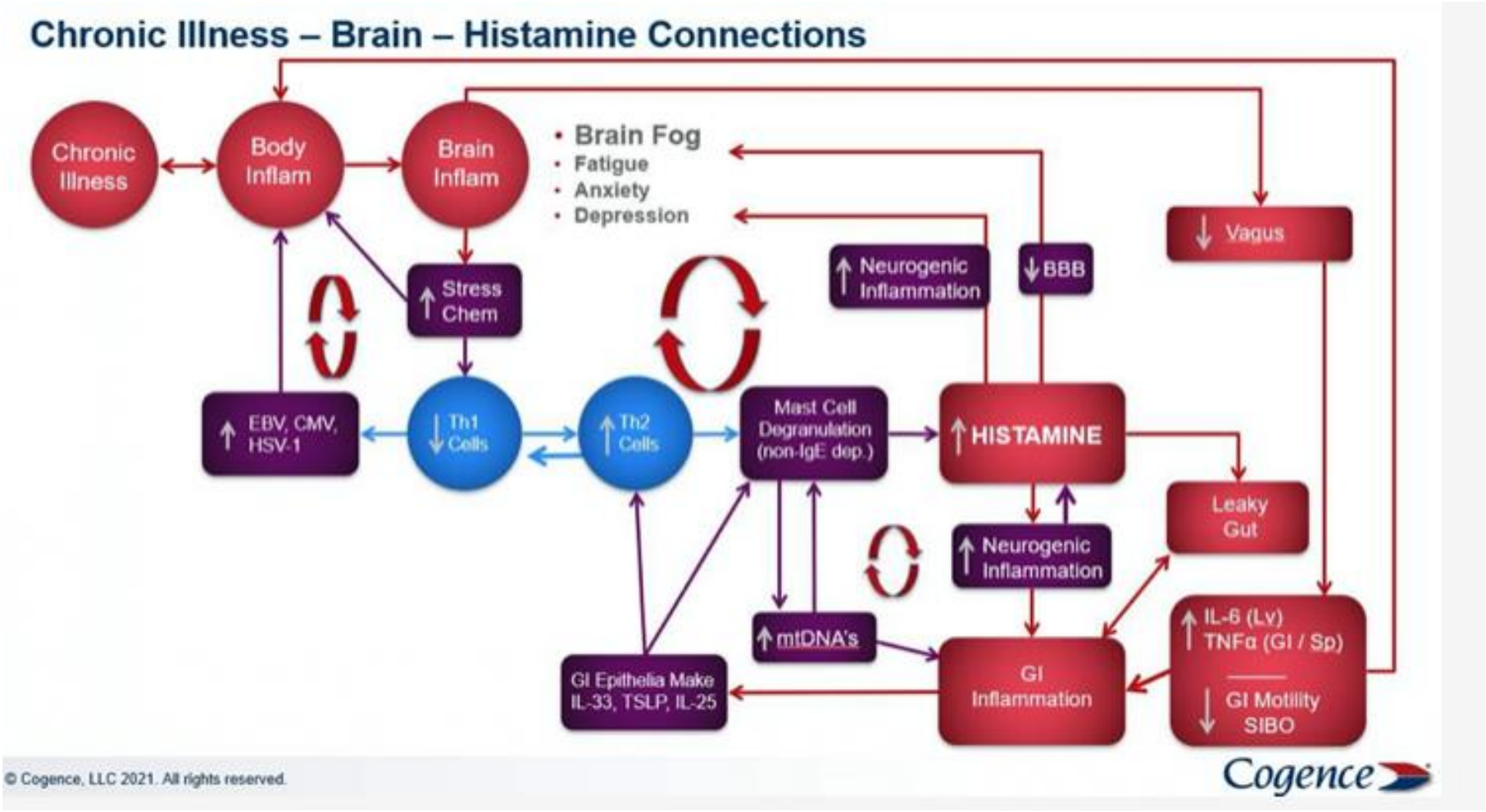
Gut Brain

GI bacterial peptides increase circulating pro-inflammatory cytokines , e.g.
IL-1 and IL-6 stimulate hypothalamic release of CRH



Scientists at the University of Colorado Boulder conducted a study to find out if sleep can be improved by prebiotics – dietary. The research suggested that the answer to a good night's sleep may lie in the gut. "We found that dietary prebiotics can improve non-REM sleep, as well as REM sleep after a stressful event"- Robert Thompson, the first author of the study published in the journal *Frontiers in Behavioural Neuroscience*

Insomnia; Stress & Immune



Nervous System

3g bedtime

Montmorency Cherries, contains a natural source of melatonin+ 3g Glycine

L-theanine, magnesium, a novel organic extract of Saffron with active-form vitamin B6

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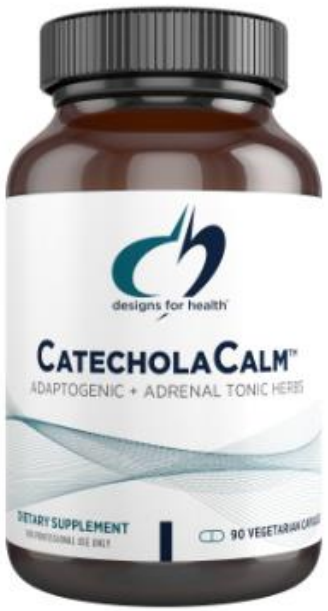
Nervous –Cortisol



Vitamin C (As Ascorbic Acid)
Thiamin (Vitamin B-1) (As Thiamin HCl)
Riboflavin (Vitamin B-2) (As Riboflavin-5-Phosphate)
Vitamin B-6 (As Pyridoxal-5-Phosphate)
Vitamin B-12 (As Methylcobalamin)
Pantothenic Acid (D-Calcium Pantothenate)
Magnesium (As Di-Magnesium Malate)
Taurine
L-Theanine
Lemon Balm (Melissa officinalis) (Leaves) [Standardized to contain 3% rosmarinic acid]
Passion Flower (Passiflora incarnate) (Flower) [Standardized to contain 3.5% flavonoids]
Valerian (Valeriana officinalis) (Root) [Standardized to contain 0.8% valerenic acid]
Ashwagandha (Withania somnifera) (Root) [Standardized to contain 1.5% withanolides]
Phosphatidylserine (From sunflower lecithin)

resilience builder reduce anxiety and improve sleep and energy

4 softgels (they are v small) first thing or with breakfast for 2 weeks, then reduce the dose to 2 first thing or with breakfast

Anxious, wired , "manic"
Hyper vigilant

Magnolia with Phellodendron (Relora®)
Phosphatidylserine
L-theanine & Lemon Balm

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Hypervigilant = Neurological suppo

- Use in

  Post infection

-
- LPS-induced neuroinflammation
- RG3 prevents neuronal damage in continual stress & hyper cortisol types

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Gut- Sleep

- Bifidobacterium longum 1714
- Lemon balm leaf extract (Melissae officinalis L)
- L-theanine

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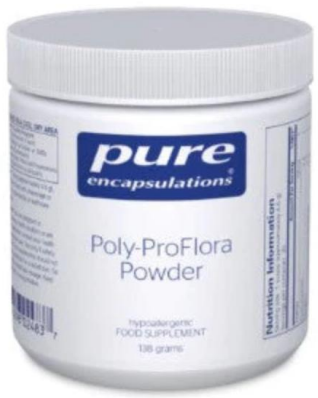
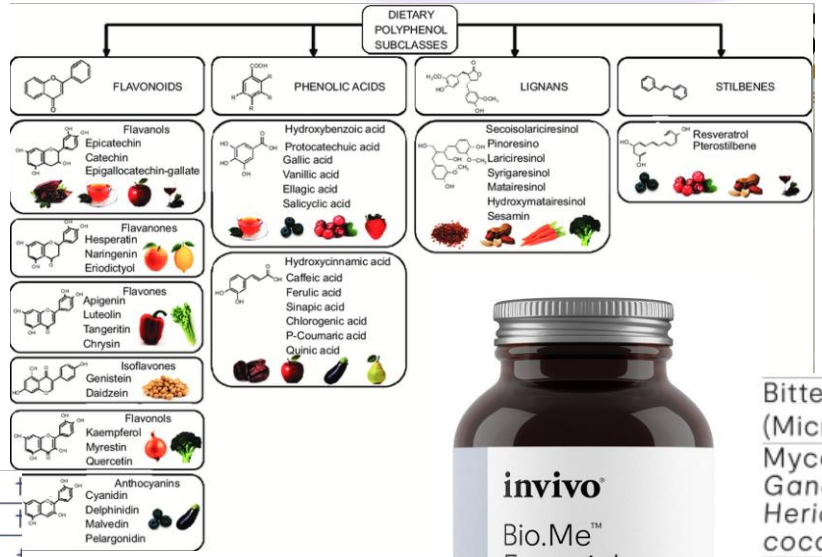
Polyphenols



PreticX™ xylooligosaccharide (XOS)	1.4 g	†
BioEcolians® α-glucooligosaccharide (α-GOS)	1 g	†
Cranberry (*Vaccinium macrocarpon*) fruit extract (standardized to contain 12 mg proanthocyanidins [PACs])	1.2 g	†
Blueberry (*Vaccinium angustifolium*) fruit extract (standardized to contain 4% polyphenols)	100 mg	†
Pomegranate (*Punica granatum*) fruit juice powder	500 mg	†



Bitter Orange Bioflavonoid Extract (MicrobiomeX®)	500mg
MycoMix®Immun (*Cordyceps spp., Ganoderma lucidum, Lentinula edodes, Hericium erinaceus, Grifola frondosa, Poria cocos, Trametes versicolor, Agaricus blazei*)	300mg
Ashwagandha Root Extract (1.5% Withanolide)	250mg
Cocoa Extract (20% Theobromine)	200mg
Blackcurrant Extract (11% Anthocyanins)	200mg
Pomegranate Powder	200mg
Green Tea Powder	100mg
Grapeseed Extract 10:1 (95% Proanthocyanins)	100mg
Chamomile Powder	75mg
Lemon Balm	50mg

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Mind and Sleep

Affron® Crocus sativus (Saffron) extract

equivalent stigma dry

Passiflora incarnata (Passionflower) extract

equivalent passiflora incarnata herb dry

Matricaria chamomile (Chamomile) extract

equivalent chamomile flower dry

Withania somnifera (Withania) extract

equivalent withania root dry

Lavender oil

the bioactive peptide – alpha
casozepine – from casein.

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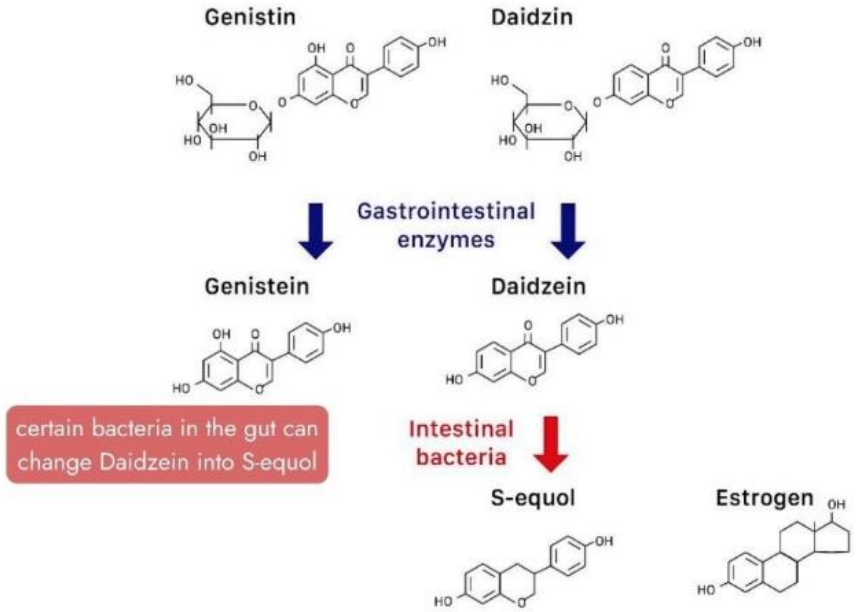
Phytoestogen – EQUOL



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Coming soon.....

SLEEP OIL

SLEEP GEL

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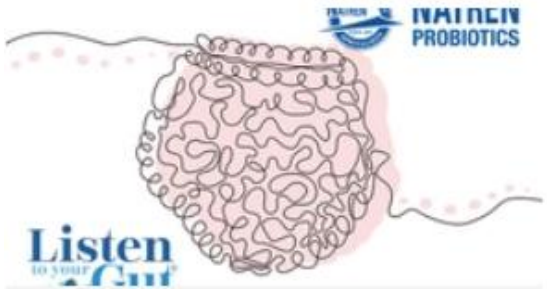
What's coming

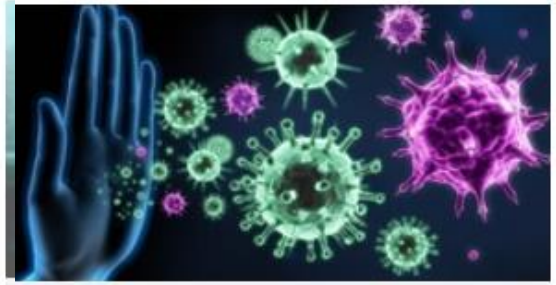


Ultimate Gut Health with Jini and Natasha

Jini Patel Thompson (author of international bestseller, Listen To Your Gut) and Natasha Trenev (founder...

Read more

2nd of May at 7:00 pm



Designs for Health® | Integrative Strategies for Supporting Immunity &...

In this webinar, Michael Jurgelewicz will take you through our favourite Immune Designs for Health®...

Read more

15th May at 7 pm

The Roadmap Series V: Mapping Reflux & GERD with Debbie...

21st of May at 12:30 pm

Register https://www.amritanutrition.co.uk/pages/educational-events

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