

# Support for Insomnia / Sleep

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# Sleep

- Sleep helps regulate:
  - Circadian rhythms, including learning and memory
  - Growth hormone
  - Cellular repair
  - Regulation of immunity
  - Insulin and glucose regulation
  - WEIGHT
  - Inflammatory processes
  - Core body temperature
  - Melatonin secretion by the pineal gland
  - Plasma levels of DHEA and cortisol

# Sleep

- Most individuals should obtain at least 7-9 hours of quality sleep a night
  - (Centers for Disease Control, CDC, 2011). Centers for Disease Control (CDC). [www.cdc.gov](http://www.cdc.gov).
- 67% of Americans experience frequent problems sleeping
- 43% say lack of sleep interferes with their daily activities.
- Between 9-12% of the population are clinically diagnosed with insomnia.
  - National Sleep Foundation. [www.sleepfoundation.com](http://www.sleepfoundation.com).
  - Ohayon MM. Epidemiology of insomnia: what we know and what we still need to learn. Sleep Med Rev. 2002;6(2):97-111.

# Sleep Deprivation and Weight Gain Linked

- Subjects that avg. 4 hr. sleep/night:
  - ↓ Leptin (18%), ↑ Ghrelin (28%)
  - ↑ reported hunger (24%), ↑ carb cravings, especially sweets, salty, and starchy high calorie snacks
  - (Ann Intern Med, 2004, vol. 141, pp. 846—850)
- > 1,000 volunteers: those that avg. , 5 hr sleep had ↓ leptin (15.5%), ↑ ghrelin (14.9%), ↑ BMI (3.6%). Results were regardless of the subjects diet and exercise habits.

(Mignot et al, Stanford School of Medicine Dec. 2004)

# Sleep Deprivation/Weight Gain Linked

- Heymsfield and Gangwisch analyzed NHANES I data: reported subjects with avg. 5hr./night sleep had 73% increased likelihood of obesity over those who slept 7-9 hr/night. ( Findings reported at the annual scientific meeting of the North American Society for the Study of Obesity. Nov, 2004)
- Study reported a linear relationship: reduced amounts of sleep are associated with overweight and obesity (Arch. Intern Med, 2005;165:25-30)

# Sleep Deficits

- Chronic partial sleep loss associated with decreased glucose tolerance, decreased leptin levels, increases in evening cortisol levels, adverse cardiovascular events
- Lack of sleep increases heart attack risk and development of arterial plaques
- Lack of quality sleep negatively effects athletic performance

Spiegel et al. Lancet 1999 354; 1435-39.

Spiegel et al. J Clin Endocrin Metab 2004, 89(11);5762-71.

Taylor DJ, et al. Sleep. 2007;30(2):213-18

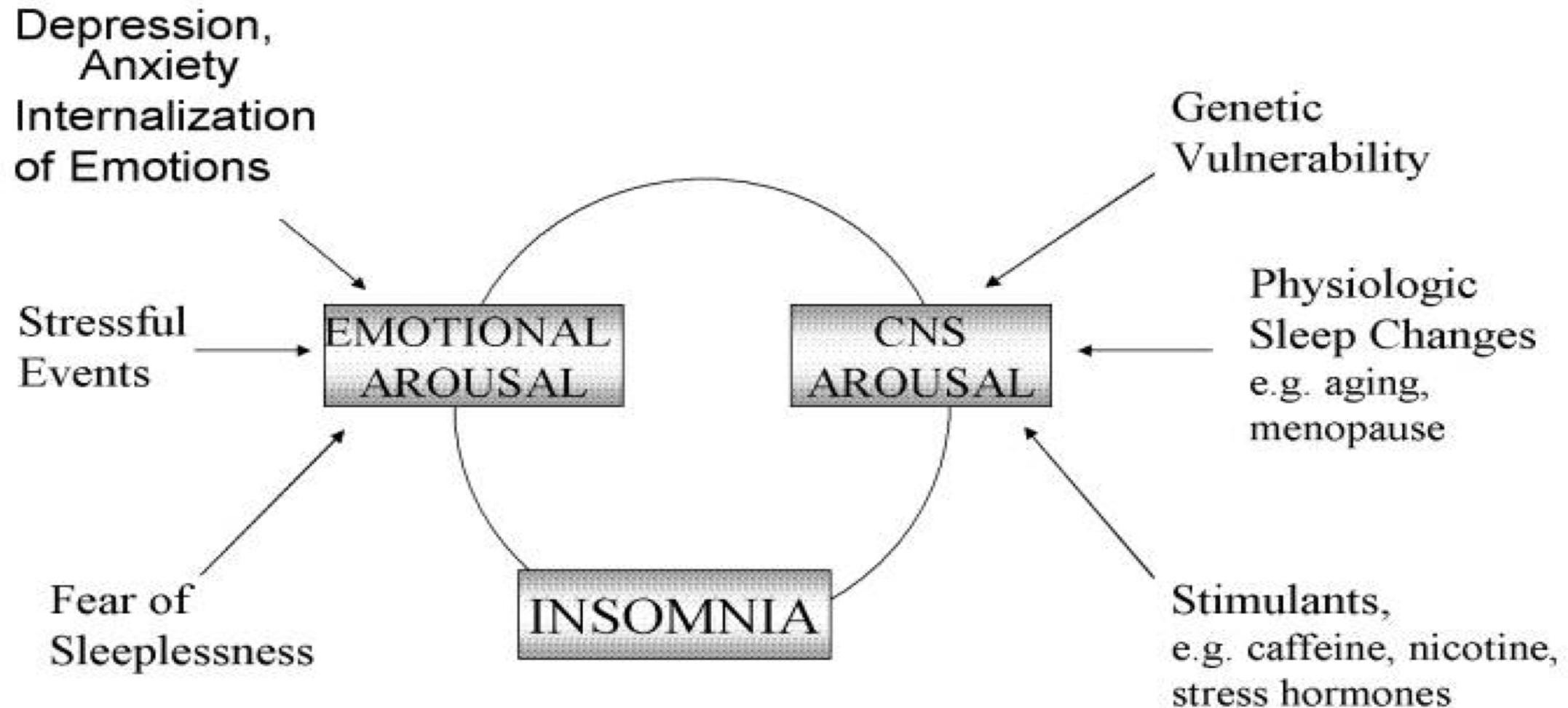
Kapsimalis F, et. al. Sleep Med. 2007 Nov 15 [Epub ahead of print]

# Daytime Sleepiness for Insomniacs

- Most chronic insomniacs do not complain of daytime sleepiness in fact they show increased alertness versus controls leading to the 24 hour hyperarousal.

Stepanski AJ, Glovinsky PB. Daytime alertness patterns in patients with chronic insomnia compared to asymptomatic control subjects *Sleep* 1988;11(1):54-60

# Hyperarousal Hypothesis (Emotional and Physiological)



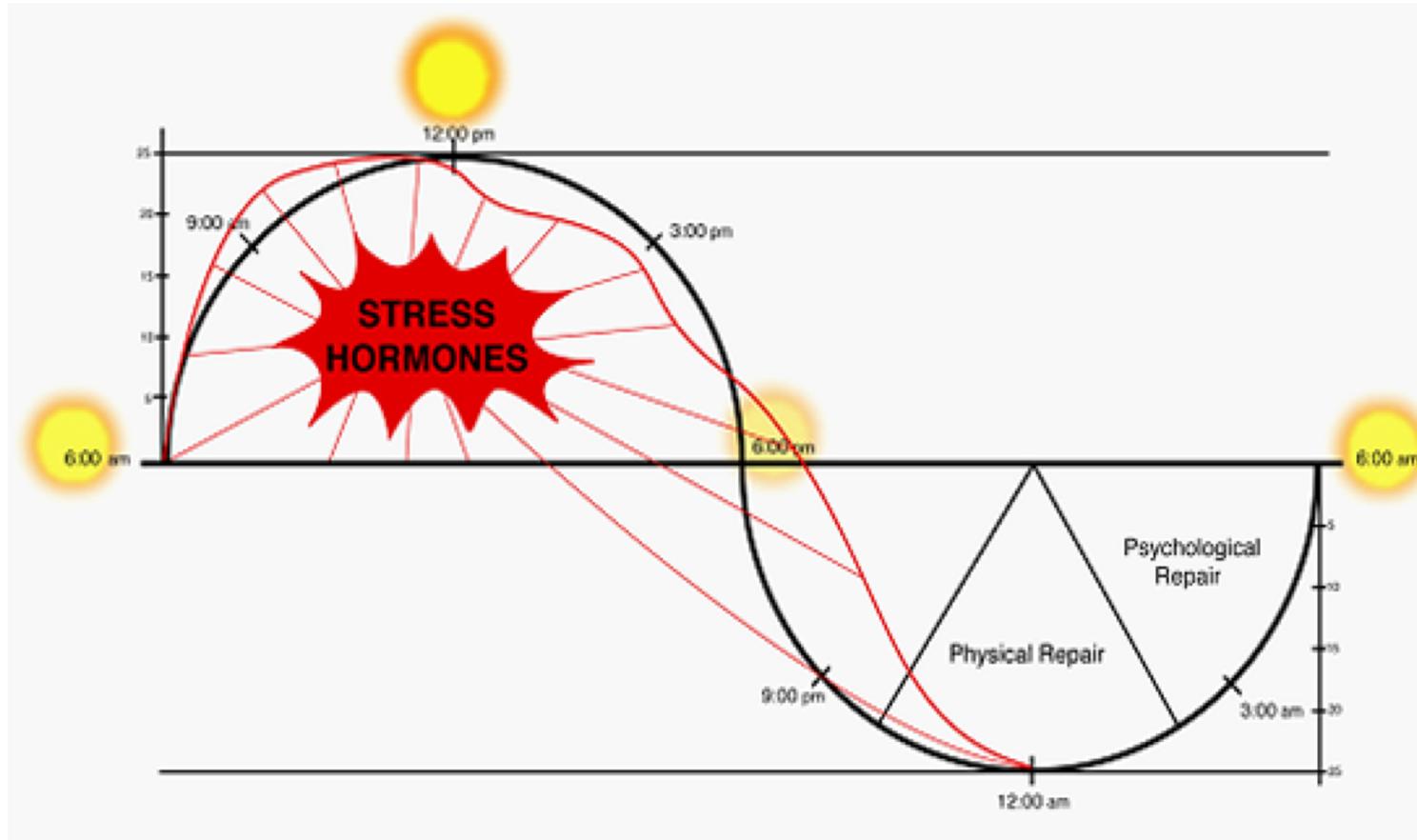
# Stress and Sleep Deprivation

- Elevated cortisol decreases serotonin and melatonin
- Also causes PM blood glucose alterations
- Elevated evening cortisol disrupts sleep and is the primary cause of insomnia
- Sleep disturbances
  - Inability to “turn off” the day
  - Waking in the middle of the night

# Cortisol and Sleep

- Cortisol release is controlled in slow-wave sleep by decreases in corticotropin-releasing hormone (CRH) and increases in growth hormone (GH)
- Exposure to chronic stressors imbalances HPA axis and disrupts normal diurnal pattern of GH, CRH and ACTH release
- Results in a paradoxical rise in cortisol in evening hours and initial sleep phases
- *Nocturnal hypercortisolism* can lead to sleep fragmentation, increasing cortisol even more

# Normal Diurnal Hormone Release



# Supplements for Sleep Should...

- Support HPA stress effects on sleep patterns
- Support sleep quality and quantity
- Support the ability to fall asleep
- Improve neurochemical balance – GABA, serotonin, dopamine, glutamate, histamine
- Improve melatonin levels
- Improve sleep patterns

# Magnolia/Phellodendron Combo



- Proprietary blend of Chinese herbs *Magnolia* and *Phellodendron* (bark)
- Used for Stress and Stress-related appetite control
- Anti-anxiety and anti-stress properties rival benzodiazepines, yet non-sedating and no “hangover” effect
- Improves cortisol balance

Kuribara H, Kishi E, Hattori N, Okada M, Maruyama Y. The anxiolytic effect of two oriental herbal drugs in Japan attributed to honokiol from magnolia bark. *J Pharm Pharmacol.* 2000;52(11):1425-9.

Maruyama Y, Kuribara H, Morita M, Yuzurihara M, Weintraub ST. Identification of magnolol and honokiol as anxiolytic agents in extracts of saiboku-to, an oriental herbal medicine. *J Nat Prod.* 1998;61:135-8.

Kalman et al. Effect of a proprietary Magnolia and Phellodendron extract on stress levels in healthy women: a pilot, double-blind, placebo-controlled clinical trial. *Nutr J.* 2008;7(1):11.

# Magnolia/Phellodendron Study

- Double blind-placebo controlled clinical study (n=26)
  - Overweight, otherwise healthy premenopausal females
  - 250mg tid x 6 weeks
  - Significantly reduced transitory anxiety and stress-related eating

Kuribara H, Kishi E, Hattori N, Okada M, Maruyama Y. The anxiolytic effect of two oriental herbal drugs in Japan attributed to honokiol from magnolia bark. *J Pharm Pharmacol.* 2000;52(11):1425-9.

Maruyama Y, Kuribara H, Morita M, Yuzurihara M, Weintraub ST. Identification of magnolol and honokiol as anxiolytic agents in extracts of saiboku-to, an oriental herbal medicine. *J Nat Prod.* 1998;61:135-8.

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# Magnolia/Phellodendron Study

- 2013 clinical study (n=56) published in Journal of International Society of Sports Nutrition
- 250mg bid x 4 weeks
- Improved salivary cortisol
- Improved mood
- Improved overall well-being and decreased stress

# Holy Basil (*Ocimum sanctum*)



- In Hindi known as Tulsi
- Used for 3000 years – The “Elixir of Life” in Ayurveda
- Adaptogenic – cortisol / stress HPA support
- Anti-fatigue
- Immunomodulatory – increase NK and T-helper cells in humans
- Cognitive/mood improvement in humans

Jamshidi N, et al. Clinical Efficacy and Safety of Tulsi in Humans: A Systematic Review of the Literature. *Evid Based Complement Alternat Med.* 2017;2017:9217567.

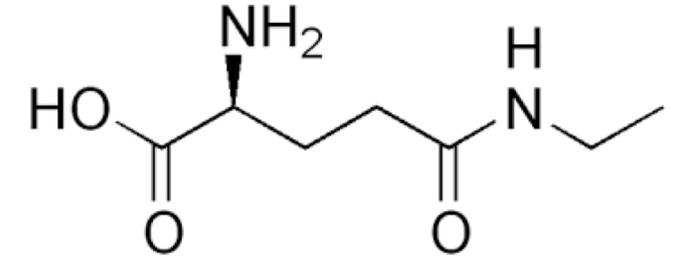
Bhargava KP, Singh N. Anti-stress activity of *Ocimum sanctum* Linn. *Indian Journal of Medical Research.* 1981;73:443–451.

# Holy Basil Clinical Study - Stress

- 2011 Study (n=79, 6 weeks) to evaluate a proprietary holy basil extract in stress
- 1,200mg daily x 6 weeks
- Results = 39% improvement in stress symptoms vs. placebo
- No adverse events/ well tolerated



# L-Theanine



- Unique amino acid from green tea
- Used if :
  - Cortisol optimal but stress and anxiousness present
  - Daytime drowsiness present
- Improves alpha wave sleep – restful sleep
- Dampens PEA
- 600-1,200mg/day – 200-400mg TID



# Kava root – *Piper methysticum*



- Kava = S. Pacific plant related to pepper; used as beverage in traditional ceremonies to induce “closeness to God”
- Used in anxiety + restlessness preservation without cravings
- Leads to sedation in larger doses
- Kava may increase drowsiness or impair ability to drive an automobile or operate heavy machinery
- Dose = 250-500mg QD std 30% kavalactones

# Kava

- 2013 double-blind placebo-controlled clinical trial n= 75 , 6 weeks
  - Studied effects of Kava on generalize anxiety disorder (GAD)
  - Significant reduction in anxiety vs. placebo
  - 26% remission in symptoms in kava group vs. 6% placebo
  - Well-tolerated, minor SE headaches
- A Cochrane Database review and meta-analysis of 7 randomized clinical trials using kava for the treatment of generalized anxiety symptoms reported a significant reduction of anxiety on the Hamilton Anxiety Rating Scale (HAM-A) for kava compared with placebo
- Hepatotoxicity may occur in larger doses in compromised patients or those taking pharmaceutical concurrently
  - Large doses may increase liver enzymes particularly GGT

- Sarris J, et al. Kava in the treatment of generalized anxiety disorder ; a double-blind randomized placebo-controlled study. J Clin Psychopharmacol. 2013;33(5):643-8.

- Pittler MH, Ernst EE. Efficacy of kava extract for treating anxiety: systematic review and meta-analysis. J Clin Psychopharm. 2000;20(1):84–9.

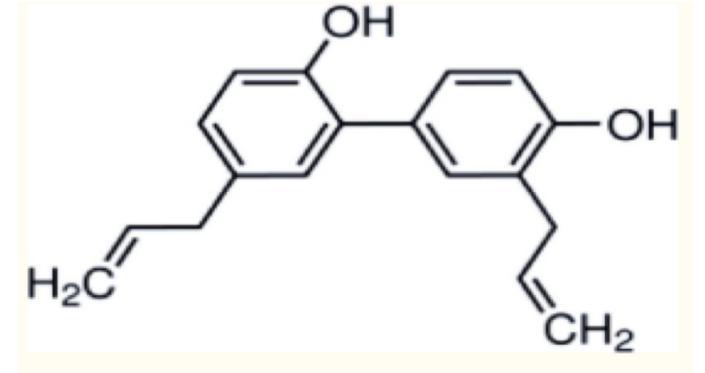
# Magnesium

- Magnesium bisglycinate chelate or threonate
  - Co-factor in over 300 biochemical reactions
  - May help support sleep quality and quantity
  - Helps improve restless leg syndrome
  - 600mg HS

Abbasi B, et al. The effect of magnesium supplementation on primary insomnia in elderly: A double-blind placebo-controlled clinical trial. *J Res med Sci.* 2012;17(12):1161-9.

# *Magnolia officinalis* bark extract

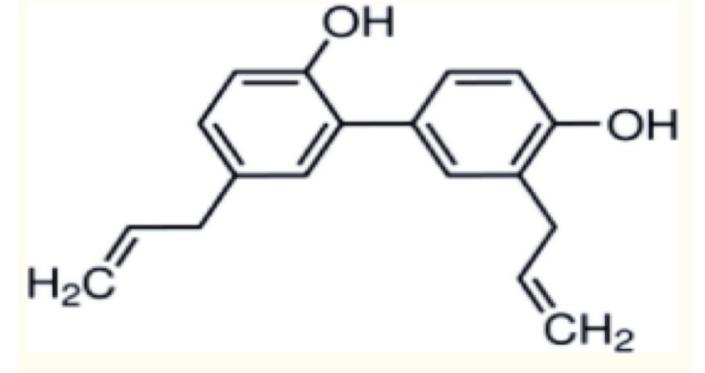
- Std. to 98% honokiol
- Honokiol is reported to bind to GABA<sub>A</sub> receptors
- Decreases sleep latency to NREM sleep
- Increases NREM sleep
- NMDA antagonist
- Anti-inflammatory – decreases microglial activation



Kuribara H, Kishi E, Hattori N, Okada M, Maruyama Y. The anxiolytic effect of two oriental herbal drugs in Japan attributed to honokiol from Magnolia bark. *J Pharm Pharmacol* (2000) 52(11):1425–910.

# *Magnolia officinalis* bark extract

- Readily crosses BBB
- Decreases LPS induced memory deficit
- Antianxiety
- Pain modulation
- Endocannabinoid binding CB1 only
- 100mg HS



Kuribara H, Kishi E, Hattori N, Okada M, Maruyama Y. The anxiolytic effect of two oriental herbal drugs in Japan attributed to honokiol from Magnolia bark. J Pharm Pharmacol (2000) 52(11):1425–910.

# Jujube (*Ziziphus jujube*) Fruit Extract

- Jujube (*Ziziphus jujuba*) fruit extracts (4:1)
- Reported to improve sleep quality
- Anxiolytic, sedative and hypnotic effects in laboratory studies
- Neuroprotection
- Increases hippocampal neurogenesis
- Decreases neuro-oxidative stress
- Improves memory and learning
- 265mg HS

# Melatonin

- Natural sleep hormone
- Levels decrease with aging
- Decreases with stress, hormonal imbalances
- Improves circadian insulin production
- Used for sleep problems
- Antioxidant
- 1-20mg before bedtime
- Watch for paradoxical effects

Li T, et al. Exogenous melatonin as a treatment for secondary sleep disorders: a systematic review and meta-analysis. *Front Neuroendocrinol.* 201;52:22-28.

# Melatonin depleted by:

- Beta-blockers
- Calcium channel blockers
- Benzodiazepines
- Estrogen-containing medications
- Hydralazine
- Loop diuretics
- Theophylline
- Antidepressants, including SSRI (Selective serotonin reuptake inhibitors)
- NSAIDs (Non-steroidal anti-inflammatory drugs)