ETIOLOGY OF INSOMNIA
&
TREATMENT IMPLICATIONS

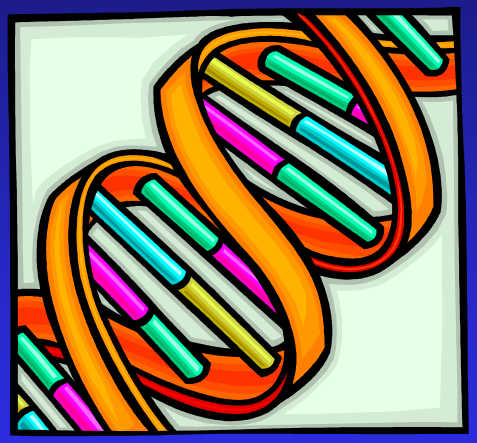
WHO NEEDS A MODEL OF INSOMNIA ?

“The only problem with insomniacs is they don’t get enough sleep”

IT’S THAT SIMPLE
AND
IT’S NOT THAT SIMPLE

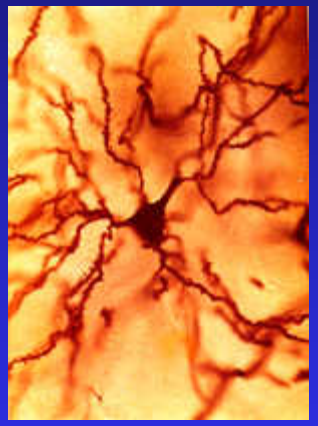
HOW DOES THIS CONDITION DEVELOP ?
WHAT IS IT ?

WHAT IS THE ETIOLOGY OF INSOMNIA ?



UNKNOWN

WHAT IS THE PATHOPHYSIOLOGY OF INSOMNIA ?



UNKNOWN

ANY IDEAS ABOUT WHAT INSOMNIA IS AND HOW IT DEVELOPS ?

ACTUALLY THERE ARE MORE THAN A FEW

60

Etiology and Pathophysiol

Michael L. Perlis
Michael T. Smith
Wilfred Pigeon

ABSTRACT

Of all the sleep disorders, insomnia is perhaps the only one where there has been a substantial amount of top-down theo rization. This may be the case because a framework is requirec to comprehend a disorder that has multiple causes and ar insidious and progressive course. In this chapter, four genera models of the etiology and pathophysiology of insomnia an summarized and critically evaluated. In particular, we review how each model characterizes the hyperarousal that is though to be responsible for disturbing sleep continuity. Additiona information is provided on how sleep homeostasis and circa dian considerations may mediate, moderate, or interact with th hyperarousal.

Insomnia is often considered a disorder of hyperarousal; that is the patient has a level of arousal that is incompatible with th initiation or maintenance of sleep. The concept of hyper arousal is, however, likely to be quite complex. What is mean by arousal? How does it become elevated? Is hyperarousal tonic phenomenon, and if not, what factors mediate or mod erate its occurrence or intensity? Is arousal a singular construct and are hyperarousal and sleep necessarily mutually exclusive

In this chapter, we review physiologic, cognitive, behav toral, and neurocognitive models of insomnia. Each of thes will be summarized as it pertains to primary insomnia an sleep state misperception insomnia (paradoxical insomnia) These models may also be relevant to the extrinsic or second ary insomnias, which, when chronic, have a great deal in com mon with primary insomnia.[1,2] In addition to reviewing th four models, we also summarize how sleep homeostasi and circadian considerations mediate, moderate, or interac with hyperarousal. Finally, we review a recent hypothesis tha suggests that hyperarousal may be better conceptualized as failure of wakefulness inhibition.

PHYSIOLOGIC MODEL OF INSOMNIA

The physiologic model suggests that chronic insomnia may b understood as a condition in which the patient has a trait leve of arousal, or a level of arousal prior to or during the preferre sleep period, that is incompatible with good sleep continuity This model assumes that physiologic arousal and sleep an mutually exclusive. Studies evaluating physiologic arousal i insomnia have used a variety of techniques, including basi psychophysiologic measures, whole-body metabolic rate heart rate variability, caffeine-induced insomnia, neuroen docrine measures, and functional neuroimaging. The studie discussed next support the general concept of physiologi

Etiology and Pathophysiology of Insomnia

Michael Lloyd Perlis; Jason Gordon Ellis; Jacqueline DeMichele Kloss; Dieter Riemann

Chapter 82

Chapter Highlights

- Since the 1990s there has been a proliferation of theoretical perspectives on the etiology of insomnia that now includes nine human models. The *central concepts* for the nine models include the following:
  - Stress-diathesis
  - Stimulus dyscontrol and classical conditioning
  - The interaction of basal arousal and sleep requirement
  - Sleep extension and the mismatch between sleep opportunity and ability
  - Altered sensory and information processing and an attenuation of the normal mesograde amnesia of sleep
  - Appraisal as a determinant of the patient's perception of disease
  - The concept of "the inhibition of sleep-related dearousal" (vs. hyperarousal)
  - The role of attention, intention, and effort
  - The etiologic importance of daytime deficits, selective attending to sleep-related threats, and safety behaviors
  - Chronic insomnia as a hybrid state that occurs in association with local neuronal wakefulness during non–rapid eye movement and rapid eye movement sleep

Until the late 1990s there were only two models regarding the etiology and pathophysiology of insomnia. The relative lack of theoretical perspectives was due to at least three factors. First, the widespread conceptualization of insomnia as owing directly to hyperarousal (levels of physiologic or central nervous system (CNS) arousal that are sufficiently high as to directly prohibit sleep) may have made it appear that further explanation was not necessary. Second, the long-time characterization of insomnia as a symptom carried with it the clear implication that insomnia was not itself worth modeling as a disorder or disease state. Third, for those inclined toward theory, the acceptance of the behavioral models (i.e., the three-factor model [3P] and the stimulus control model[1,2]) and the treatments that were derived from them might have had the untoward effect of discouraging the development of alternative or elaborative models. Since the 1990s there has been a proliferation of theoretical perspectives on the etiology and pathophysiology of insomnia that includes both human and animal models. In this chapter, nine of the human models are described and critiqued. The models presented span from the classical behavioral perspectives, to the traditionally cognitively focused frameworks, to the more modern cognitive information–processing perspectives, to an interaction paradigm that takes into account basal arousal and sleep requirement, to the neurocognitive and neurobiologic models that essentially frame insomnia, from a functional and neurophysiologic point of view, as a hybrid state (part wake and part non–rapid eye movement [NREM] sleep).

DEFINITION OF INSOMNIA

The *Diagnostic and Statistical Manual of Mental Disorders*, fifth edition (DSM-5)[3] and *International Classification of Sleep Disorders*, third edition (ICSD3[4]) define *insomnia disorder* as difficulty initiating or maintaining sleep on three or more nights per week for at least 3 months. This definition further stipulates that the diagnosis of insomnia must take into account sleep opportunity, level of daytime impairment and distress, whether symptom presentation (in the case of children and elders) varies with caregiver presence, and the possibility that the insomnia is not better explained by (or does not occur exclusively during the course of) other sleep disorders or medical or psychiatric illnesses.

This definition is different from the DSM-IV-TR and the ICSD2 in several important ways. First, the diagnostic terms *primary insomnia* and *secondary insomnia* have been replaced to reflect the change that insomnia is now viewed as a disorder, regardless of whether it is comorbid with other disorders. Second, although quantitative values are not given for insomnia severity (i.e., that sleep latencies or wake after sleep onset durations must be greater than some minimum duration to be of clinical significance), insomnia frequency and chronicity are explicitly stated. The frequency criterion is new, and the

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Chapter 78

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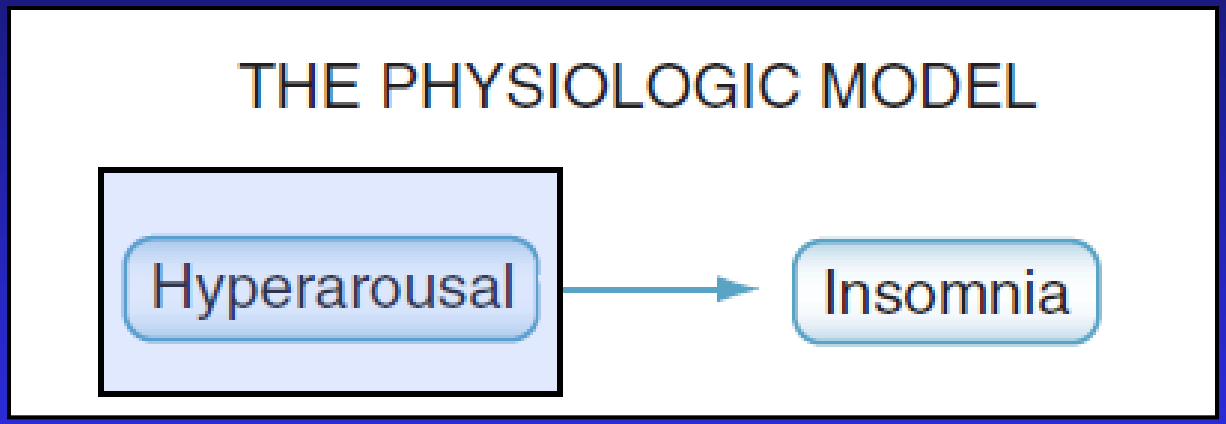
ry. A simple conditioning history, wherein a stimulus ways paired with a single behavior, yields a high prob- y that the stimulus will yield only one response. A plex conditioning history, wherein a stimulus is paired a variety of behaviors, yields a low probability that timulus will yield only one response. In persons with nnia, the normal cues associated with sleep (e.g., bed, oom, bedtime, etc.) are often paired with activities r than sleep. For instance, in an effort to cope with nnia, the patient might spend a large amount of time e bed and bedroom awake and engaging in activities r than sleep. The coping behavior appears to the nt to be both reasonable (e.g., staying in bed at least its the patients to rest) and reasonably successful aging in alternative activities in the bedroom some- s appears to result in cessation of the insomnia). These tices, however, set the stage for stimulus dyscontrol, owered probability that sleep-related stimuli will elicit desired response of sleepiness and sleep. Figure 78-1 ides as schematic representation of stimulus control stimulus dyscontrol.

ngths and Weaknesses

treatment that is derived from stimulus control theory e of the most widely used behavioral treatments, and fficacy has been well established.[8-12] The success of the apy, however, is not sufficient evidence to say that ulus dyscontrol is the factor, or one of the factors, onsible for predisposition to, the precipitation of, or erpetuation of insomnia.[8] This is the case because the apy includes active components that are not based y on learning or behavioral theory. For instance, the ment specifies that the patient should spend awake somewhere other than the bed and that the sleep dule should be fixed. These two interventions also ence the homeostatic and circadian regulation of sleep. s, the efficacy of stimulus control therapy does not ssarily provide evidence for the stimulus control model. ct, one investigation found that the reverse of stimulus rol instructions also improved sleep continuity.[13] nother limitation of the stimulus control perspective is it focuses solely on instrumental conditioning. That ere are activities that can be engaged in that reduce hance the probability of the occurrence of sleep. The nal model does not explicitly delineate how classical litioning might also be an operational factor. That is, egular pairing of the physiology of wake with sleep- ed stimuli might lead to a scenario where sleep-related uli become conditioned stimuli for wakefulness. This r possibility, although not part of the classical stimulus rol perspective, is clearly consistent with it.

nceptual time frame for causality in terms of "predisposition, precipitation, rpetuation" was first articulated as part of the 3P model. It is used in this t to illustrate the complexity of modeling what "cause" insomnia.

THE PHYSIOLOGIC PERSPECTIVE


THE PHYSIOLOGIC MODEL
Hyperarousal
Insomnia

WHAT IS HYPERAROUSAL ?

DO PATIENTS WITH INSOMNIA EXHIBIT THIS ?

WHAT IS HYPERAROUSAL ?

A LEVEL OF PHYSIOLOGIC AROUSAL THAT INTERFERES WITH THE INITIATION AND MAINTENANCE OF SLEEP

CLASSICAL MEASURES

- **HEART RATE (HR)**
- **RESPIRATION RATE (RR)**
- **MUSCLE TONUS (EMG)**
- **TEMPERATURE (CBT)**
- **STARTLE RESPONSE (GSR)**

DO INSOMNIA PATIENTS EXHIBIT INCREASED PHYSIOLOGIC AROUSAL ?

	Monroe 1967	Haynes 1974	Haynes 1981	Freedman 1982	Adam 1985	Stepanski 1994
Subject Issues						
Mean Age (PS and GS)	25/26	18/18	19/19	31/27	51/51	34/34
Sample Size (PS and GS)	16/16	??/??	10/11	12/12	18/18	24/25
Recruitment Source	Univ.	Univ.	Univ.	Comm.	PCP[2]	Comm.
Recruitment (indicated Insomnia Research)	Yes	No	??	Yes	No	Yes
Medical Screening	??	??	??	Yes	??	Yes
Psych Screen	??	??	??	Yes	Yes	Yes
Sleep Dx Screen	??	??	??	Yes	??	Yes
Insomnia Complaint (for the PS)	No	??	Yes	Yes	Yes	Yes
PSG study	Yes	No	Yes	Yes	Yes	Yes
PSG Confirmed Insomnia	Yes	No	Yes	Yes	Yes	Yes
Measures -						
Heart rate - During the Day					**ns**	**ns ?**
Heart Rate - Prior to Sleep Onset	↑		↑	↑	**ns**	↑
Heart rate - During Sleep	↑			**ns**	**ns**	↑
Respiration Rate - During the Day						
Respiration Rate - Prior to Sleep Onset	↑			↑		
Respiration Rate - During Sleep	↑			**ns**		
Temperature[1]- During the Day					↑	
Temperature - Prior to Sleep Onset	↑			**ns**	↑	
Temperature - During Sleep	↑			**ns**	↑	
Muscle Tension - During the Day		↑				
Muscle Tension - Prior to Sleep Onset				↑		
Muscle Tension - During Sleep				**ns**		
Skin Resistance - During the Day	↑					
Skin Resistance - Prior to Sleep Onset				↑		
Skin Resistance - During Sleep				**ns**		
Peripheral Vasoconstrictivity- During the Day	↑					**ns**
Peripheral Vasoconstrictivity- Prior to Sleep Onset				**ns**		
Peripheral Vasoconstrictivity- During Sleep				**ns**		**ns**

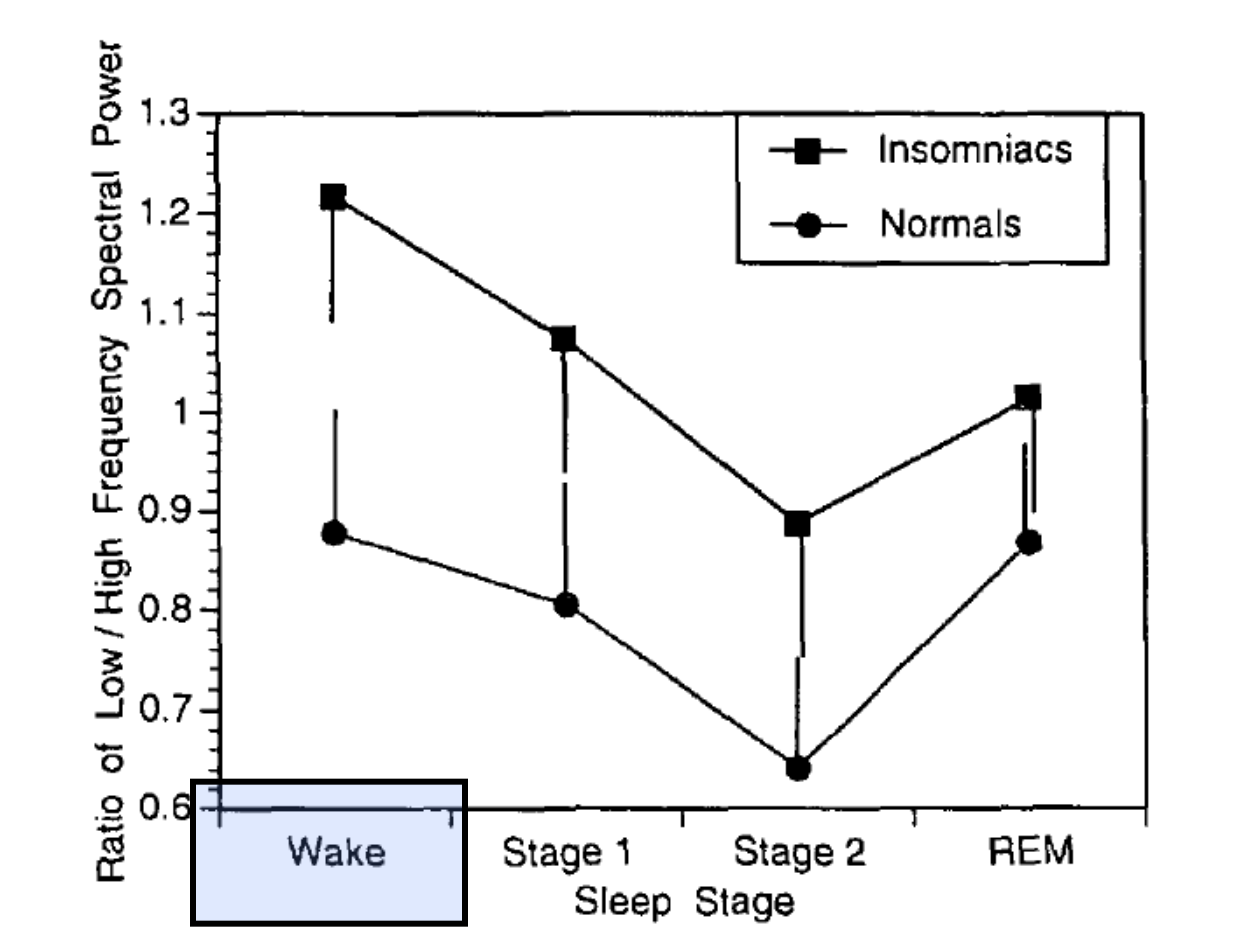
WHAT IS HYPERAROUSAL ?

A LEVEL OF PHYSIOLOGIC AROUSAL THAT INTERFERES WITH THE INITIATION AND MAINTENANCE OF SLEEP

CONTEMPORARY MEASURES

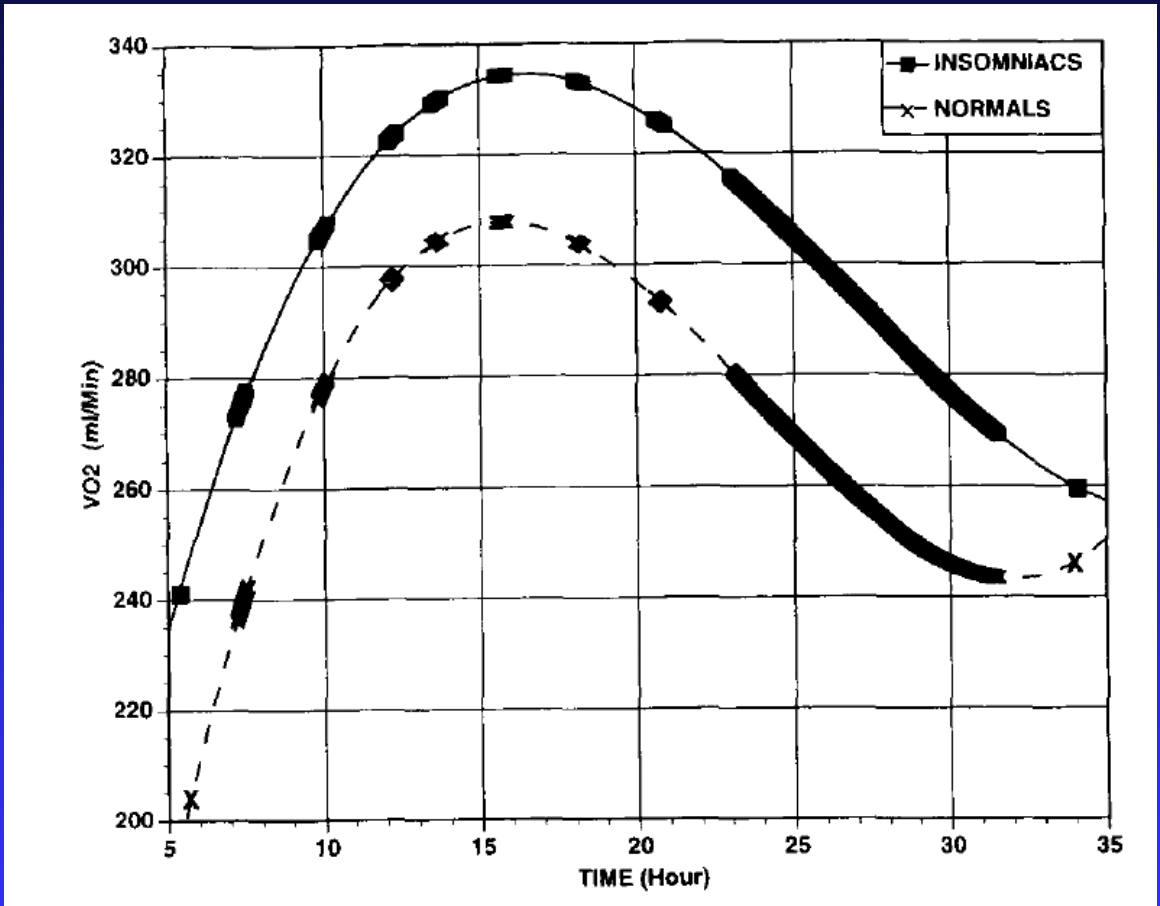
- HEART RATE VARIABILITY (HRV)
- METABOLIC RATE
- CORTISOL LEVEL

HRV



Bonnet et al, Psychosom Med. 1998 Sep-Oct;60(5):610-5.

METABOLIC RATE



Bonnet et al. Sleep 1995; 18(7):581-588.
Bonnet et al. Psychosom Med 1997; 59(5):533-540.

HPA AXIS ABNORMALITIES

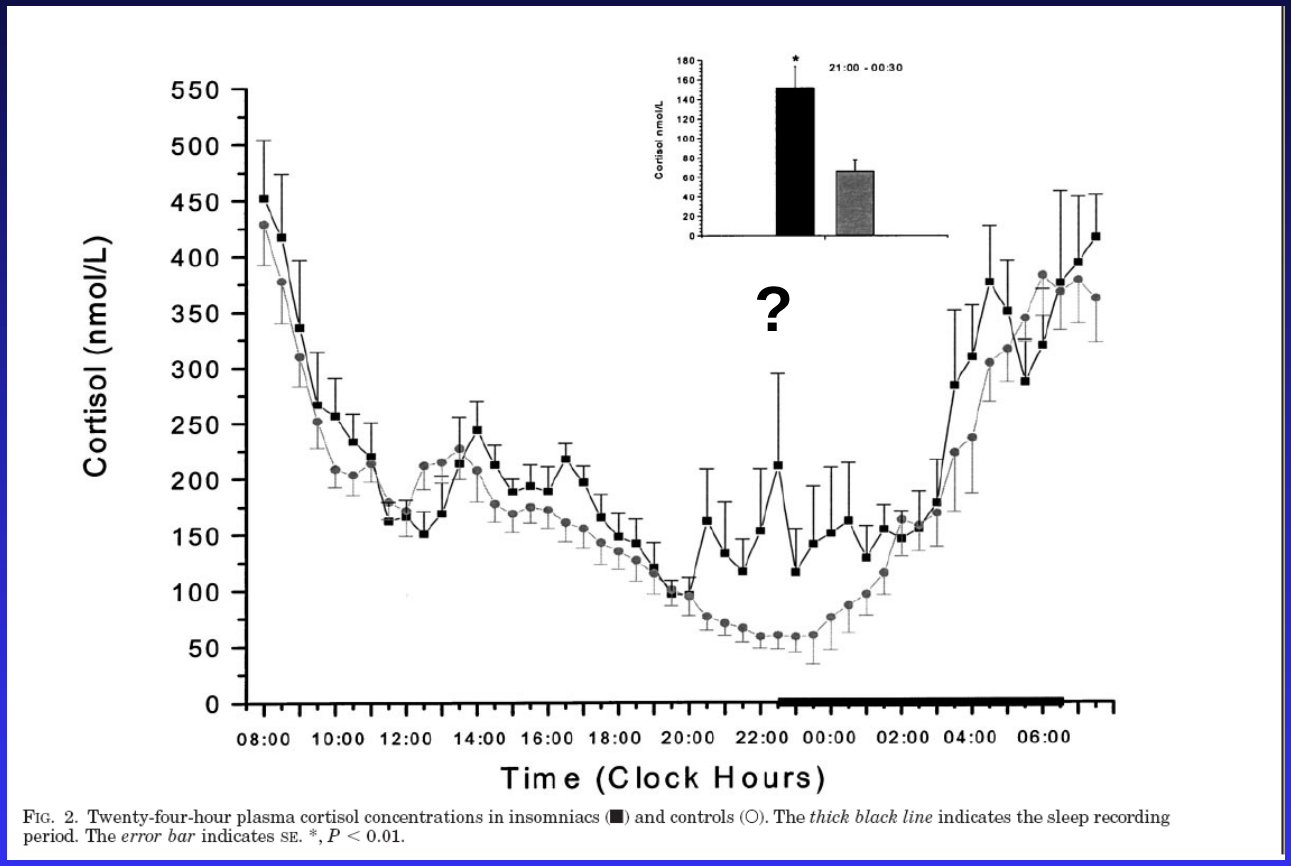
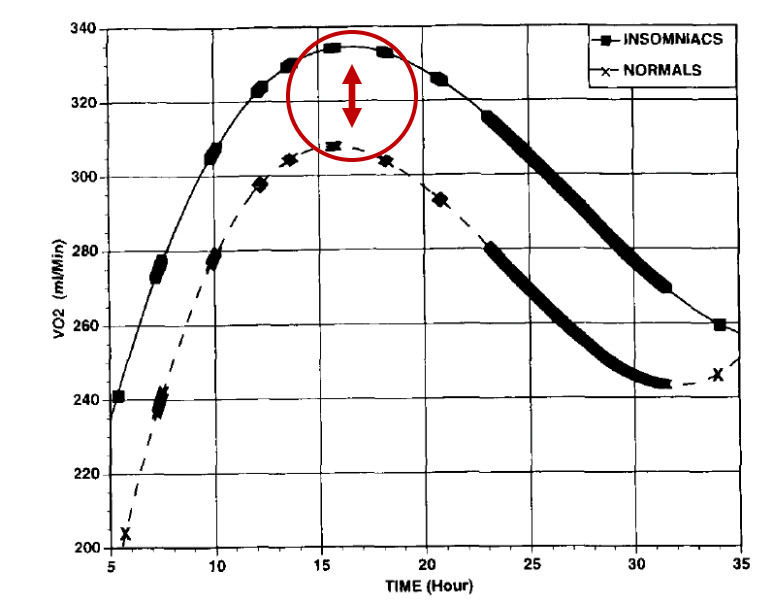


FIG. 2. Twenty-four-hour plasma cortisol concentrations in insomniacs (■) and controls (○). The *thick black line* indicates the sleep recording period. The *error bar* indicates SE. *, $P < 0.01$.

Vgontzas et al. 2001. Journal of Clinical Endocrinology & Metabolism



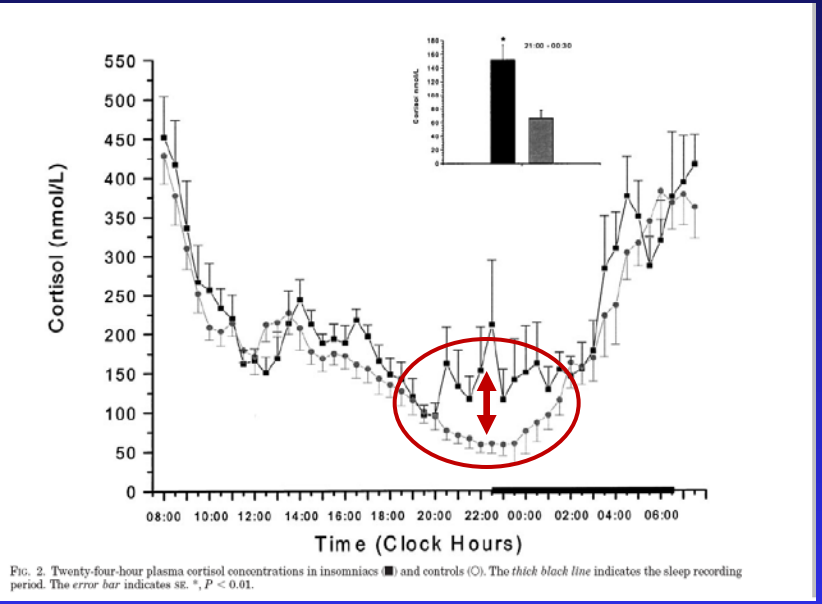


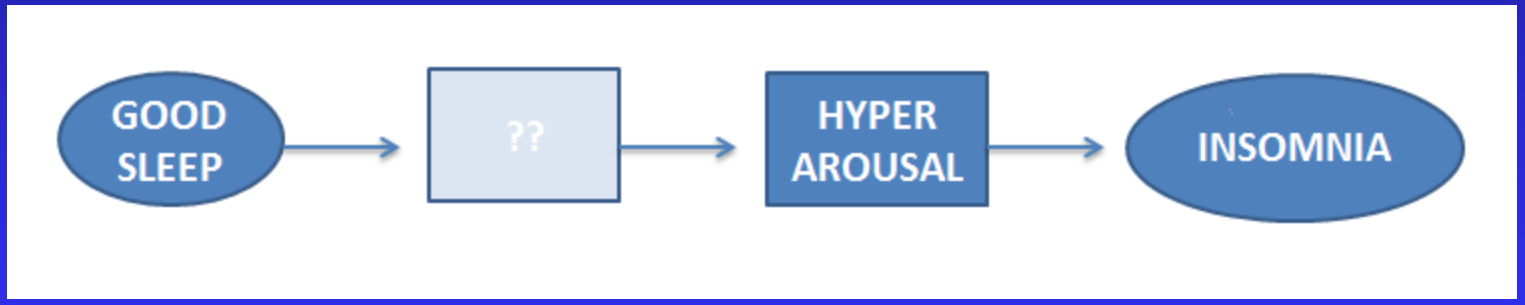
FIG. 2. Twenty-four-hour plasma cortisol concentrations in insomniacs (■) and controls (○). The *thick black line* indicates the sleep recording period. The *error bar* indicates SE. *, $P < 0.01$.

Q: IS THE LEVEL OF AROUSAL ENOUGH TO INTERFERE WITH SLEEP INITIATION OR MAINTENANCE ?

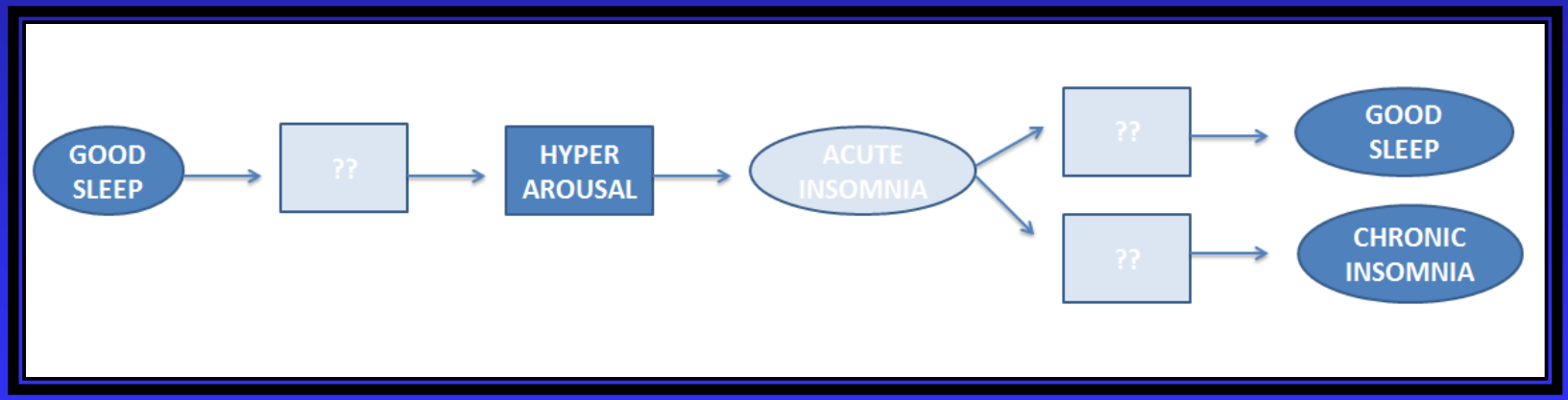
DOES THE AROUSAL LEVEL COMPARE TO THIS ?!

IT’S DOUBTFUL

DOES THE MODEL EXPLAIN HOW THE HYPERAROUSAL CONDITION COMES INTO EXISTENCE ?



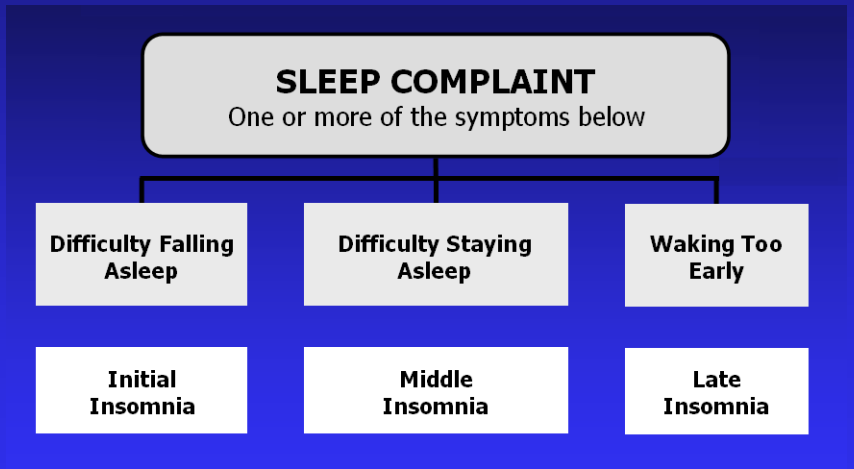
DOES THE MODEL EXPLAIN HOW ACUTE INSOMNIA BECOMES CHRONIC AND HOW HOW THE CONDITIONS DIFFER ?



CAN THIS MODEL EXPLAIN THE VARIOUS INSOMNIA PHENOTYPES (TYPES AND SUBTYPES)

PRIMARY INSOMNIA / INSOMNIA DISORDER

PSYCHOPHYSIOLOGIC INSOMNIA
IDIOPATHIC INSOMNIA
PARADOXICAL INSOMNIA
SLEEP HYGIENE DISORDER
PHYSIOLOGIC INSOMNIA
INSOMNIA NOS



FOR A GOOD REVIEW OF THE EVIDENCE

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CLINICAL REVIEW

The hyperarousal model of insomnia: A review of the concept and its evidence

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Keywords:
Insomnia
Hyperarousal

SUMMARY

Primary insomnia is defined as difficulties in falling asleep, maintaining sleep or non-restorative sleep accompanied by significantly impaired daytime functioning in the absence of a specific physical, mental or substance-related cause. The current review provides substantial support for the concept that hyperarousal processes from the molecular to the higher system level play a key role in the pathophysiology of primary insomnia. Autonomous, neuroendocrine, neuroimmunological, electrophysiological and neuroimaging studies demonstrate increased levels of arousal in primary insomnia during both night and daytime. In the light of neurobiological theories of sleep–wake regulation, primary insomnia may be conceptualized as a final common pathway resulting from the interplay between a genetic vulnerability for an imbalance between arousing and sleep-inducing brain activity, psychosocial/medical stressors and perpetuating mechanisms including dysfunctional sleep-related behavior, learned sleep preventing associations and other cognitive factors like tendency to worry/ruminate.

Introduction

Insomnia as a diagnostic entity is defined as a complaint of prolonged sleep latency, difficulties in maintaining sleep, the experience of non-refreshing or poor sleep coupled with impairments of daytime functioning, including reduced alertness, fatigue, exhaustion, dysphoria and other symptoms. The complaints have to endure for at least 4 weeks to be diagnosed as insomnia. The Diagnostic and Statistical Manual of the American Psychiatric Association (DSM)[1] classifies insomnias into primary insomnia (PI), insomnia related to a medical or mental disease and insomnia related to the intake or abuse/dependency from substances. The International Classification of Sleep Disorders (ICSD)[2] goes beyond that approach and specifies 11 insomnia subtypes encompassing among others acute, psychophysiological, paradoxical, idiopathic and substance-induced insomnia.

Insomnia as a symptom is a highly prevalent health complaint afflicting up to 50% of the general population depending on criteria applied. Estimates for the prevalence of PI as a diagnostic entity in the general population range from 3 to 5%.[3] Research diagnostic criteria for insomnia[4] now provide operationalized and standardized criteria for the diagnosis of insomnia and its subtypes.

Polysomnographic research on insomnia revealed a remarkable discrepancy between the subjective experience of insomnia and polysomnographically rather undisrupted sleep in many patients with primary insomnia.[5,6] Thus, polysomnography (PSG), in contrast to other fields of clinical sleep medicine, has not become the via regia to the diagnosis of insomnia.[7] Insomnia diagnosis and assessment is based on subjective reports (sleep questionnaires) of sleep behavior and relies on sleep diaries filled out every evening and morning (for an overview of relevant instruments see[8,9]).

The effectiveness of cognitive-behavioral treatment for insomnia (CBT-I)[10–12] compared to the risks inherent with pharmacological insomnia treatment (e.g., benzodiazepines[13]) may have added to the conceptualization of PI as primarily a psychological disorder and negligence to study its biological aspects (compared to other sleep disorders or other disorders in the field of mental health).

The "hyperarousal" perspective of insomnia[14–16] has gained widespread attention as an integrative approach to the pathophysiology of insomnia (especially primary insomnia (PI) or psychophysiological

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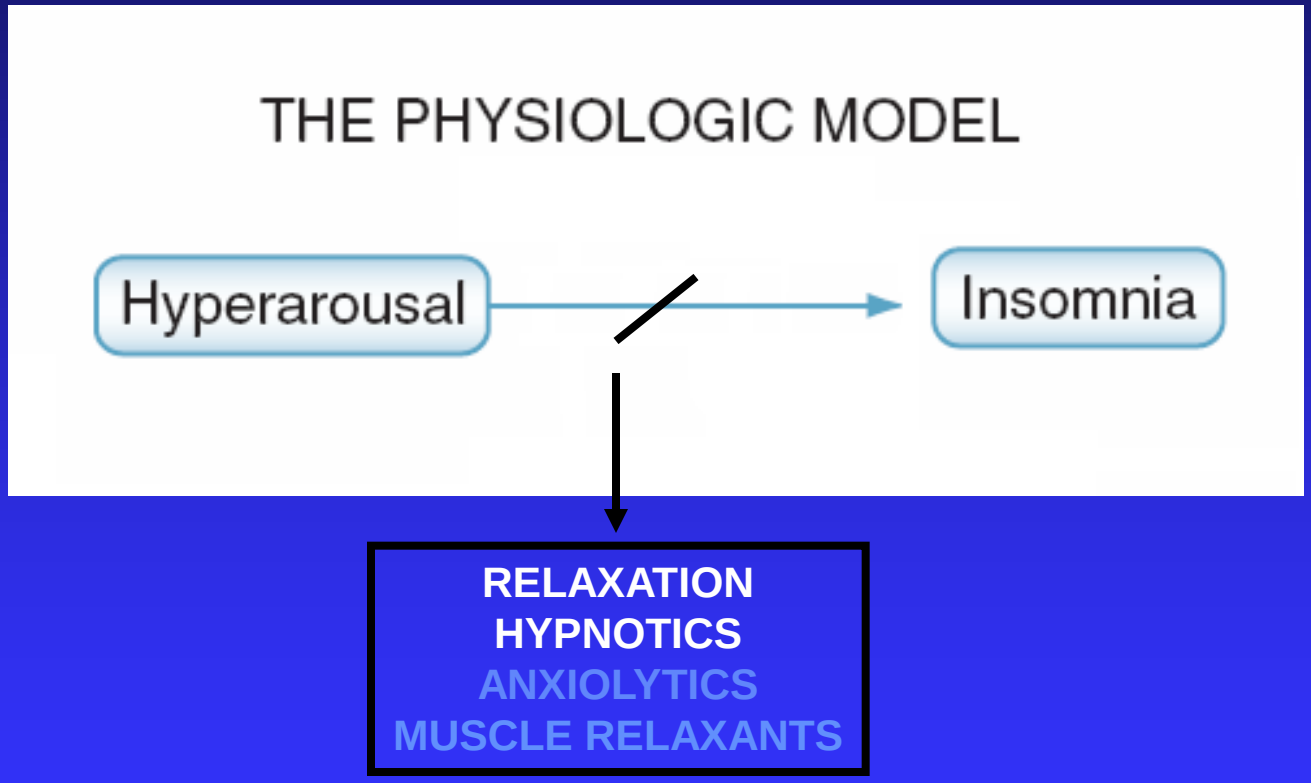
[c] Tel.: +49 761/270 6589; fax: +49 761/270 6523.
[d] Tel.: +49 761/270 6824; fax: +49 761/270 6523.
[e] Tel.: +49 761/270 6603; fax: +49 761/270 6523.
[f] Tel.: +49 761/270 6506; fax: +49 761/270 6523.
[g] Tel.: +1 585 737 2531.
[h] Tel.: +49 761/270 6630; fax: +49 761/270 6523.

TARGETS FOR TREATMENT

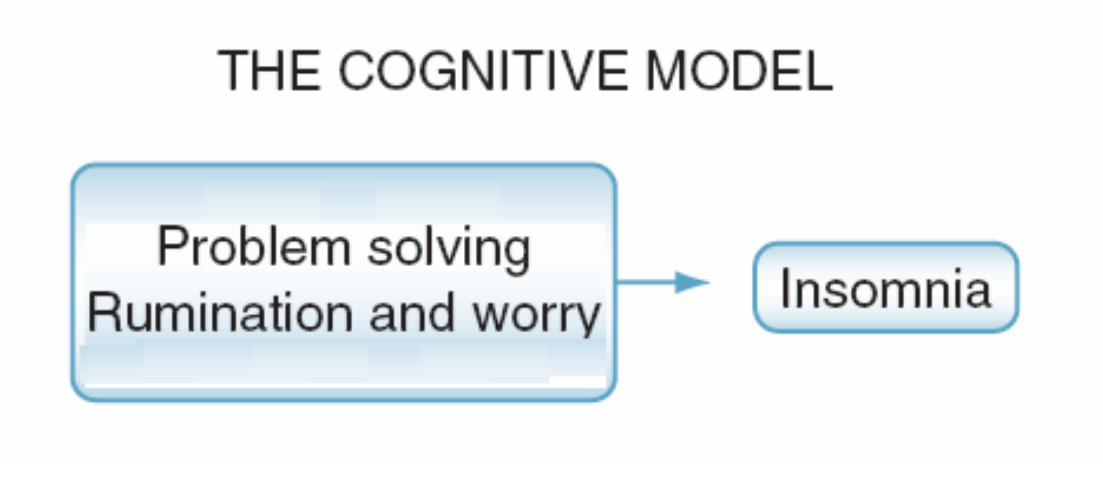
PHYSIOLOGIC MODEL OF INSOMNIA (GENERAL)



ACTUALLY SRT !

THE COGNITIVE PERSPECTIVE

COGNITIVE MODEL OF INSOMNIA (GENERAL)



INSOMNIA OCCURS AS A RESULT OF WORRY

WORRY – CLASSIC

WORRY – CONTEMPORARY

DOES CHRONIC INSOMNIA OCCUR BECAUSE OF

WORRY

RUMINATION

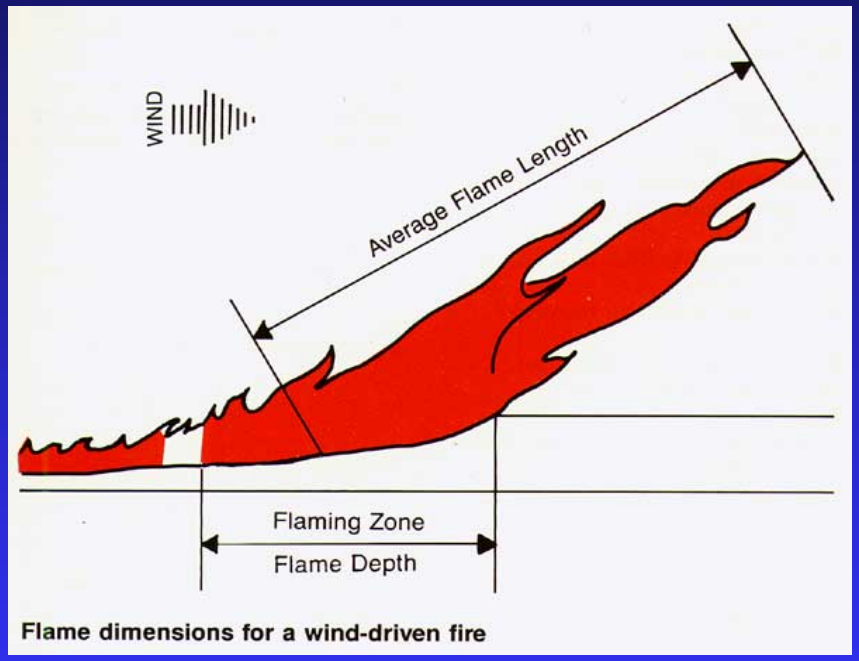
INTRUSIVE THOUGHTS

SELECTIVE ATTENTION

SLEEP-RELATED INTENTION AND EFFORT

MAYBE

OR MAYBE THE COGNITIVE FACTORS ARE “WIND TO THE FLAME”



Flame dimensions for a wind-driven fire

THAT IS, COGNITIVE FACTORS SERVE TO MAKE THE INSOMNIA MORE SEVERE AND MORE CHRONIC

CONSIDER THIS:

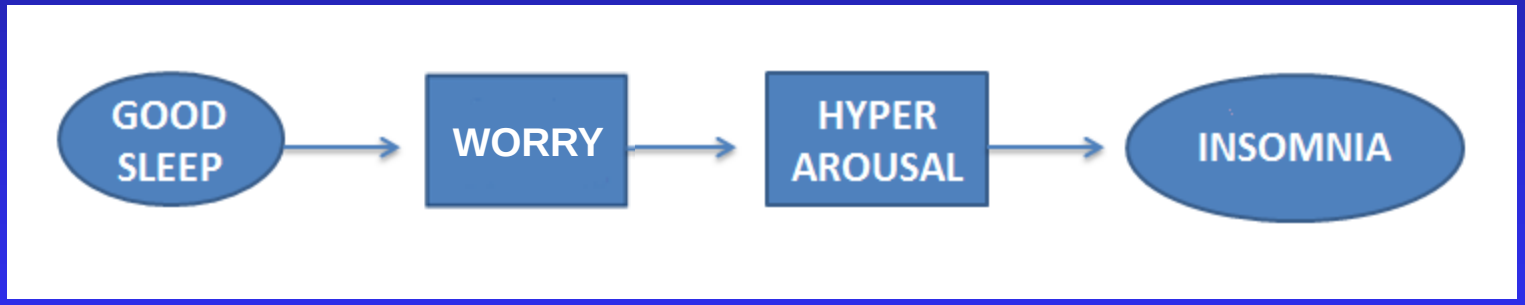
IN THE CASE OF CHRONIC INSOMNIA

IS IT THE CASE THAT WORRY KEEPS ONE AWAKE

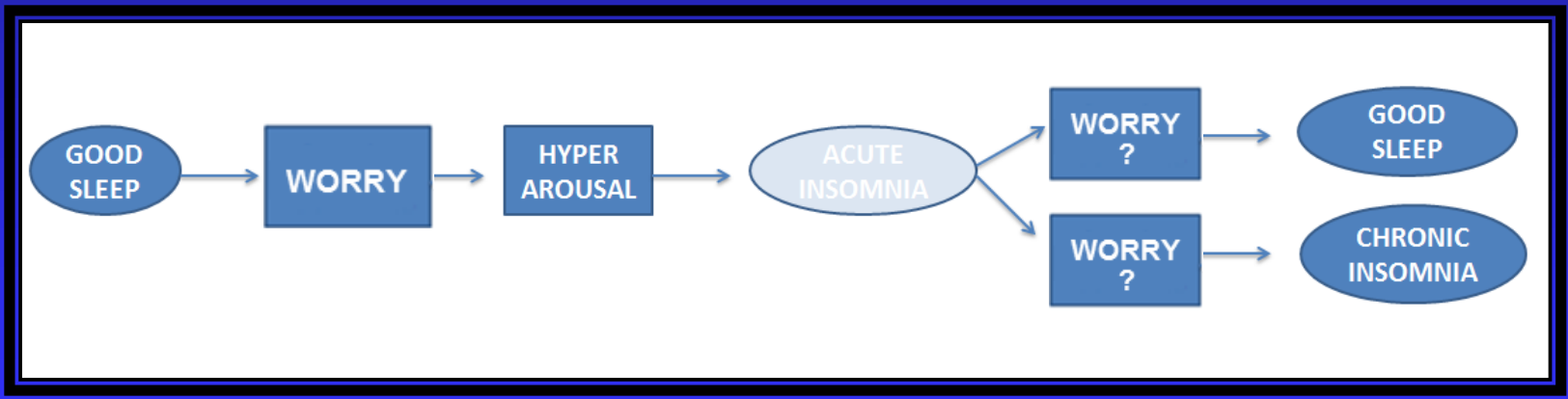
OR

THAT ONE WORRIES BECAUSE ONE IS AWAKE ?

DOES THE MODEL EXPLAIN HOW THE HYPERAROUSAL CONDITION COMES INTO EXISTENCE ?



DOES THE MODEL EXPLAIN HOW ACUTE INSOMNIA BECOMES CHRONIC AND HOW THE CONDITIONS DIFFER ?



CAN THIS MODEL EXPLAIN THE VARIOUS INSOMNIA PHENOTYPES (TYPES AND SUBTYPES)

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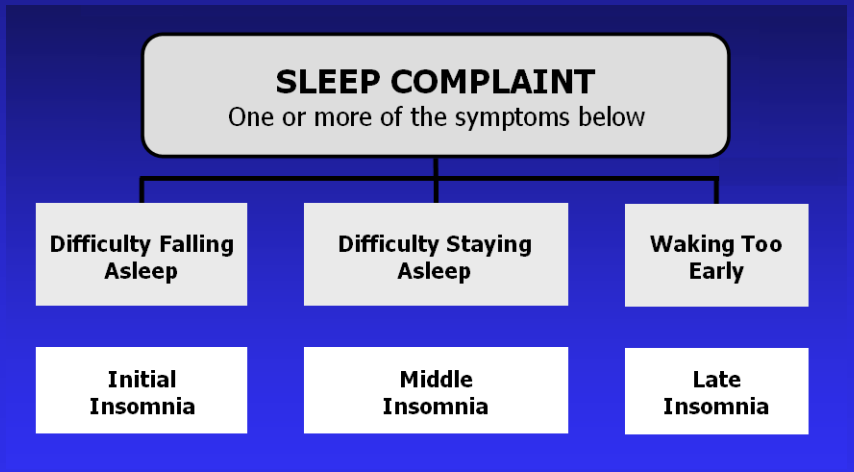
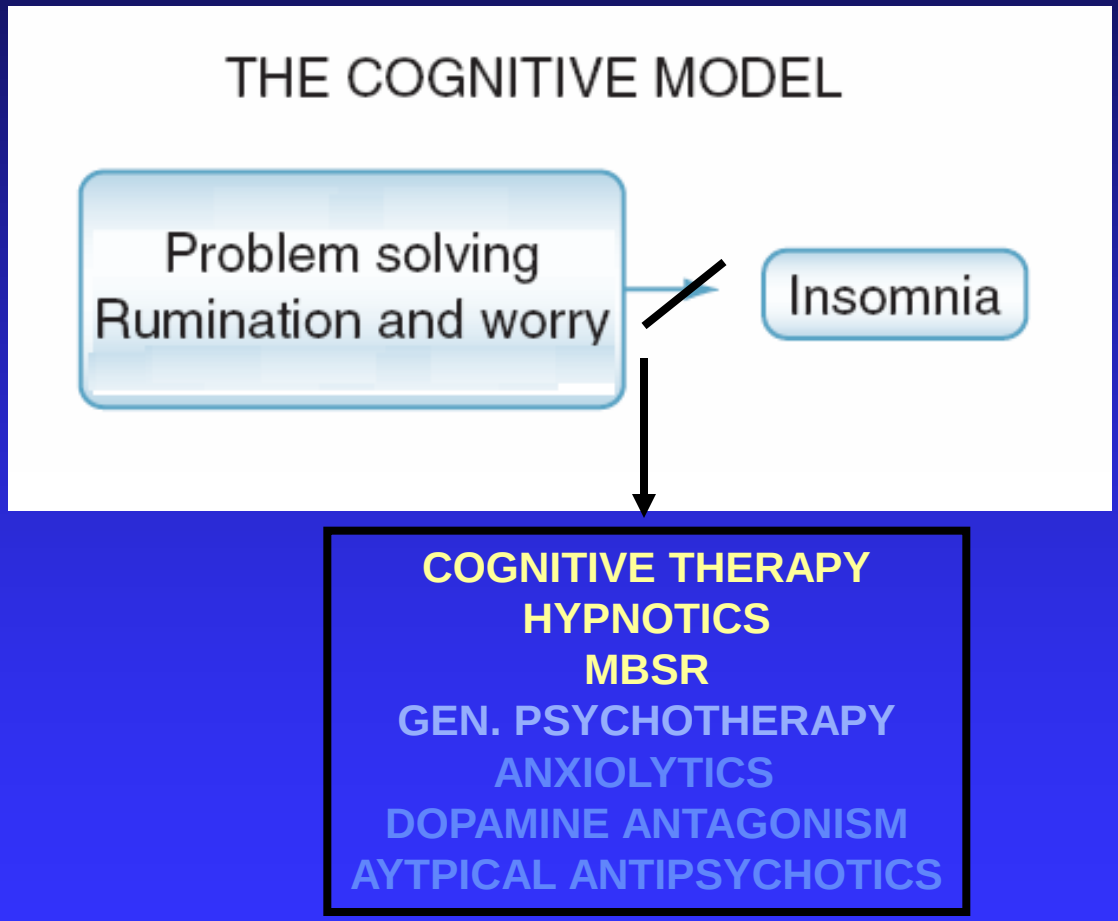


TARGETS FOR TREATMENT

COGNITIVE MODEL OF INSOMNIA (GENERAL)



ACTUALLY SRT & SCT

THE BEHAVIORAL PERSPECTIVE

THE SPIELMAN MODEL
(AKA 3 FACTOR OR 3P MODEL)

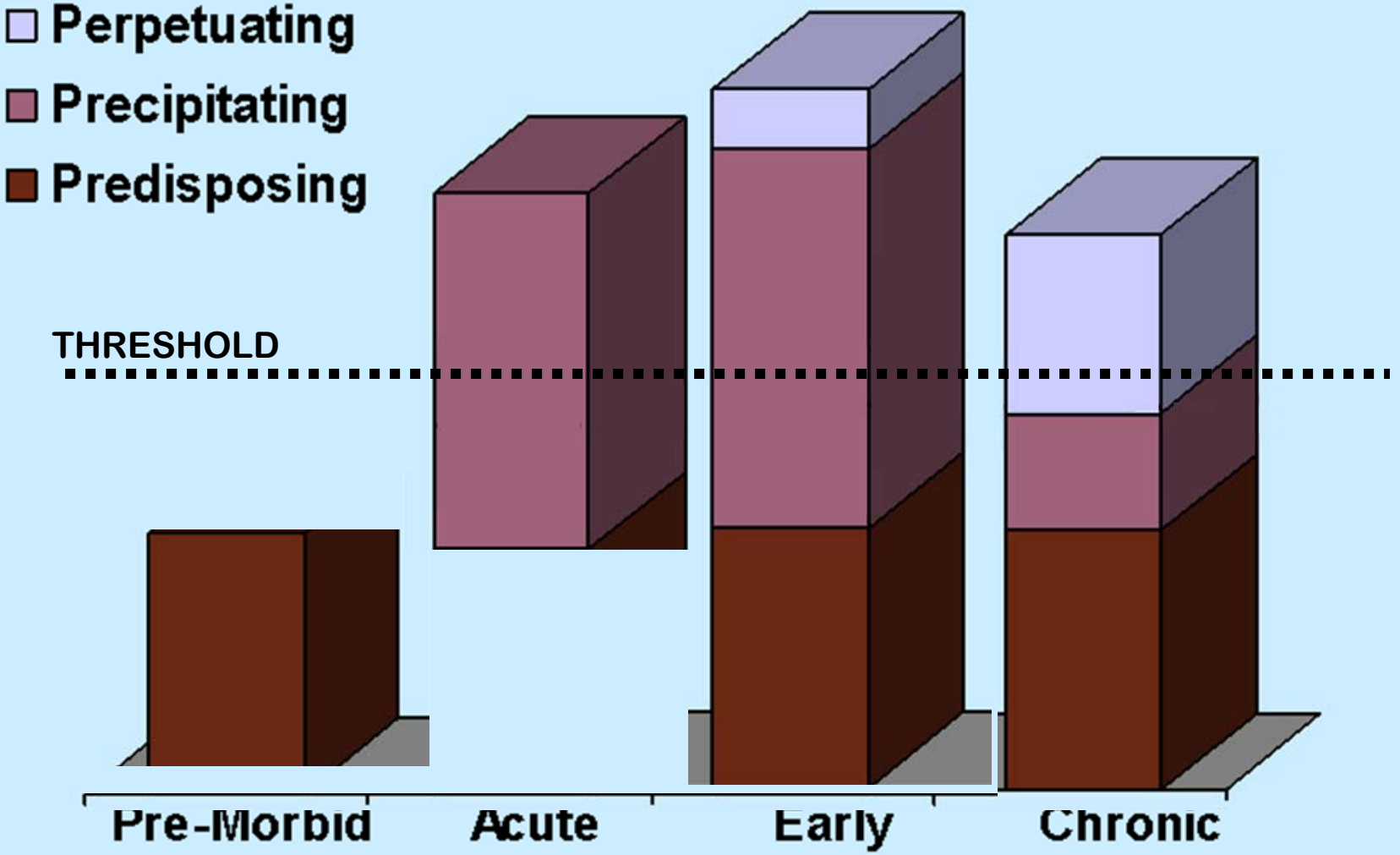
Spielman A. et al. A behavioral perspective on insomnia treatment. Psychiatric Clinics of North Am 1987; 10(4):541-553.

“The best cure for insomnia is to get a lot of sleep”

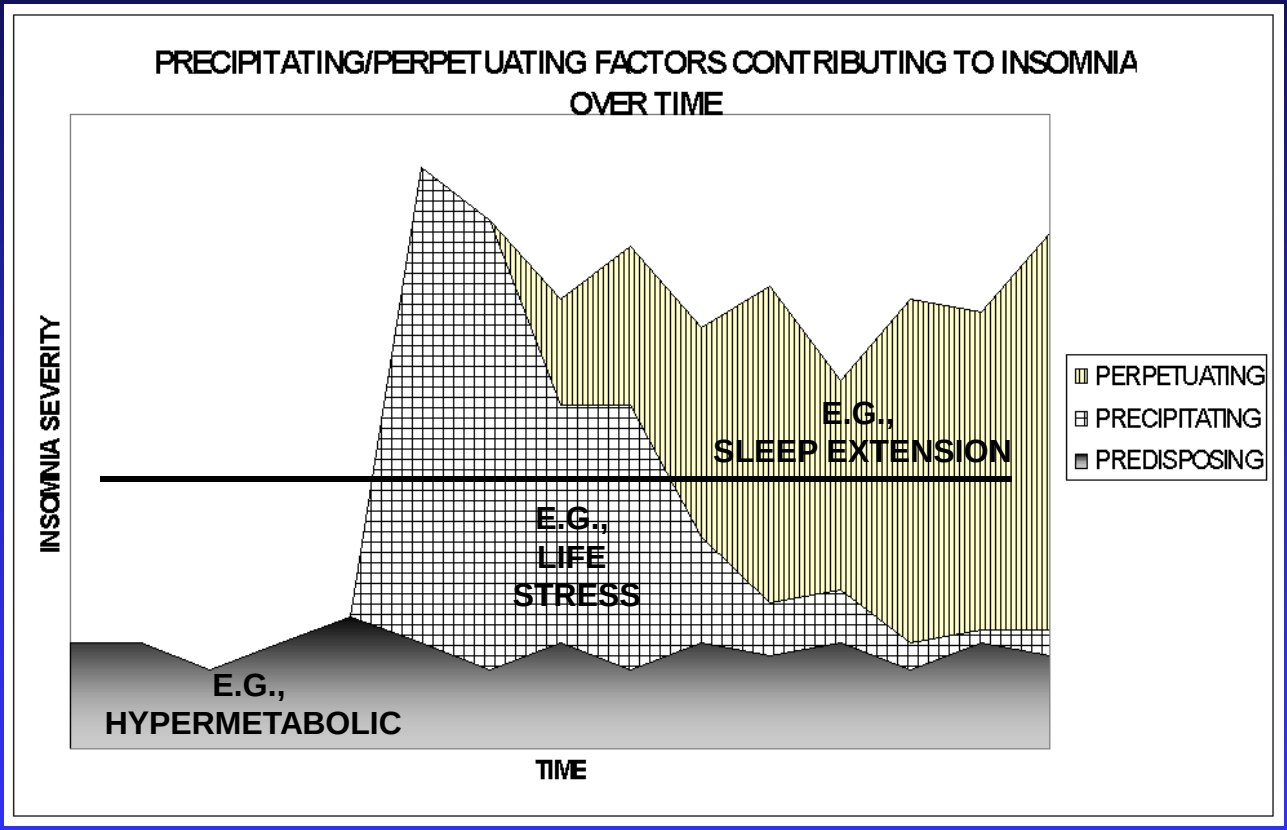
-- W.C. Fields

NATURE OF INSOMNIA OVER TIME

3 FACTOR MODEL

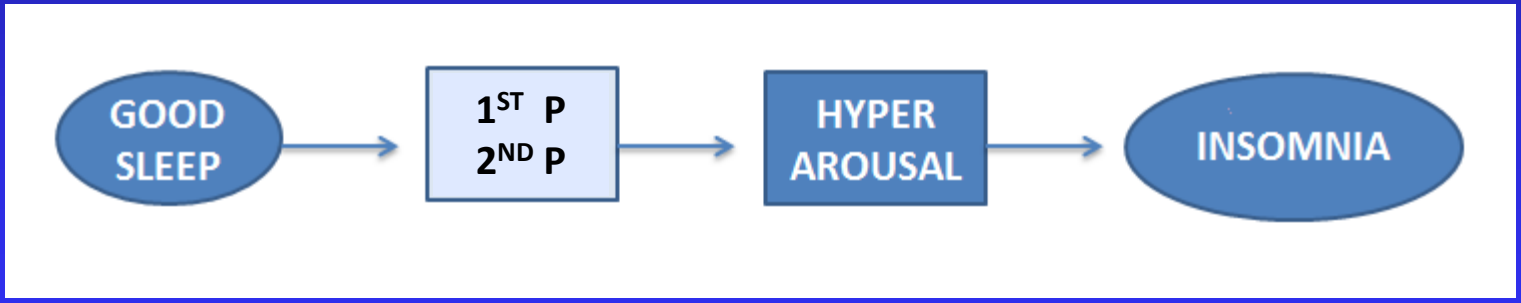


SPIELMAN'S NEW MODEL



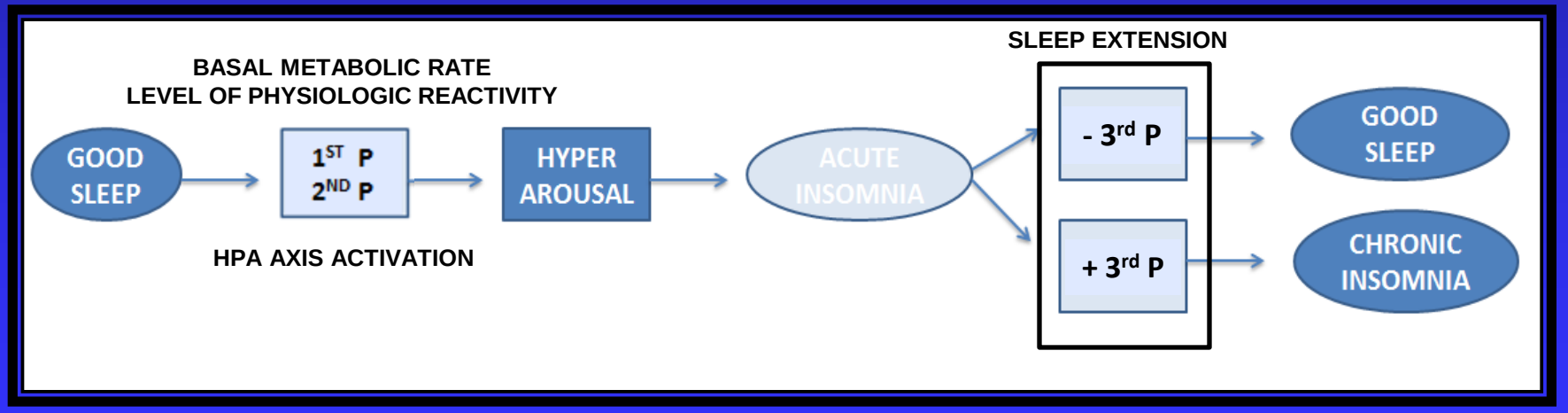
DOES THE MODEL EXPLAIN HOW THE HYPERAROUSAL CONDITION COMES INTO EXISTENCE ?

YES.



DOES THE MODEL EXPLAIN HOW ACUTE INSOMNIA BECOMES CHRONIC AND HOW THE CONDITIONS DIFFER ?

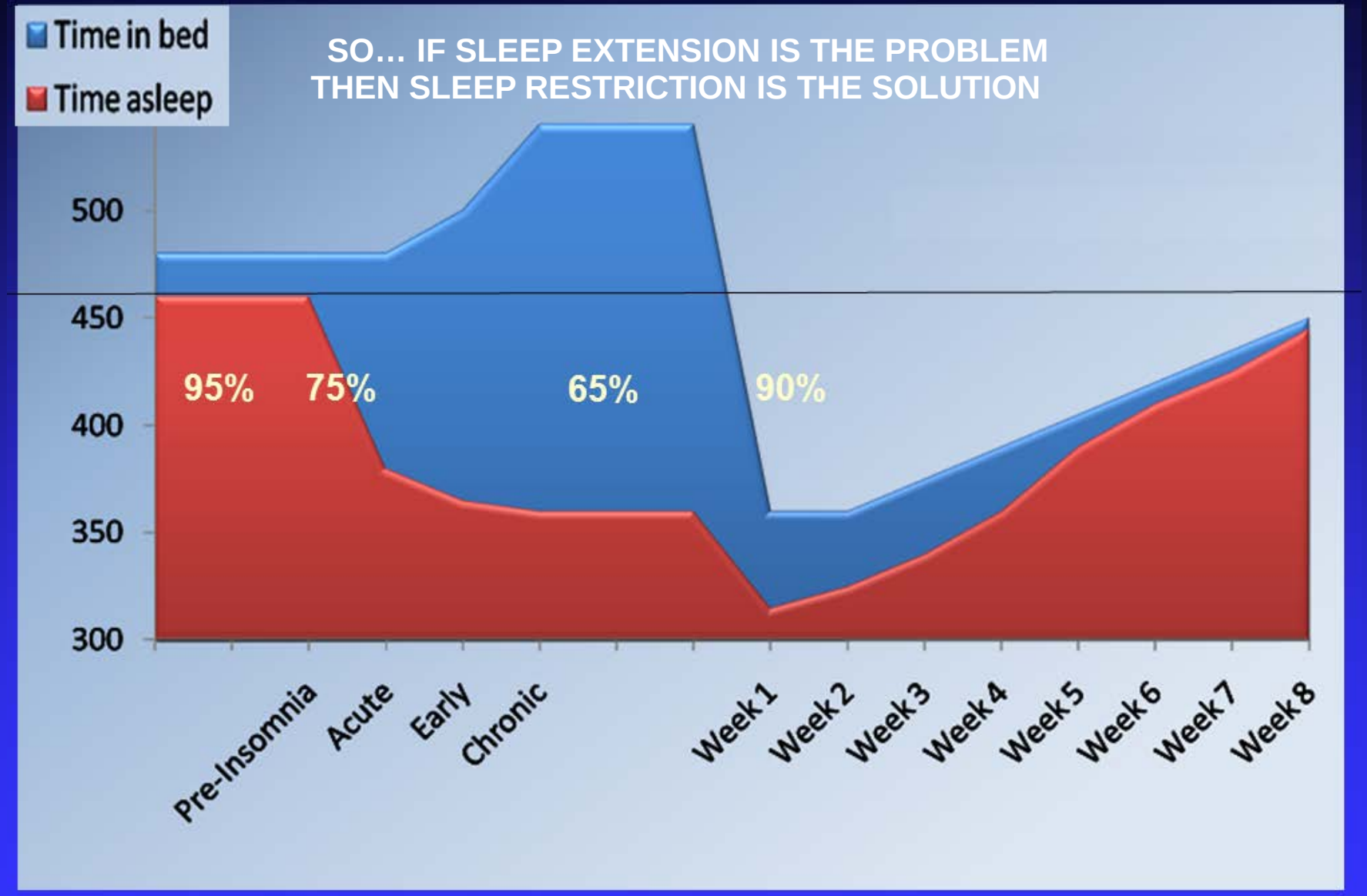
YES.



3rd P – SLEEP EXTENSION

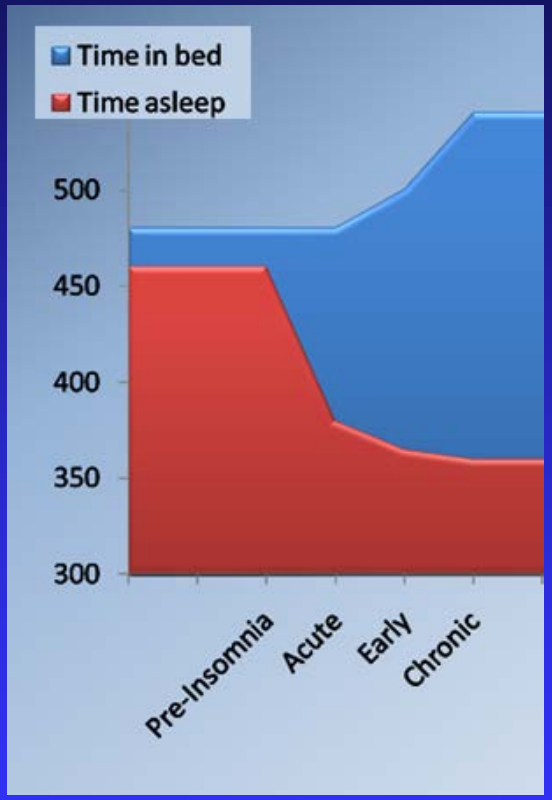
HOW TIME IN BED VARIES WITH INSOMNIA

HOW SLEEP OPPORTUNITY IS EXPANDED TO RECOVER LOST SLEEP

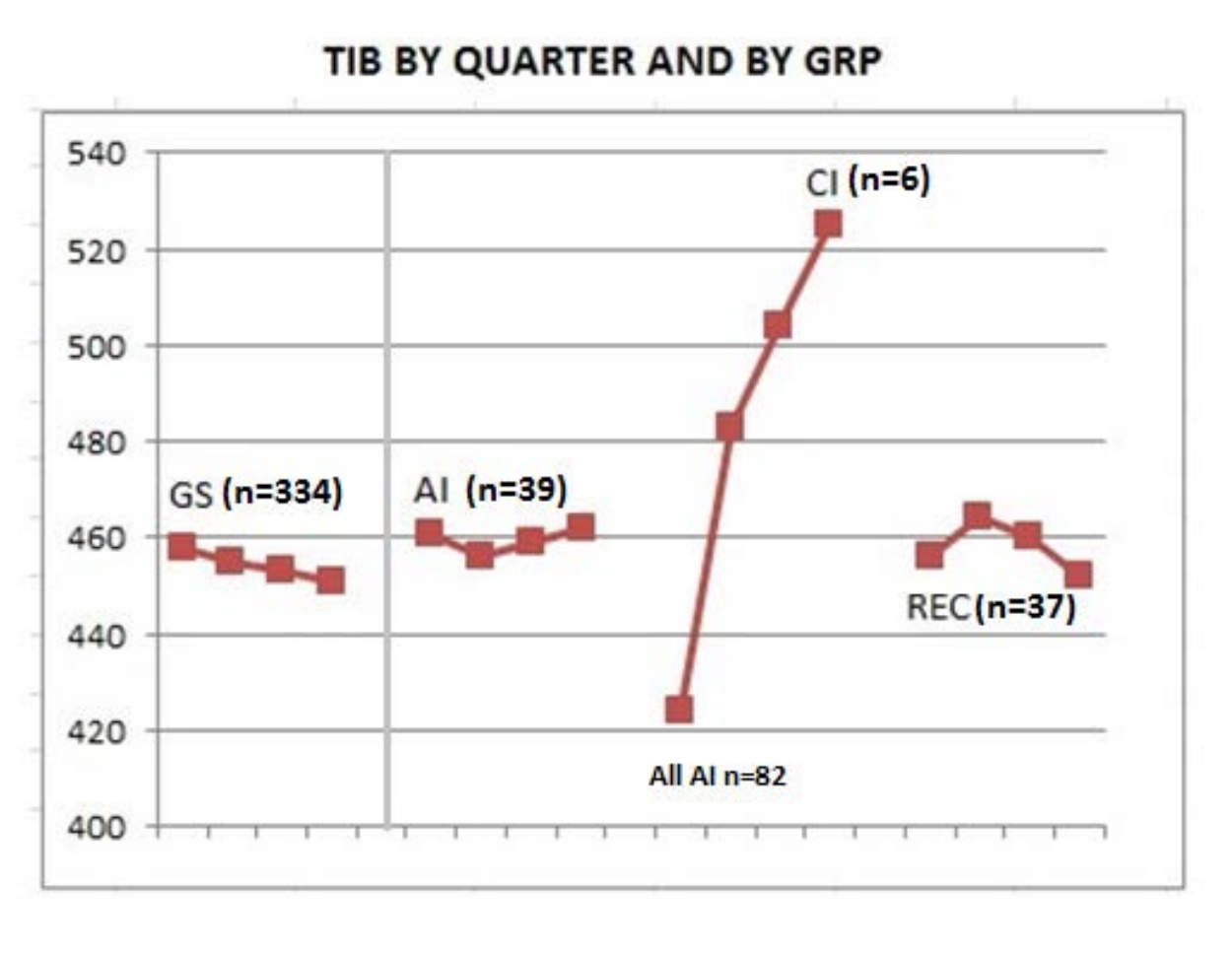


Schematic representation by Michael Grandner PhD

IS THIS TRUE ?


Time in bed
Time asleep
500
450
400
350
300
Pre-Insomnia
Acute
Early
Chronic

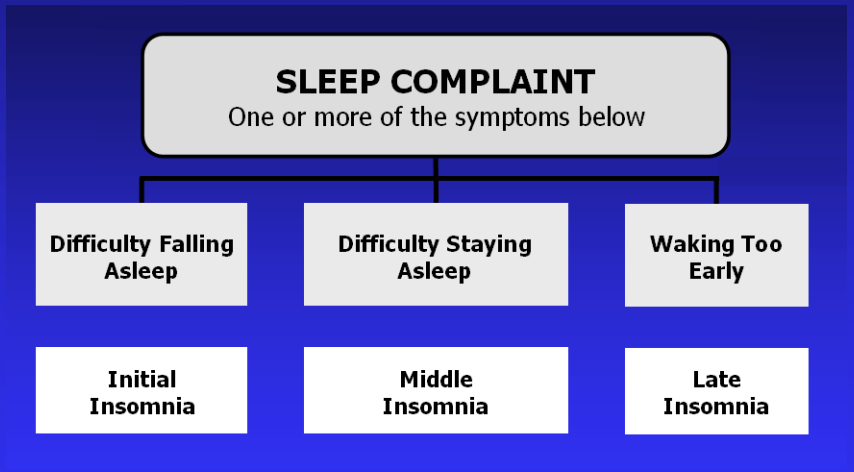
SO FAR…


TIB BY QUARTER AND BY GRP
540
520
500
480
460
440
420
400
GS (n=334)
AI (n=39)
CI (n=6)
REC (n=37)
All AI n=82

CAN THIS MODEL EXPLAIN THE VARIOUS INSOMNIA PHENOTYPES (TYPES AND SUBTYPES)

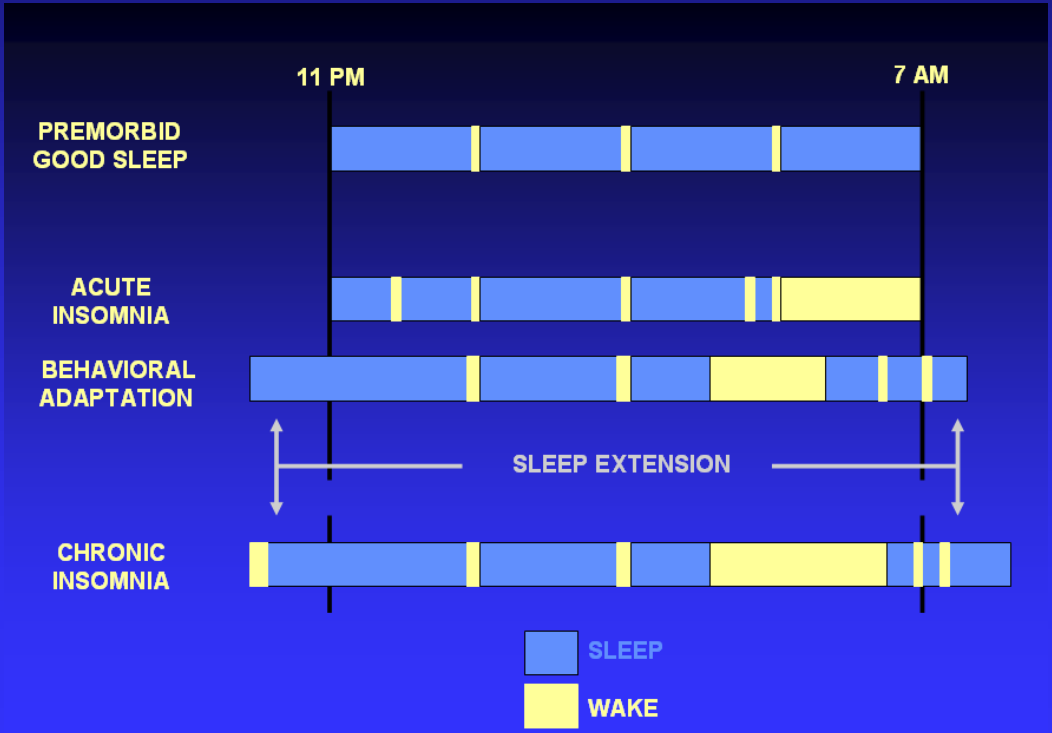
PRIMARY INSOMNIA / INSOMNIA DISORDER

PSYCHOPHYSIOLOGIC INSOMNIA
IDIOPATHIC INSOMNIA
PARADOXICAL INSOMNIA
SLEEP HYGIENE DISORDER
PHYSIOLOGIC INSOMNIA
INSOMNIA NOS



PROBABLY NOT

DOES CHRONIC INSOMNIA OCCUR SOLELY IN RELATION TO SLEEP EXTENSION ?



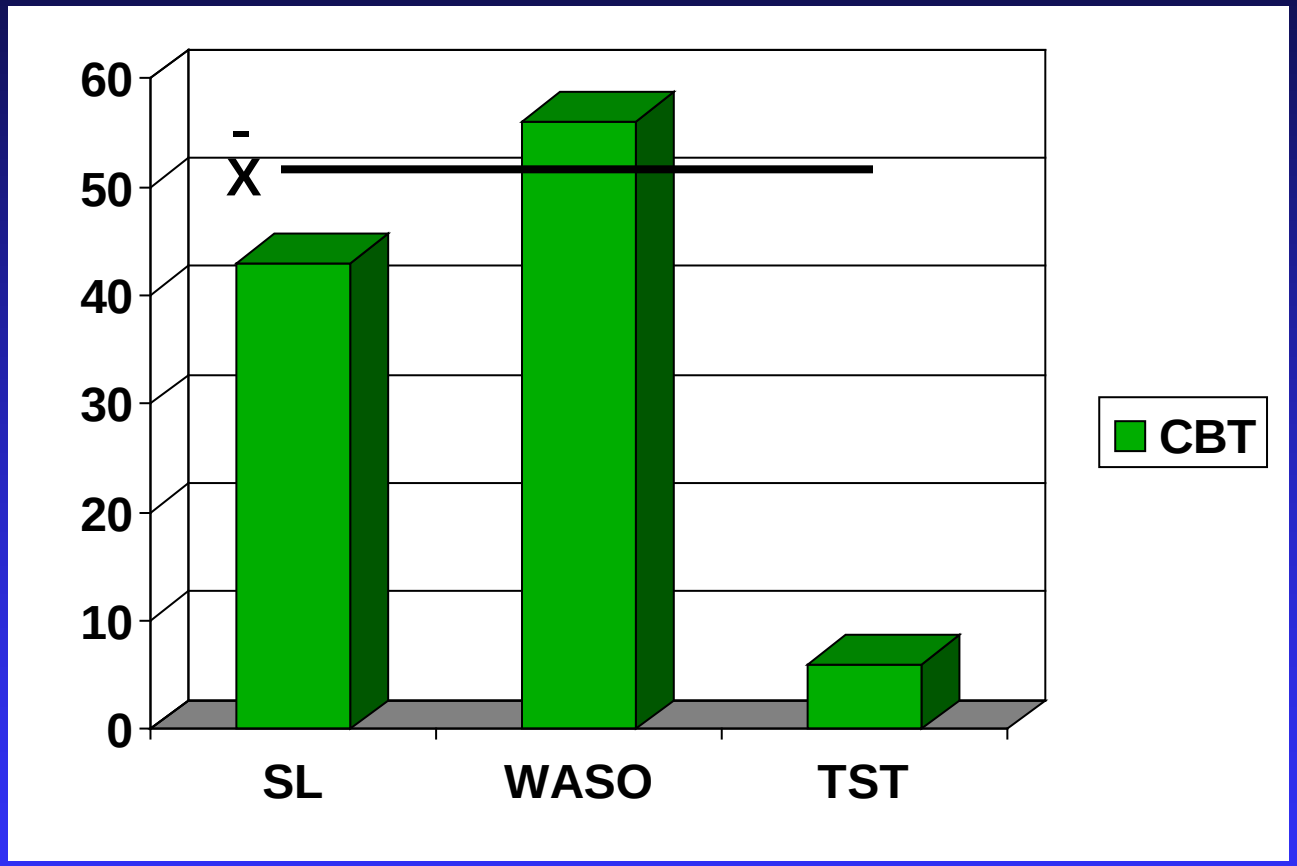
Schematic representation by Michael Smith PhD

PROBABLY NOT

ASSUMING TX (CBT-I) ENTIRELY ELIMINATES THE BEHAVIORS THAT PERPETUATE INSOMNIA

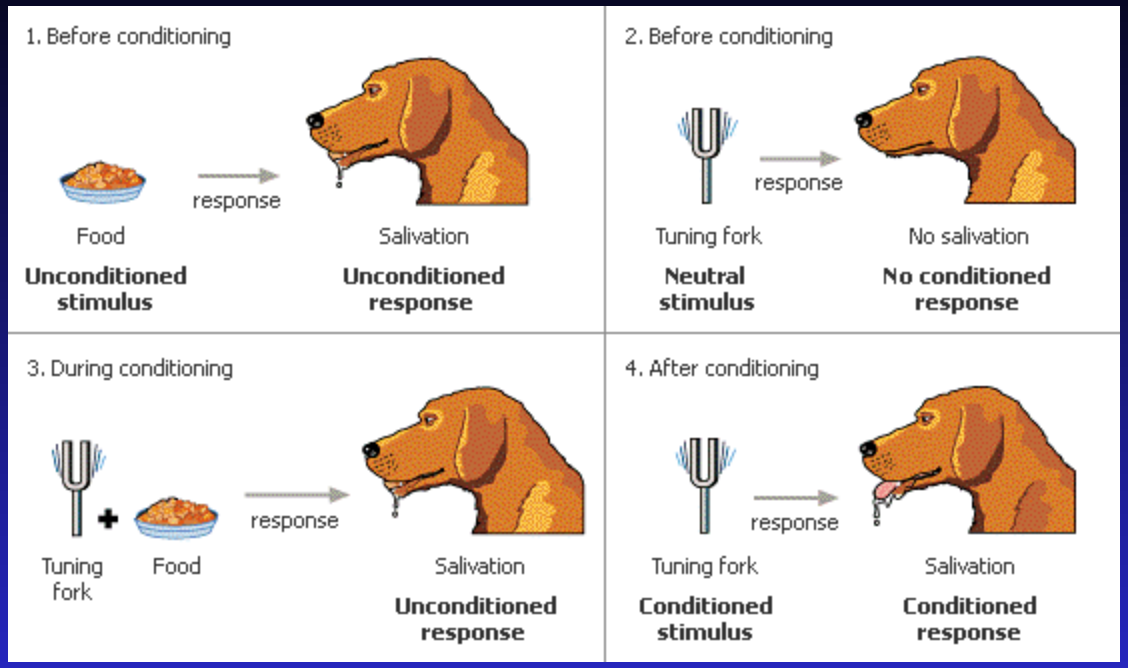
WHY ARE PATIENTS NOT CURED ?

AVERAGE RESPONSE = ~ 50%



Smith et al. American Journal of Psychiatry. 159: 5-11. 2002.

IS THERE SOMETHING MISSING FROM THE BEHAVIORAL MODEL ?



THE BEHAVIORAL MODEL FOCUSES ON INSTRUMENTAL AND NOT CLASSICAL CONDITIONING

CLASSICAL CONDITIONING

NORMAL SITUATION

BEDROOM/BEDTIME ➔ SLEEPINESS & SLEEP

ACUTE INSOMNIA SITUATION

BEDROOM/BEDTIME + LIFE STRESS INDUCED SOMATIC AROUSAL ➔ SCD

BEDROOM/BEDTIME + LIFE STRESS INDUCED CORTICAL AROUSAL ➔ SCD

CHRONIC INSOMNIA SITUATION

BEDROOM/BEDTIME ~~+ LIFE STRESS~~ INDUCED SOMATIC AROUSAL ➔ SCD

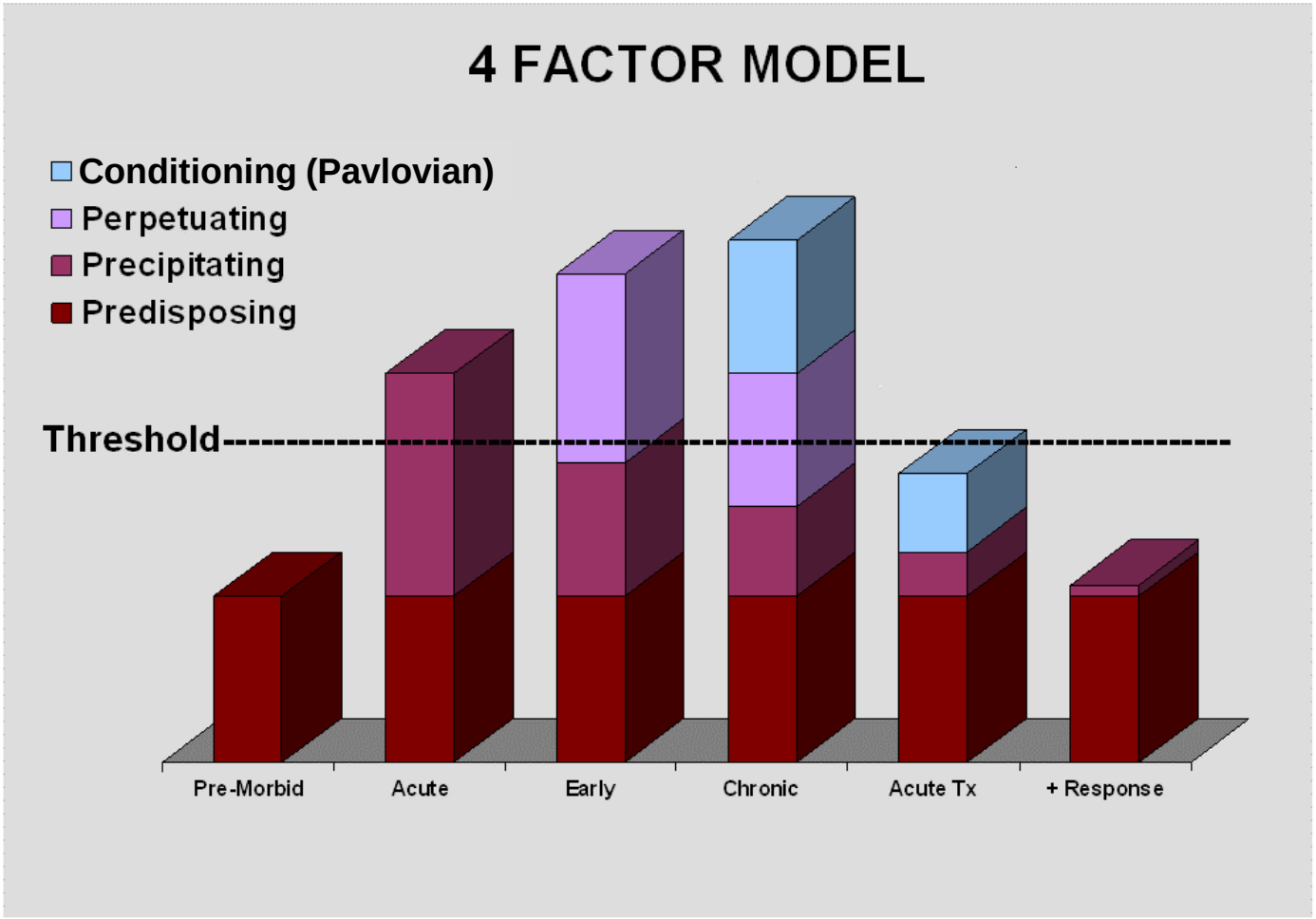
BEDROOM/BEDTIME ~~+ LIFE STRESS~~ INDUCED CORTICAL AROUSAL ➔ SCD

PATIENT'S TELL YOU ABOUT THIS ALL THE TIME !

SO IF ONE TAKES INTO ACCOUNT CONDITIONING

THE THREE FACTOR MODEL COULD BE REPRESENTED AS A FOUR FACTOR MODEL

THE FOUR FACTOR MODEL

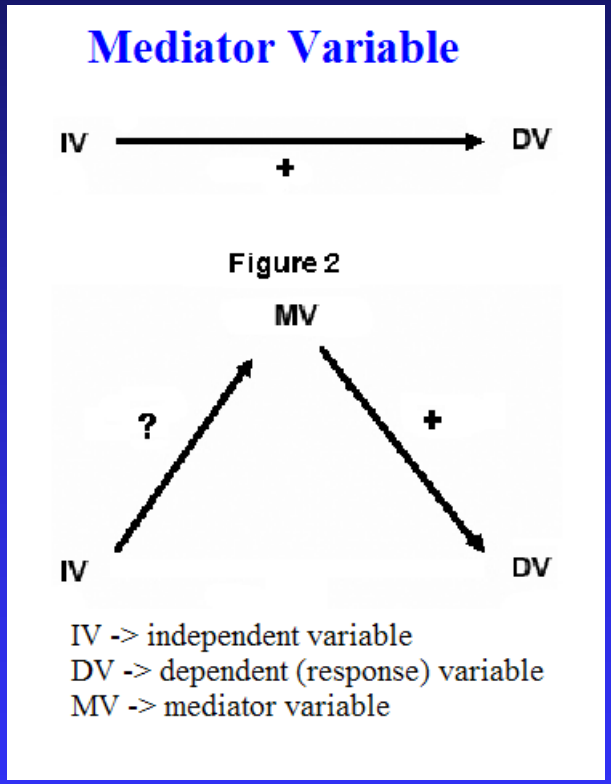


Perlis, Pigeon and Smith; Principles and Practice of Sleep Medicine Chapter 60

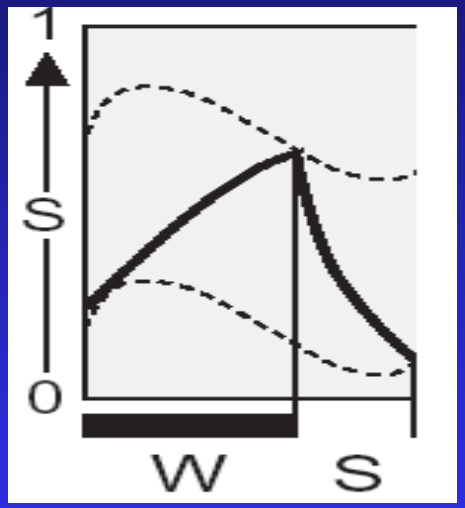
DOES CHRONIC INSOMNIA OCCUR SOLELY IN RELATION TO PHYSIOLOGIC, COGNITIVE, AND BEAHVIORAL FACTORS ?

PROBABLY NOT

IT'S LIKELY THAT MODERATORS & MEDIATORS ARE AT PLAY



WHAT'S MISSING ?



29

Sleep Homeostasis and Models of Sleep Regulation

Alexander A. Borbély
Peter Achermann

The level of electroencephalographic (EEG) slow wave activity (SWA) is determined by the duration of prior sleep and waking. SWA is a marker of nonrapid eye movement (NREM) sleep intensity and may serve as an indicator of NREM sleep homeostasis. Power in the range of sleep spindles (spindle frequency activity, SFA) shows in part an inverse relationship to SWA. This observation can be accounted for by neurophysiological data. Thalamocortical neurons exhibit oscillations in the range of sleep spindles at an intermediate level of hyperpolarization (corresponding to superficial NREM sleep), and slow oscillations at a high level of hyperpolarization (corresponding to deep NREM sleep). Although the homeostatic NREM sleep process is largely independent of circadian factors, it interacts with the circadian rhythm of sleep propensity.

The two-process model of sleep regulation is based on the homeostatic process S and the circadian process C. Advanced versions of its homeostatic part can simulate the SWA pattern for a variety of experimental schedules. Essential aspects of the model have been validated by results from forced desynchrony protocols. Other models include the two-oscillator model, the reciprocal interaction models, and combined models. The incorporation of rapid eye movement (REM) sleep homeostasis is still at an early stage.

There is recent evidence for a local, use-dependent facet of sleep regulation. This concept is derived from unihemispheric sleep experiments in marine mammals, and from studies revealing specific regional effects in the sleep EEG of humans. The modeling approach could be extended to local sleep.

Three basic processes underlie sleep regulation: (1) a homeostatic process determined by sleep and waking; (2) a circadian process, a clock-like mechanism defining the alternation of periods with high and low sleep propensity and being basically independent of sleep and waking; and (3) an ultradian process occurring within sleep and represented by the alternation of the two basic sleep states—nonrapid eye movement (NREM) sleep and rapid eye movement (REM) sleep. This chapter focuses on "sleep homeostasis." Homeostasis has been defined as "the coordinated physiological processes which maintain most of the steady states in the organism."[1] The term *sleep homeostasis*[2] refers to the sleep-wake–dependent aspect of sleep regulation, as homeostatic mechanisms counteract deviations from an average "reference level" of sleep. They augment sleep propensity when sleep is curtailed or absent, and they reduce sleep propensity in response to excess sleep.

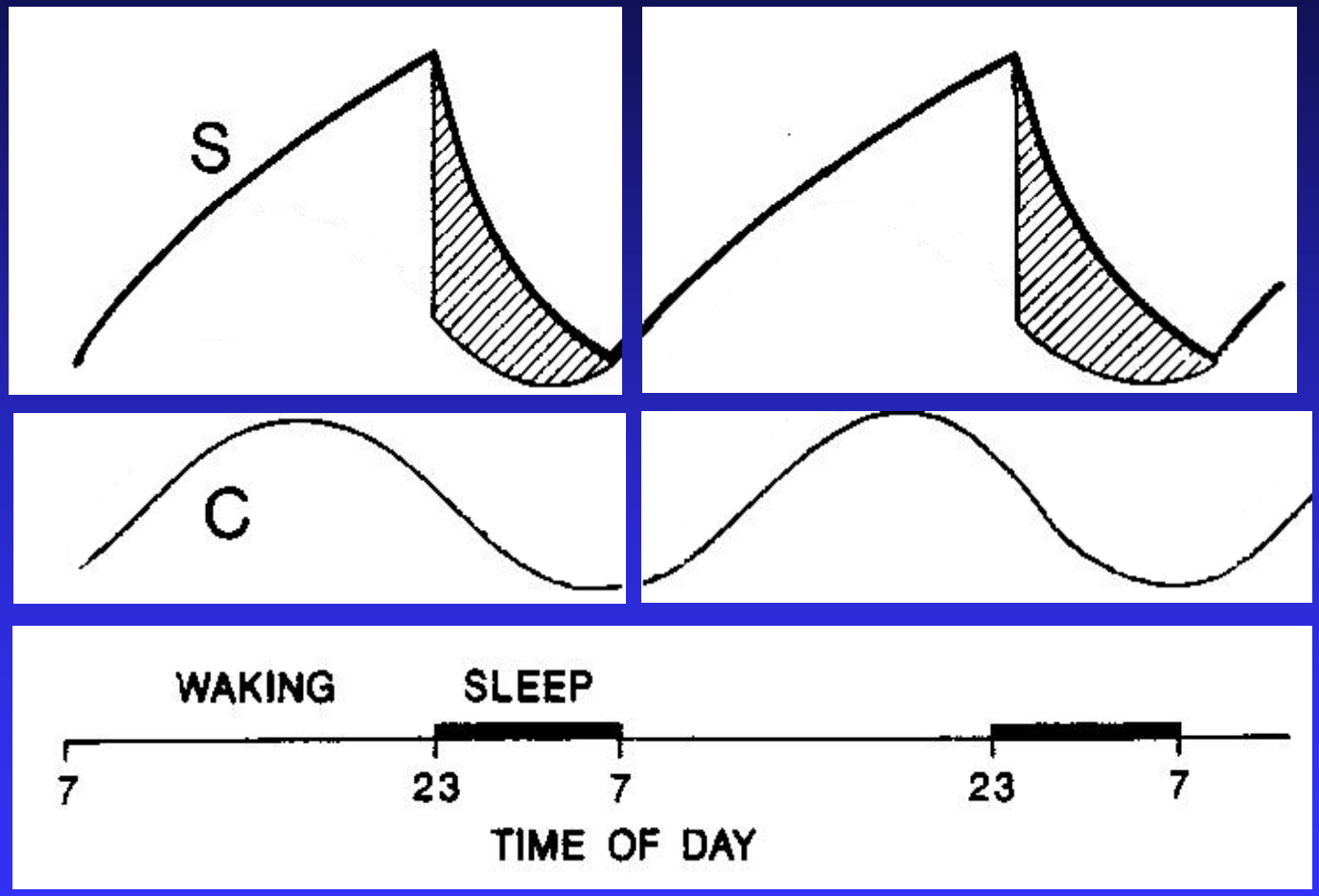
The interest in modeling the processes underlying sleep regulation has increased over the past decade. In the research briefing report of the Institute of Medicine,[3] a panel of leading North American experts in basic sleep research recommended that "the homeostatic and circadian influences need to be integrated into a single functional model that can describe both the timing of sleep and its quality." Models help delineate the processes involved in the regulation of sleep and thereby offer a conceptual framework for the analysis of existing and new data.

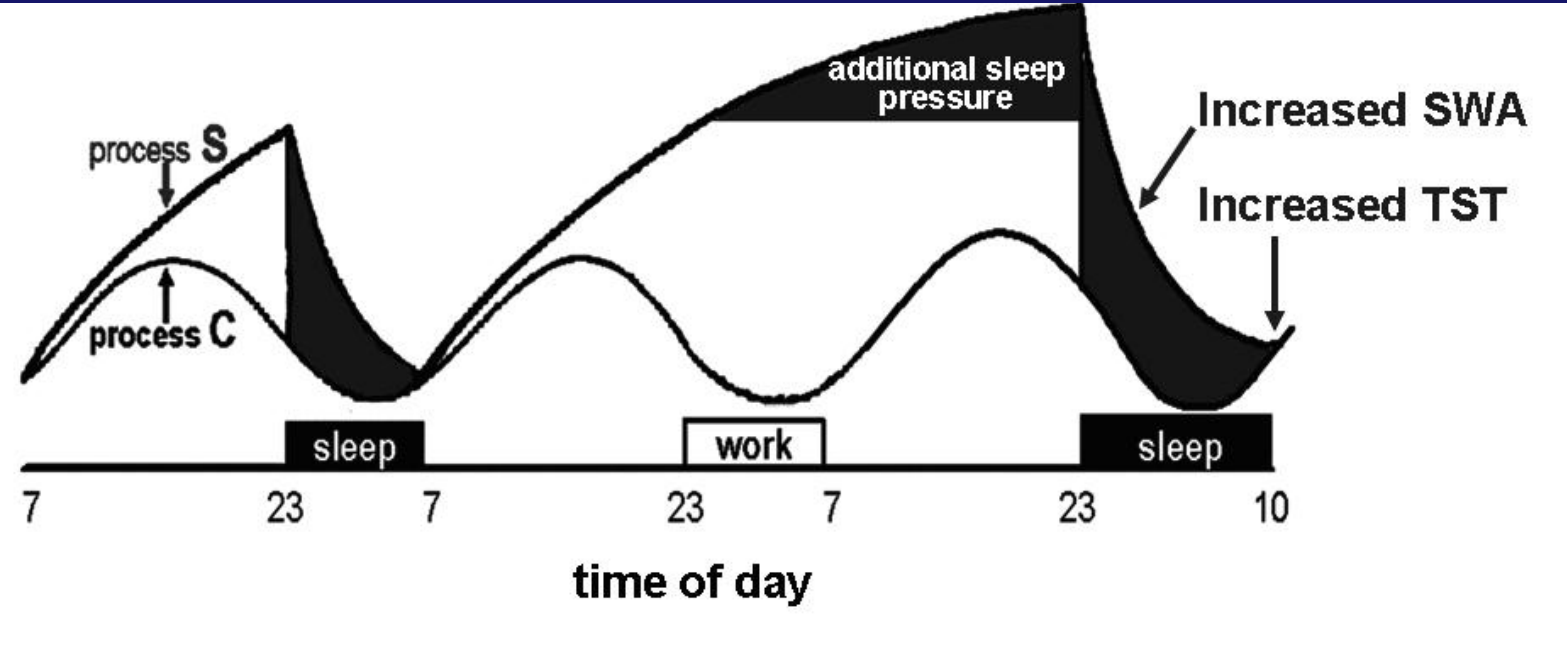
HOMEOSTATIC REGULATION OF SLEEP

Electroencephalographic Slow Wave Activity: A Physiological Indicator of NREM Sleep Homeostasis

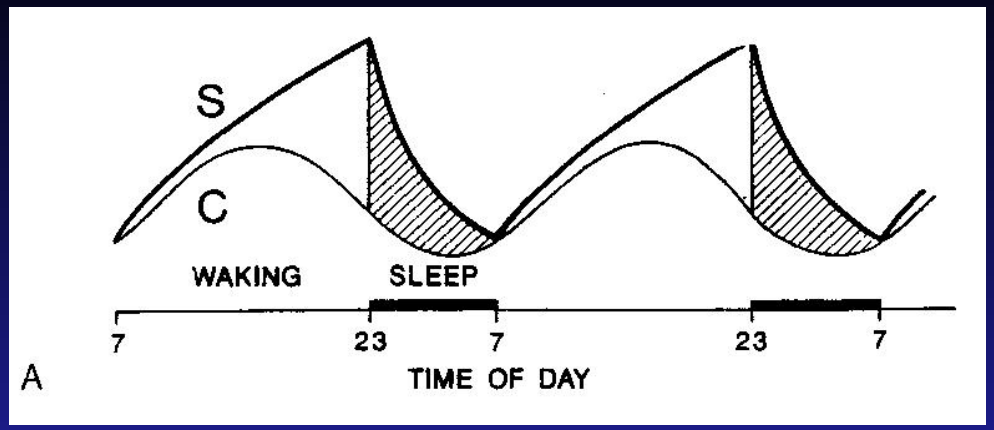
Slow-Wave Sleep and Slow Wave Activity. NREM sleep is not a homogeneous substate of sleep, but can be subdivided according to the predominance of electroencephalographic (EEG) slow wave activity (SWA). The percentage of slow waves (frequency, 0 to 2 Hz; minimum peak-to-peak value, 75 μV) is the major criterion for scoring human NREM sleep into the stages 2, 3, or 4.[4] Stages 3 and 4 are commonly referred to as slow-wave sleep (SWS). However, the conventional sleep scoring method is inadequate for a quantitative analysis, because the sleep stages are based on rather general and arbitrary criteria. Presently, EEG parameters can be assessed by computer-aided methods of signal analysis. One of the most important functional EEG parameters will be referred to as "slow wave activity." It is equivalent to "delta activity" and encompasses components of the EEG signal in the frequency

BORBELY'S 2 PROCESS MODEL OF NORMAL SLEEP





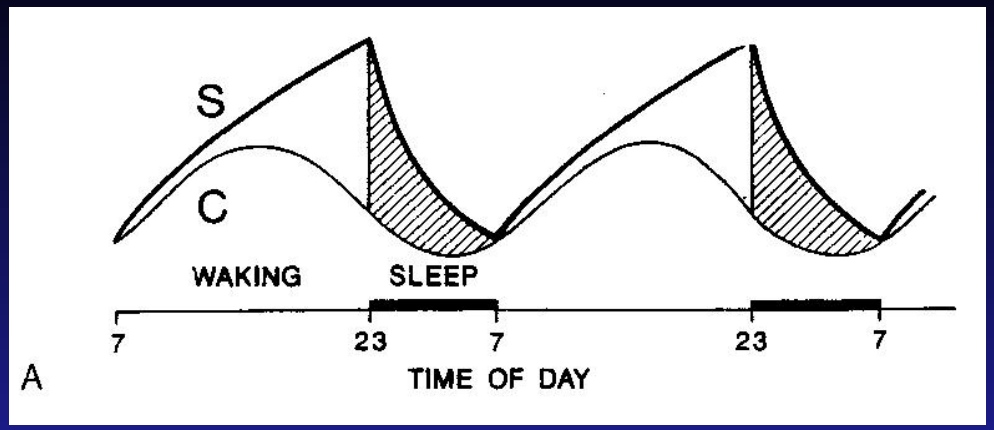
WHAT ABOUT INSOMNIA ?



THE TWO PROCESS MODEL HELP ACCOUNT FOR INSOMNIA SUBTYPE

INITIAL AND LATE INSOMNIA MAY OCCUR WITH SUBTLE PHASE SHIFTS OR SLEEPING OUT OF ONE'S PREFERRED SLEEP PHASE

INITIAL, MIDDLE, OR LATE, MAY OCCUR AS SLEEP HOMEOSTASIS DYSREGULATTION (DEPRIME OR EXCESSIVE OPPORTUNITY)

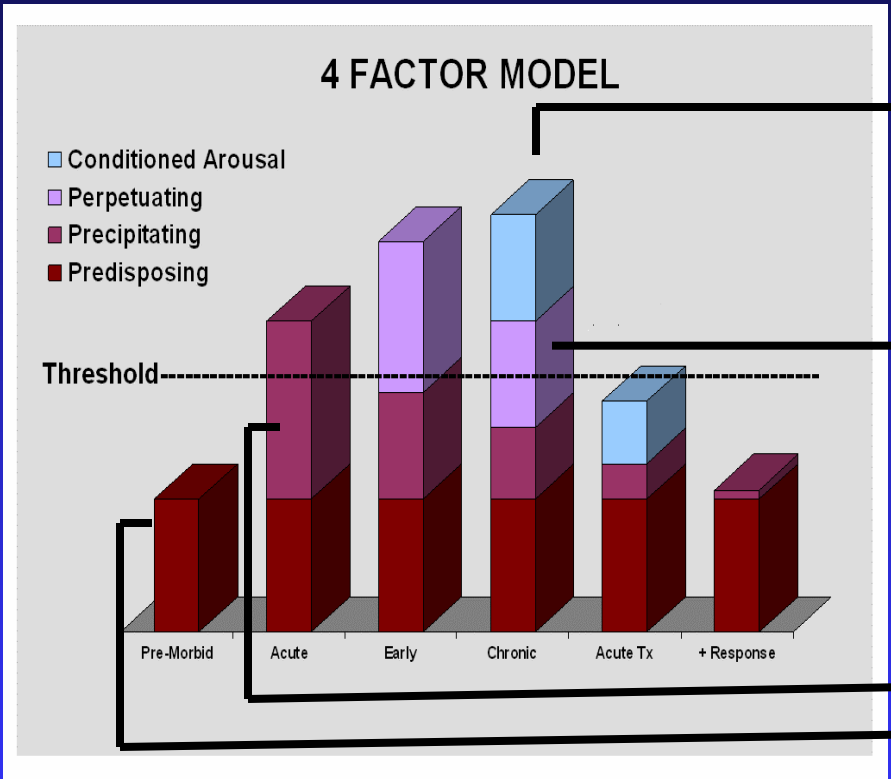


THE TWO PROCESS MODEL HELPS ACCOUNT FOR WHY SLEEP EXTENSION IS A PROBLEM AND WHY SLEEP RESTRICTION WORKS

"IF SLEEP EXTENSION IS THE PROBLEM, SLEEP RESTRICTION IS THE SOLUTION"

TARGETS FOR TREATMENT

FOUR FACTOR MODEL



STIMULUS CONTROL INST
HYPNOTICS
SADs
OREXIN ANTAGONISM

SLEEP RESTRICTION
STIMULUS CONTROL INST

EXERCISE
RELAXATION
GEN. PSYCHOTHERAPY

SO THESE ARE THE BASIC MODELS

THERE ARE OTHER MODELS WORTH STUDYING DOWN THE ROAD

THE LUNDH MODEL

THE NEUROCOGNITIVE MODEL

THE HARVEY MODEL

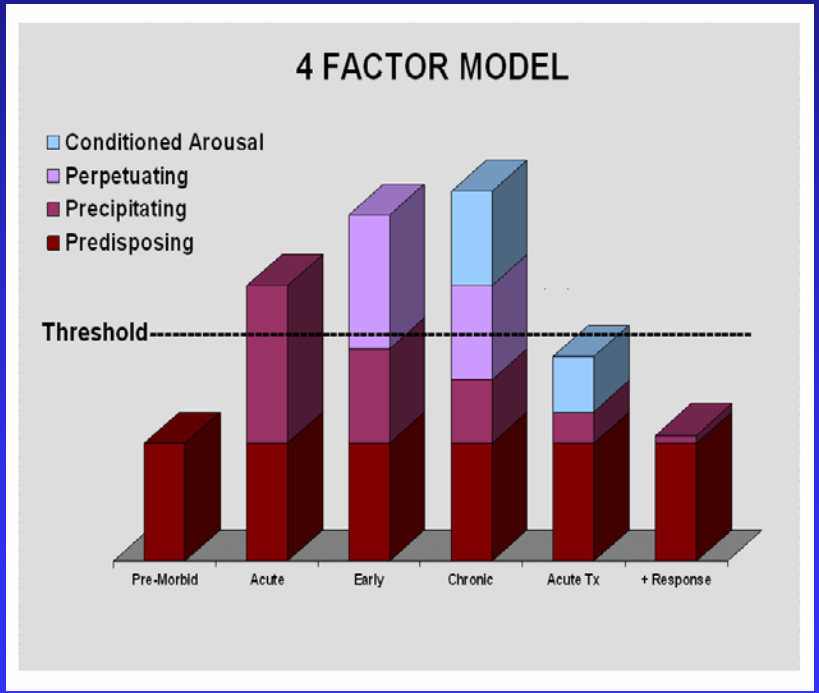
THE PSYCHOBIOLOGICAL INHIBITION MODEL

THE NEUROBIOLOGICAL MODEL

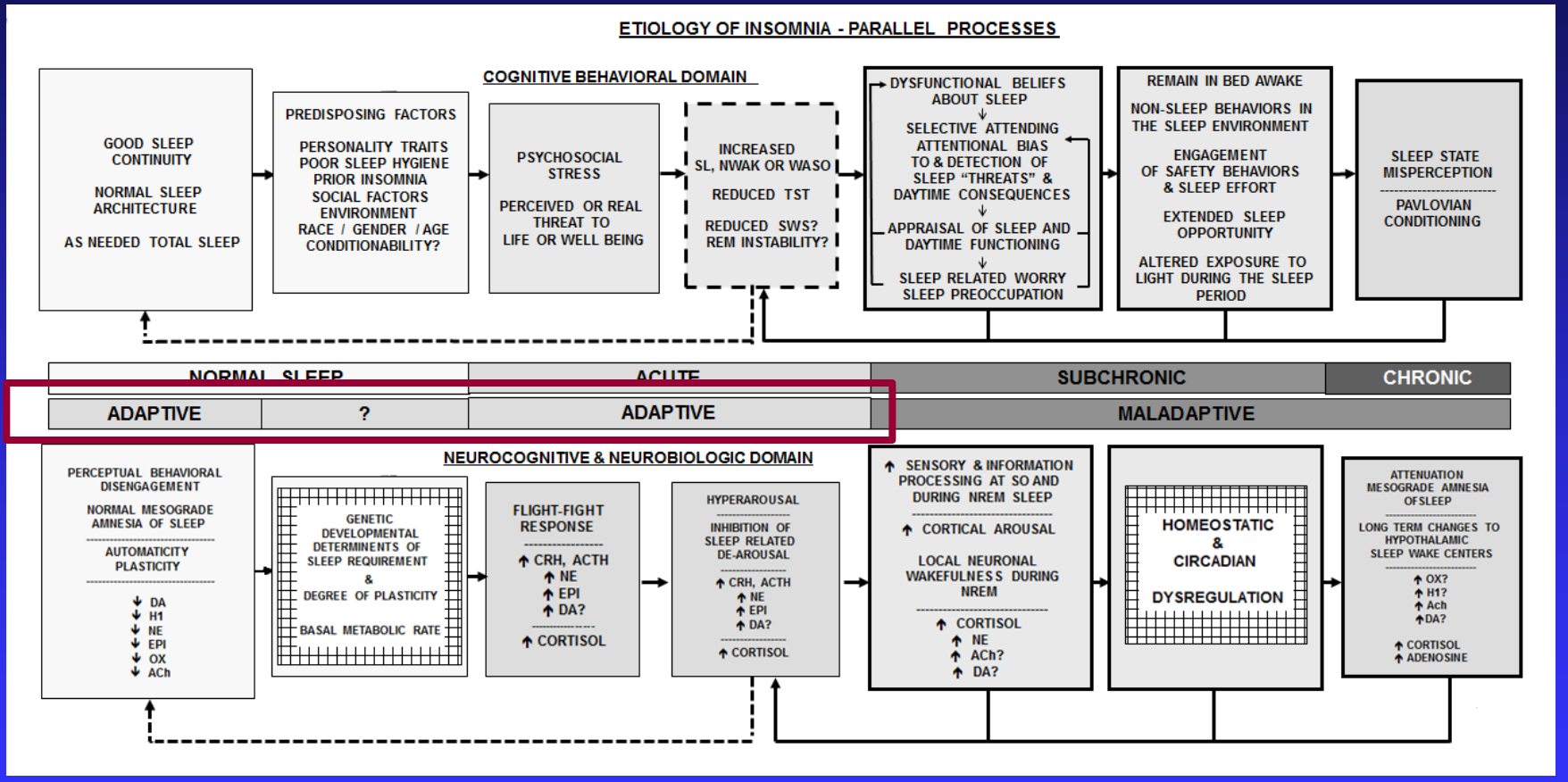
THE DROSOPHILA MODEL
THE RODENT MODEL

THE PARALLEL PROCESS MODEL

FROM A CLINICAL POINT OF VIEW



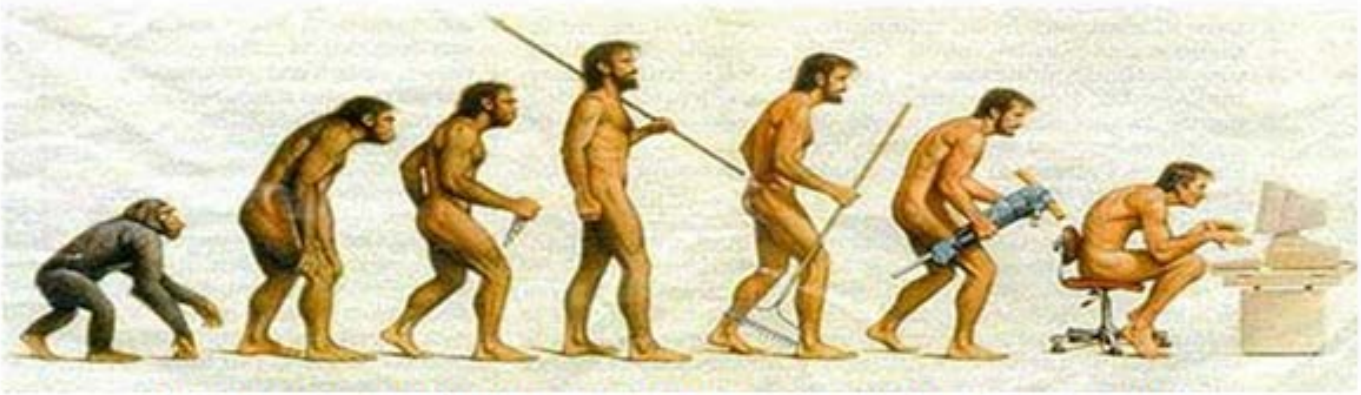
FROM A RESEARCH POINT OF VIEW



“No matter how important sleep may be, it was adaptively deferred when the mountain lion entered the cave.”

SPIELMAN ET AL. 1991

Thank you Jay !

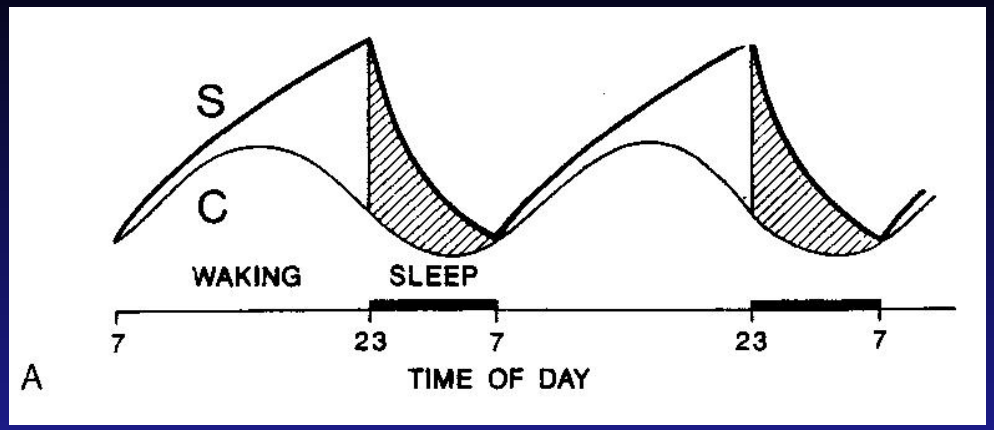


WE LIVE WITH INSOMNIA TODAY BECAUSE, AT SOME POINT, IN OUR EVOLUTIONARY HISTORY INSOMNIA ALLOWED US TO LIVE'

DEAN HANDLEY
SEPRACOR
CIRCA 2005
DINNER

The University of Pennsylvania

Michael Perlis PhD
Director, Upenn Behavioral Sleep Medicine Program
mperlis@upenn.edu



GIVEN THE TWO PROCESS MODEL

WHAT SHOULD BE THE KEY QUESTIONS OF RELEVANCE FOR TX

1. HOW LONG IS THE INDIVIDUAL AWAKE DURING THE DAY ?
2. DOES THE INDIVIDUAL NAP (AND WHEN) ?
3. WHAT TIME IS THE INDIVIDUAL GOING TO BED ?
4. WHAT TIME IS THE INDIVIDUAL GETTING OUT OF BED ?