

**ETIOLOGY OF INSOMNIA
&
TREATMENT IMPLICATIONS**



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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**



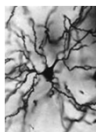
**HOW DOES THIS CONDITION DEVELOP ?
WHAT IS IT ?**

**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



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Etiology and Pathophysiology of Insomnia

Michael L. Perl, Jason Gordon Elin, Jacqueline Delbecq, Dieter Bannasch

INTRODUCTION

It is a well-known fact that insomnia is a common sleep disorder. It is characterized by difficulty falling asleep, staying asleep, or waking up too early. The prevalence of insomnia is estimated to be between 10% and 30% in the general population. The condition can have a significant impact on a person's quality of life, leading to daytime fatigue, irritability, and difficulty concentrating. The etiology of insomnia is complex and multifactorial, involving a combination of genetic, environmental, and psychological factors. The pathophysiology of insomnia is also complex, involving dysregulation of the body's circadian rhythm and the sleep-wake cycle. This chapter provides a comprehensive overview of the current understanding of the etiology and pathophysiology of insomnia, highlighting the latest research findings and clinical implications.

DEFINITION OF INSOMNIA

Insomnia is defined as a persistent difficulty in falling asleep, staying asleep, or waking up too early, despite adequate opportunity for sleep. The condition is typically diagnosed based on a clinical history and a sleep diary. The International Classification of Sleep Disorders (ICSD-2) defines insomnia as a disorder characterized by a complaint of difficulty in falling asleep, staying asleep, or waking up too early, despite adequate opportunity for sleep. The condition is typically diagnosed based on a clinical history and a sleep diary. The ICSD-2 defines insomnia as a disorder characterized by a complaint of difficulty in falling asleep, staying asleep, or waking up too early, despite adequate opportunity for sleep.

Chapter 82

Insomnia

Chapter 78

Insomnia

ISBN 978-0-12-0208-1-2 PLS 8078-0-12-0208-12000-0 Author: Elin, J., Perl, M. L.

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	Verma 1974	Verma 1981	Frederick 1982	Adam 1985	Chapman 1994
Subject Issues						
Mean Age (PS and OS)	29/26	18/11	18/11	21/21	21/21	24/24
Sample Size (PS and OS)	18/18	75/77	10/11	1,21/2	18/18	24/25
Recruitment Source	Lab	Lab	Lab	Comm	Lab	Comm
Recruitment (indicated insomnia research)	Yes	No	??	Yes	No	Yes
Medical Screening	??	??	??	Yes	??	Yes
Psych Screen	??	??	??	Yes	Yes	Yes
Sleep Lab Screen	??	??	??	Yes	??	Yes
Insomnia Complaint (for PS)	No	??	Yes	Yes	Yes	Yes
PSQ study	Yes	No	Yes	Yes	Yes	Yes
PSQ 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	↑
Respiration Rate - During the Day						
Respiration Rate - Prior to Sleep Onset	↑					
Respiration Rate - During Sleep	↑				ns	
Temperature* - 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 Vasoconductivity - During the Day	↑					ns
Peripheral Vasoconductivity - Prior to Sleep Onset					ns	
Peripheral Vasoconductivity - During Sleep					ns	ns

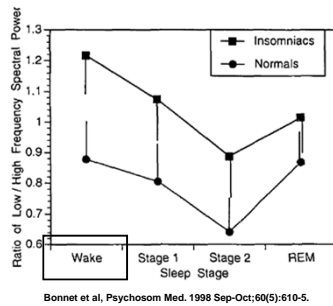
WHAT IS HYPERAROUSAL ?

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

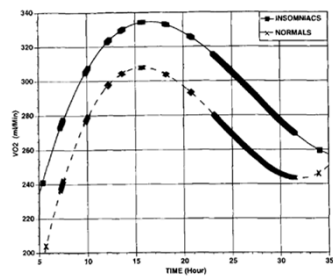
CONTEMPORARY MEASURES

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

HRV



METABOLIC RATE



HPA AXIS ABNORMALITIES

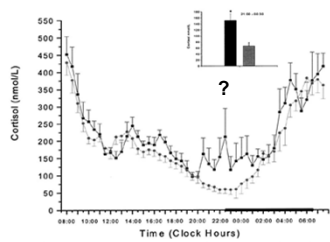


FIG. 2. Twenty-four-hour plasma cortisol concentrations in normals (●) and normals (○). The thick black line indicates the sleep recording period. The error bar indicates ± 1 SD ($P < 0.05$).

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

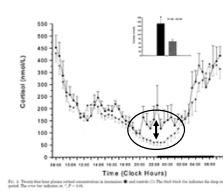
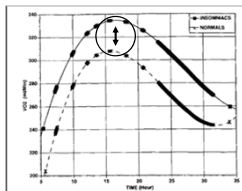
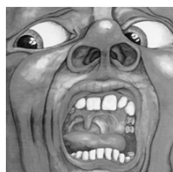


FIG. 2. Twenty-four-hour plasma cortisol concentrations in normals (●) and normals (○). The thick black line indicates the sleep recording period. The error bar indicates ± 1 SD ($P < 0.05$).

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

**DOES THE AROUSAL LEVEL COMPARE TO
THIS ?!**

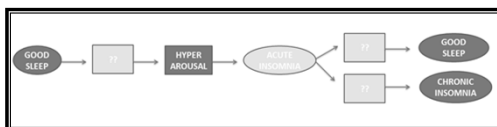


IT'S DOUBTFUL

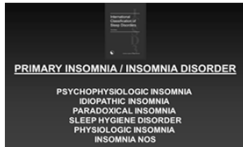
DOES THE MODEL EXPLAIN HOW THE
HYPERAROUSAL CONDITION COMES INTO
EXISTENCE ?



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)



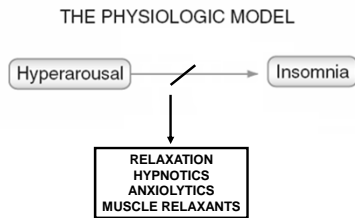
FOR A GOOD REVIEW OF THE EVIDENCE





TARGETS FOR TREATMENT

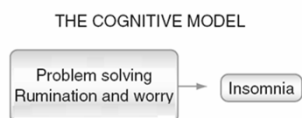
PHYSIOLOGIC MODEL OF INSOMNIA (GENERAL)



THE COGNITIVE PERSPECTIVE



COGNITIVE MODEL OF INSOMNIA (GENERAL)



**INSOMNIA OCCURS AS A
RESULT OF WORRY**

WORRY – CLASSIC



WORRY – CONTEMPORARY



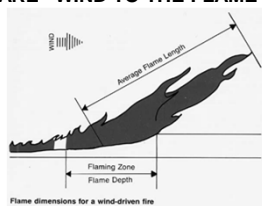
**DOES CHRONIC INSOMNIA OCCUR
BECAUSE OF**

**WORRY
RUMINATION
INTRUSIVE THOUGHTS**

**SELECTIVE ATTENTION
SLEEP-RELATED INTENTION AND EFFORT**

MAYBE

**OR MAYBE THE COGNITIVE FACTORS
ARE "WIND TO THE FLAME"**



**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**

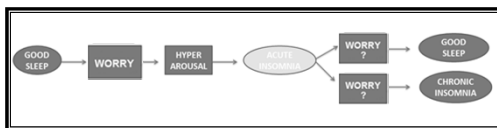
OR

**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 ?**



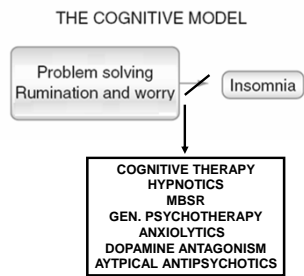
**CAN THIS MODEL EXPLAIN THE VARIOUS
INSOMNIA PHENOTYPES (TYPES AND SUBTYPES)**





TARGETS FOR TREATMENT

COGNITIVE MODEL OF INSOMNIA (GENERAL)



THE BEHAVIORAL PERSPECTIVE

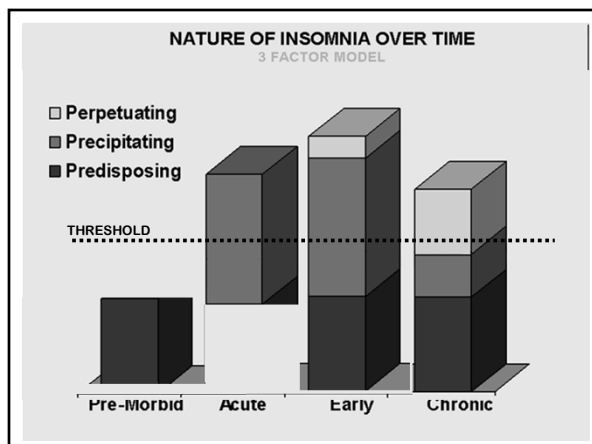


THE SPIELMAN MODEL (AKA 3 FACTOR OR 3P MODEL)

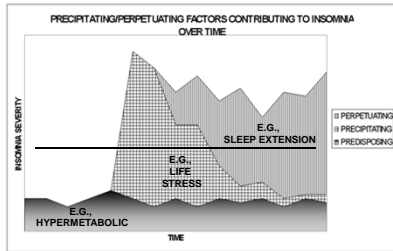
Spielman A. et al. A behavioral perspective on insomnia treatment.
Psychiatric Clinics of North Am 1987; 10(4):541-553.



**"The best cure for insomnia is to get
a lot of sleep"**
-- W.C. Fields



SPIELMAN'S NEW MODEL



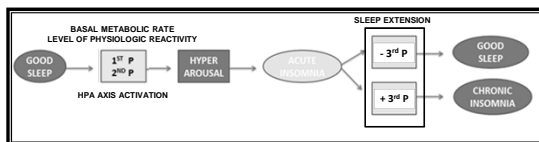
DOES THE MODEL EXPLAIN HOW THE HYPERAROUSAL CONDITION COMES INTO EXISTENCE ?

YES.



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

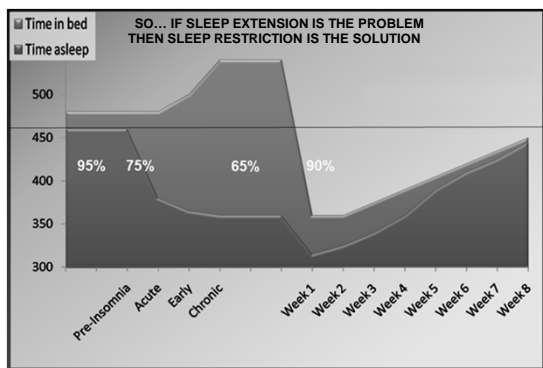
YES.



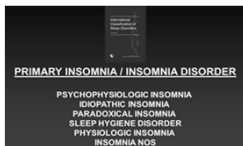
3rd P – SLEEP EXTENSION

HOW TIME IN BED VARIES
WITH INSOMNIA

HOW SLEEP OPPORTUNITY IS
EXPANDED TO RECOVER
LOST SLEEP

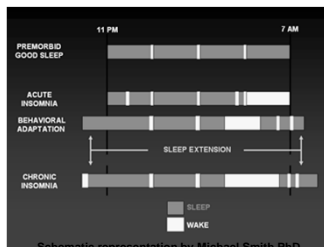


CAN THIS MODEL EXPLAIN THE VARIOUS
INSOMNIA PHENOTYPES (TYPES AND SUBTYPES)



PROBABLY NOT

DOES CHRONIC INSOMNIA OCCUR
SOLELY IN RELATION TO
SLEEP EXTENSION ?

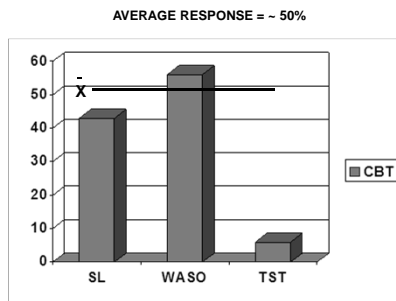


Schematic representation by Michael Smith PhD

PROBABLY NOT

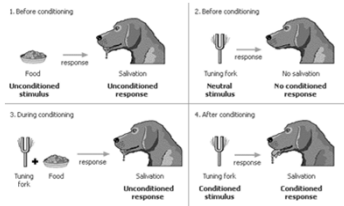
**ASSUMING TX (CBT-I) ENTIRELY
ELIMINATES THE BEHAVIORS
THAT PERPETUATE INSOMNIA**

**WHY ARE
PATIENTS NOT
CURED ?**



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

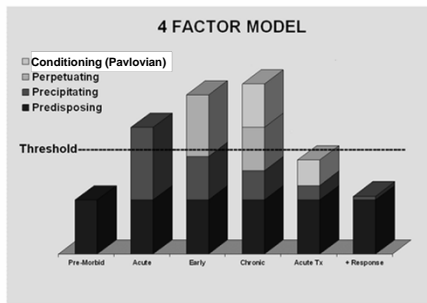
CHRONIC INSOMNIA SITUATION
BEDROOM/BEDTIME + ~~LIFE STRESS~~ INDUCED SOMATIC AROUSAL → SCD
BEDROOM/BEDTIME + ~~LIFE STRESS~~ INDUCED CORTICAL AROUSAL → SCD

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

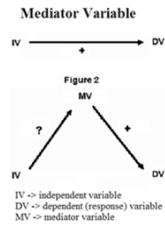


Perlis, Pigeon and Smith; *Principles and Practice of Sleep Medicine* Chapter 60

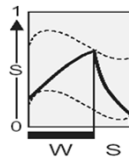
**DOES CHRONIC INSOMNIA OCCUR
SOLELY IN RELATION TO
PHYSIOLOGIC, COGNITIVE, AND
BEHAVIORAL FACTORS ?**

PROBABLY NOT

IT'S LIKELY THAT MODERATORS & MEDIATORS ARE AT PLAY



WHAT'S MISSING ?

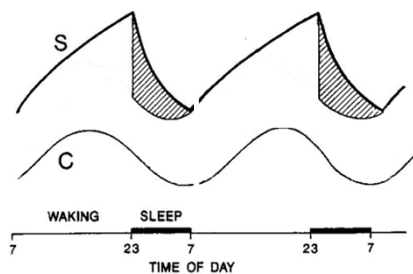


Sleep Homeostasis and Models of Sleep Regulation

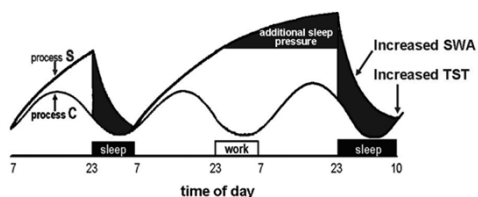
Alexander A. Borbély
 Peter Achermann

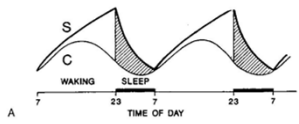
The model of homeostatic regulation of sleep proposed by Borbély and Achermann (1992) is a synthesis of the two main models of sleep regulation, the homeostatic model of Borbély and Achermann (1992) and the circadian model of Achermann and Borbély (1992). The model is based on the assumption that sleep is regulated by a homeostatic process that accumulates sleep debt during wakefulness and is restored during sleep. The model also incorporates a circadian rhythm that influences the timing of sleep. The model has been used to predict sleep patterns in various situations, including shift work and jet lag. The model is a valuable tool for understanding the regulation of sleep and for developing strategies to improve sleep quality.

BORBELY'S 2 PROCESS MODEL OF NORMAL SLEEP



WHAT ABOUT INSOMNIA ?

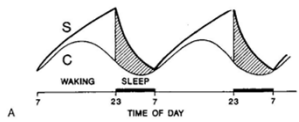




THE TWO PROCESS MODEL HELP ACCOUNT FOR INSOMNIA SUBTYPE

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
DYSREGULATION (DEPRIVE OR EXCESSIVE OPPORTUNITY)



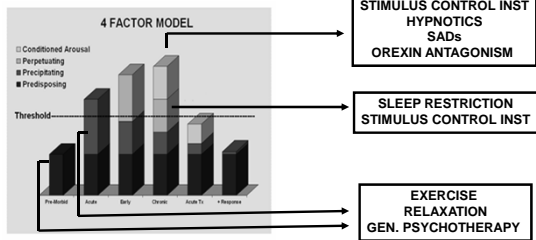
THE TWO PROCESS MODEL HELPS ACCOUNT FOR WHY SLEEP EXTENSION IS A PROBLEM AND WHY SLEEP RESTRICTION WORKS

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



TARGETS FOR TREATMENT

FOUR FACTOR MODEL

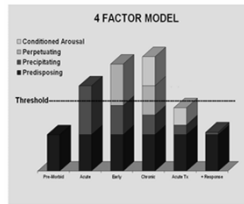


SO THESE ARE THE BASIC
MODELS

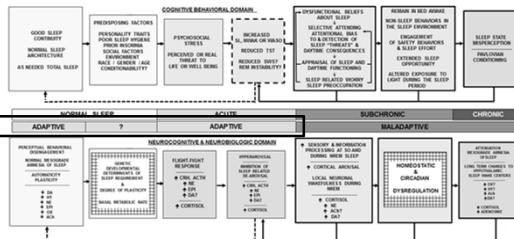


THERE ARE OTHER MODELS WORTH
STUDYING DOWN THE ROAD

- 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

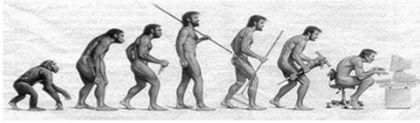


ETIOLOGY OF INSOMNIA: PARALLEL PROCESSES



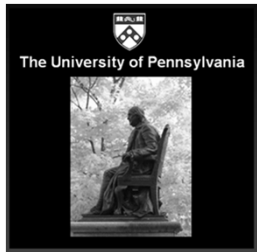
“No matter how important sleep may be, it was adaptively deferred when the mountain lion entered the cave.”

SPIELMAN ET AL. 1991
Thank you Jay !

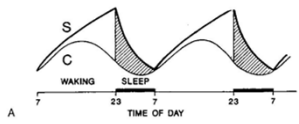


WE LIVE WITH INSOMNIA TODAY BECAUSE,
AT SOME POINT, IN OUR
EVOLUTIONARY HISTORY INSOMNIA
ALLOWED US TO LIVE'

DEAN HANDLEY
SEPRACOR
CIRCA 2005
DINNER



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 ?
