

MANAGEMENT OF INSOMNIA: BECOMING THE SANDMAN

Jeffrey W Boyle M.D., Ph.D.

Disease exists, if either sleep or watchfulness be
excessive.

Hippocrates

- ▶ No financial conflicts of interest
- ▶ I will answer questions about off label uses of antidepressant medications used as hypnotics.

DISCLOSURES

Several thin, parallel white lines of varying lengths and orientations are positioned in the bottom right corner of the slide, creating a modern, abstract graphic element.

- ▶ Define insomnia
- ▶ Explore diagnostic criteria for insomnia
- ▶ Characterize the pathophysiology of insomnia
- ▶ Review the pharmacologic and non-pharmacologic treatment of insomnia

OBJECTIVES

- ▶ Chronic insomnia 10%
- ▶ Transient insomnia 30-35%
- ▶ Children: 10-30%

DEMOGRAPHICS

- ▶ Sleep Difficulty
 - ▶ Initiating
 - ▶ Maintaining
 - ▶ Consolidating
 - ▶ Quality
- ▶ Despite adequate opportunity for sleep
- ▶ Daytime impairment
- ▶ NOT Circadian rhythm disorder, parasomnia, or sleep disordered breathing

INSOMNIA DEFINED

PETO: Falstaff!--Fast asleep... and snorting like a horse.

PRINCE HENRY: Hark, how hard he fetches breath.
Henry IV, pt 1

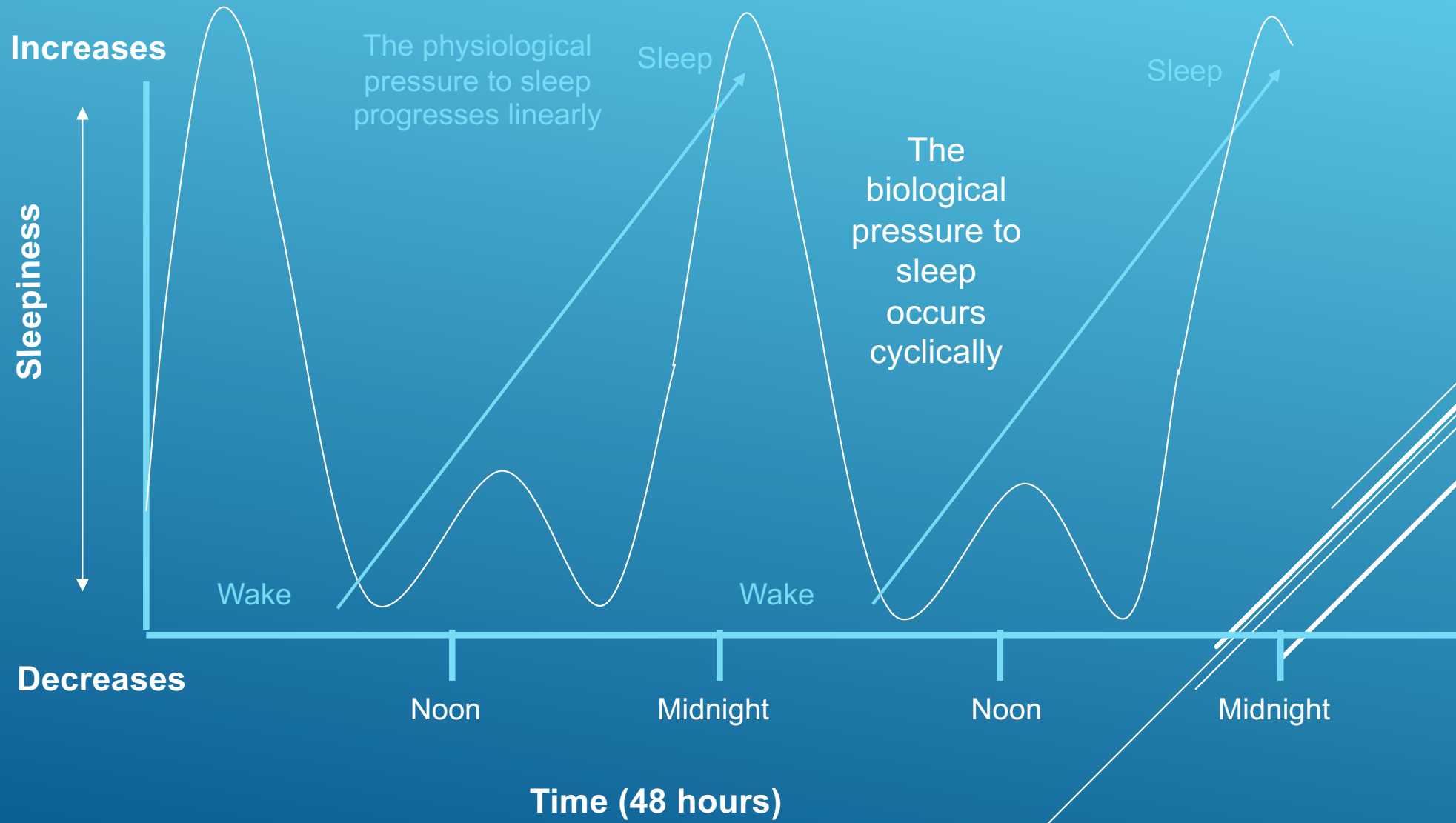
- ▶ Fatigue
- ▶ Daytime sleepiness
- ▶ Mood problems and irritability
- ▶ Behavioral problems
- ▶ General Malaise
- ▶ Cognitive Impairment
- ▶ Impaired social, family, occupational, or academic performance
- ▶ Dissatisfaction with sleep

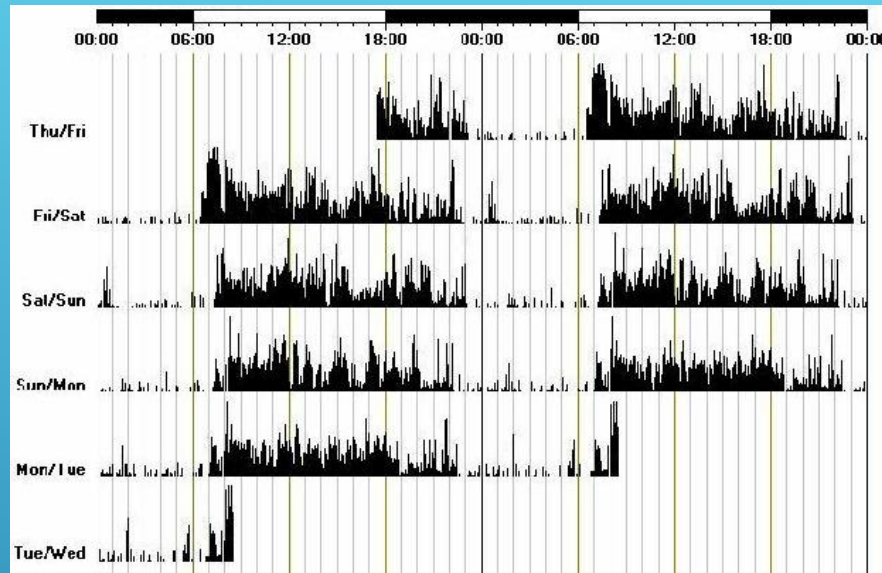
DAYTIME SYMPTOMS

- ▶ Involuntary eventual necessity
- ▶ The 2-process model (Borbely, 1982)
- ▶ Circadian rhythm
 - ▶ Modification by Light exposure
 - ▶ Modification by diet
- ▶ Homeostatic drive
 - ▶ Duration of wakefulness
 - ▶ Linear and cumulative - “sleep load” increases
 - ▶ Extracellular adenosine suppresses BF neurons

WHAT CAUSES US TO SLEEP?

COMBINED SLEEP PROCESSES



[illegible]

- ▶ Clinical diagnosis
- ▶ PSG not needed
- ▶ Sleep diary (AASM)
- ▶ Actigraphy

DIAGNOSTIC EVALUATION



- ▶ Primary Insomnia
- ▶ Adjustment Sleep disorder
- ▶ Psychophysiologic insomnia
- ▶ Paradoxical Insomnia
- ▶ Insomnia due to mental disorder
- ▶ Insomnia due to drug or substance
- ▶ Insomnia due to medical condition
- ▶ Insomnia, unspecified.

INSOMNIA DIAGNOSES

1. Consider underlying medical diagnosis
2. Consider underlying psychiatric diagnosis
3. Evaluate current medication regimen
4. Assess sleep hygiene and sleep habits
5. Evaluate for Primary sleep disorder

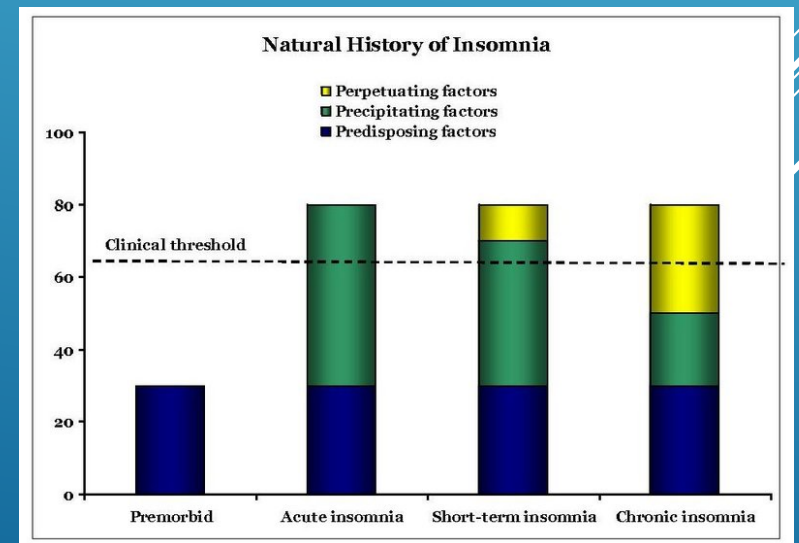
CLINICAL APPROACH

- ▶ Evaluate for associated symptoms
 - ▶ Pain
 - ▶ Constitutional symptoms
 - ▶ Anxiety
 - ▶ Depression
- ▶ Associated Conditions(Adjusted Odds Ratio)
 - ▶ Heart disease 2.27
 - ▶ Cancer 2.58
 - ▶ Neurologic disease 4.64
 - ▶ Lung disease 3.78
 - ▶ Urinary problems 3.28

SECONDARY INSOMNIA

- ▶ Largest subtype of insomnia
- ▶ Heightened arousal
- ▶ Learned sleep-preventing associations
- ▶ Large component of anxiety.
- ▶ Psychology:
 - ▶ Predisposing Factors
 - ▶ Precipitating Factors
 - ▶ Perpetuating Factors

PSYCHOPHYSIOLOGIC INSOMNIA



APPROACH TO PSYCHOPHYSIOLOGIC INSOMNIA

- ▶ Anxiety
 - ▶ Generalized anxiety
 - ▶ Performance anxiety
 - ▶ Conditioned arousal
 - ▶ Sleep better away from home (@PSG)
 - ▶ Rec. changing bedroom/habits.
 - ▶ Sleep Disruptive Cognitions
 - ▶ Beliefs and expectations
 - ▶ Catastrophizing
- 
- A series of white diagonal lines of varying lengths and thicknesses are positioned in the bottom right corner of the slide, creating a modern, abstract graphic element.

- ▶ Sleep onset is an involuntary process.
 - ▶ Autonomic Nervous system
- ▶ Train the brain, habit formation
- ▶ "Sleep hygiene" refers to a set of habits that can promote good quality, restorative sleep.

SLEEP HYGIENE

- ▶ Have a regular sleep schedule. Avoid changing bedtimes/awakening time more than one hour on the weekends.
- ▶ Have a routine prior to bed which is predictable and relaxing.
- ▶ A warm shower or bath in the evening prior to bed can promote sleep.
- ▶ Avoid reading, talking on the telephone, texting, using tablets, and watching television in bed. Do not use a TV as a night light.

SLEEP HYGIENE: PATIENT INSTRUCTIONS

- ▶ Avoid sleeping with pets or children.
- ▶ Make your room pleasant and relaxing. Look forward to going to bed.
- ▶ Do not leave work for yourself in bed, do not keep unfolded laundry or other unfinished projects in your room.
- ▶ Do not watch your clock while trying to fall asleep, but if you are not asleep by 20 minutes get up and try relaxing in a dark room.

SLEEP HYGIENE: PATIENT INSTRUCTIONS

- ▶ Stay active with regular exercise, preferably no later than 6 PM.
- ▶ Avoid napping during the day.
- ▶ Try to have adequate exposure to natural light throughout the day.
- ▶ Avoid eating large meals late at night, but don't go to bed hungry.
- ▶ Avoid drinking alcohol and exposure to nicotine at night.
- ▶ Avoid caffeinated beverages after noon. Do not drink excessive amounts of caffeine throughout the day.

SLEEP HYGIENE: PATIENT INSTRUCTIONS

- ▶ Cognitive therapy

- ▶ Administered by a trained psychologist.
- ▶ Addresses false beliefs
- ▶ Retrains maladaptive behaviors
- ▶ Paradoxical motivation
- ▶ Mindfulness training

COGNITIVE-BEHAVIORAL THERAPY

- ▶ Strategy: Make patients so tired they train themselves to sleep.
- ▶ Step 1: Determine the allowed Time in Bed.
 - ▶ How much are they sleeping? +30 minutes
 - ▶ Not less than 5 hours
- ▶ Step 2: Set a wake time.
- ▶ Step 3: Set a bed time.
- ▶ Step 4: Based on ~85% Sleep efficiency, increase Time in Bed by 15-30 minutes per week.

SLEEP RESTRICTION

And thus with little sleeping and much reading, his brains dried up...

Don Quixote, Miguel de Cervantes y Saavedra

- ▶ Antihistamines
- ▶ Benzodiazepines
- ▶ “Non-benzodiazepine” hypnotics
- ▶ Melatonin agonist
- ▶ Orexin Antagonist

Not poppy, nor madragora, nor all the drowsy syrups of the world, shall ever medicine thee to that sweet sleep...

Othello, Act 3, Scene 3

PHARMACOLOGIC MANAGEMENT

Ambien, Ambien CR (zolpidem tartrate)

Butisol sodium (butabarbital sodium)

Carbtrital (pentobarbital and carbromal)

Dalmane (flurazepam hydrochloride)

Doral (quazepam)

Edluar (zolpidem tartrate)

Halcion (triazolam)

Intermezzo (zolpidem)

Lunesta (eszopiclone)

Placidyl (ethchlorvynol)

Prosom (estazolam)

Restoril (temazepam)

Rozerem (ramelteon)

Seconal (secobarbital sodium)

Silenor (doxepin hydrochloride)

Sonata (zaleplon)

Zolpimist (zolpidem tartrate)

Belsomra (Suvorexant)

FDA APPROVED MEDICATIONS

Several thin, parallel white lines of varying lengths and angles are positioned in the bottom right corner of the slide, creating a modern, abstract graphic element.

- ▶ Elimination half life 1-1.5h
- ▶ Therapeutic effects in 5-15m
- ▶ GABA_A agonist
- ▶ Two studies failed to demonstrate any increased Kennedy-type car accidents.
- ▶ Will not prevent overnight awakenings
 - ▶ But can be considered as a PRN.

ZALEPLON

- ▶ Suvorexant
- ▶ Inhibitor of Orexin
- ▶ Indication: Insomnia
- ▶ Half life 12h
- ▶ Improvement in sleep onset: 8-10 minutes.
- ▶ Wake after sleep onset: 17-26 minutes
 - ▶ WASO: time spent awake throughout the night after falling asleep.
- ▶ Side Effects: Drowsiness, headache, dizziness, abnormal dreams, REM-related parasomnias

OREXIN ANTAGONIST

- ▶ Zolpidem (Ambien) 2.5-3.0
- ▶ Eszopiclone (Lunesta) 6h
- ▶ Alprazolam (Xanax) 12-15h
- ▶ Clonazepam (Klonopin) 10-50h
- ▶ Lorazepam (Ativan) 10-20h
- ▶ Diazepam (Valium) 20-80h
- ▶ Temazepam (Restoril) 0.4-0.6h to 3.5-18.4h
- ▶ Triazolam (Halcion) 2 h
- ▶ Midazolam (Versed) 1-4h
- ▶ Zaleplon (Sonata) 1-1.5h

HYPNOTIC AND BENZODIAZEPINE ELIMINATION PHARMACOLOGY

- ▶ Sideswipes a tractor trailer.
- ▶ “A police report said Kennedy had trouble speaking, was swaying and told an officer that she may have accidentally taken a sleeping pill earlier that day.”
- ▶ In a court appearance on July 17, 2012, Kennedy said local hospital tests found no traces of drugs and that her doctor believed she had suffered a seizure.
- ▶ A toxicology report filed on July 25, 2012, said zolpidem was found in a sample of her blood taken when Kennedy was arrested
- ▶ Kennedy was acquitted of the charges on February 28, 2014.



KERRY KENNEDY: JULY 13TH, 2012

PATRICK KENNEDY: MAY 4TH 2006

abcnews.go.com/Health/story?id=1927026&page=1

omize Links M Neurology Home Photopic Sky S... IFL interfacelift — ... DIY Dropbox alt... The SSD Optim... Neurology Boar... neuromuscular...

ABC NEWS Election U.S. World Entertainment Health Tech ... Video Live 4

BREAKING NEWS: SANDERS WINS MICHIGAN, CLINTON TAKES MISSISSIPPI; TRUMP TAKES THREE STATES ON GOP SIDE

Kennedy's Crash Highlights Dangers of Ambien

abcnews.go.com/Health/story?id=1927026&page=1

omize Links M Neurology Home Photopic Sky S... IFL interfacelift — ... DIY Dropbox alt... The SSD Optim... Neurology Boar... neuromuscular... Intergy

ABC NEWS Election U.S. World Entertainment Health Tech ... Video Live 4 Shows

BREAKING NEWS: SANDERS WINS MICHIGAN, CLINTON TAKES MISSISSIPPI; TRUMP TAKES THREE STATES ON GOP SIDE

Ambien Highlights Dangers of Kennedy's

52 SHARES

f

t

e

After he smashed his Ford Mustang into a barrier near Capitol Hill early Thursday morning, Rhode Island Rep. Patrick Kennedy released a statement, saying that he had been disoriented by two prescription medications he had taken.

One of which was Ambien, a prescription sleep aid.

While Kennedy said he was "disoriented" in his statement, police officers described him as "intoxicated."

How could using Ambien, the nation's most widely used sleep aid, explain his behavior?

Kennedy's situation echoes a growing trend, police and toxicologists say. In some states, Ambien has made it onto the lists of the Top 10 drugs found in impaired motorists.

One doctor questioned Kennedy's decision to get behind the wheel with two prescription drugs in his system.

Kennedy's Crash Highlights Dangers of Ambien


+ 'Sleepdriving' Wreaking Havoc on Roads

ANALYSIS: Donald Trump Delivers Blow to Marco Rubio

Democratic Primary Exit Poll Analysis

Republican Primary Exit Poll Analysis

Sanders Says It's Premature for Clinton to



- ▶ Elimination half life 2.5-3.0h
- ▶ Serum >50ng/mL impairs driving
- ▶ 8 hours after a 10mg IR dose
 - ▶ 15% of women
 - ▶ 3% of men
- ▶ 8 hours after a 12.5mg CR dose
 - ▶ 33% of women
 - ▶ 25% of men

ZOLPIDEM AND DRIVING

"FDA Drug Safety Communication: Risk of next-morning impairment after use of insomnia drugs; FDA requires lower recommended doses for certain drugs containing zolpidem (Ambien, Ambien CR, Edluar, and Zolpimist)". [FDA](#). January 10, 2013.

- ▶ Address insomnia with respect to primary cause and with a general assessment of precipitating and perpetuating factors
- ▶ Understanding the psychology, physiology, and pathophysiology of sleep and sleep disorders will help in treatment.
- ▶ Use non-pharmacologic therapies before pharmacologic therapies
- ▶ Warn patients who take hypnotics about driving.

SUMMARY

- ▶ A 68-year-old man presents to your clinic for insomnia. He has always considered himself a “poor sleeper”. Over the past 3 months his insomnia has worsened, however. He believes it has contributed to daytime fatigue, feeling blue, and poor appetite. A thorough review of sleep history reveals good sleep hygiene and regular sleep schedule. His wife reports mild snoring and one episode in which his wife reports that she was struck by the patient overnight when he was acting out a violent dream he was having. He has never tried a sleep aid. Associated symptoms that have come up in the past few months include a mild sense of unsteadiness and some trouble swallowing. His examination is notable for a BMI of 23, modified Mallampati score of 2, blunted affect, and a rest tremor in the right hand.
- ▶ The next most important step in evaluation and management should include:
 - ▶ a. A diagnostic polysomnogram
 - ▶ b. Referral to neurology
 - ▶ c. Zolpidem 5 mg nightly and sleep restriction therapy
 - ▶ d. Referral to psychiatry

MOC QUESTION

- ▶ Rational: This patient presents with a primary complaint of insomnia. He has other associated findings which suggest insomnia secondary to another medical problem. He does have symptoms of anhedonia and anorexia with insomnia which, in the appropriate clinical context, could suggest an affective as a primary cause to his insomnia. Additionally, he has a blunted affect. His blunted affect, however could be a sign of facial bradykinesia. The other physical findings of a unilateral rest tremor and symptoms of dream enactment raise concern for a neurological disorder as a primary cause to his insomnia. A polysomnogram could be considered if a neurologic condition is not identified to classify his parasomnia and rule out sleep disordered breathing. Zolpidem and sleep restriction therapy could be considered if other signs and symptoms of a primary cause to his insomnia were not present and he had primary psychophysiologic insomnia.

REFERENCE:

NEUBAUER, D. CHRONIC INSOMNIA. CONTINUUM
2013;19(1): 50-66.