ASSESSMENT OF EEG CORTICAL AROUSAL INTENSITY **CLINICAL RELEVANCE** AND NEED FOR NEW SCORING GUIDELINES

"More has been learned about sleep in the last 65 years than in the past 6500 years"

From REM Sleep to Circadian Physiology (First Noble Prize)

Mansoor Ahmed. MD, FACCP, FBISM
Assistant Professor of Medicine
Case Western Reserve University
Fellow American Academy of Sleep Medicine
Director Cleveland Sleep & Research Center

Portrait of personal journey

Lahore

Montreal

Toronto

Winnepeg

Sleep……. A Vital Sign if Human Health

Sleep disorders are linked with many diseases.

Summary Of Presentation

1: Nature of arousal : Conceptual Framework

A: Arousals are integral part of normal sleep

B: Arousals are a marker of sleep disruption representing a detrimental and harmful feature for sleep via their impact on autonomic system, respiratory control and sleep architect

2: Evaluation of Arousal

A: Traditional Scoring …..what have we missed?!

B: Quantifying arousal: Arousal Intensity

3: Future implications on research and clinical sleep medicine/scoring

Nature of arousal in sleep

A: Integral Part of Sleep Physiology

- Wakefulness and sleep are two different sides of vigilance. Sleep is state of reduced vigilance
- The essential features of sleep is the arousability and presence of abundant arousals
- Arousals are element of normal sleep weaved into the texture of sleep, taking part in regulation of sleep, ensuring reversibility of sleep

The nature of arousal in sleep. Halasaz P, Parrino L, Bodisz R: J Sleep Research, 2004 March 13 (1): 1-23

Arousals are element of normal sleep

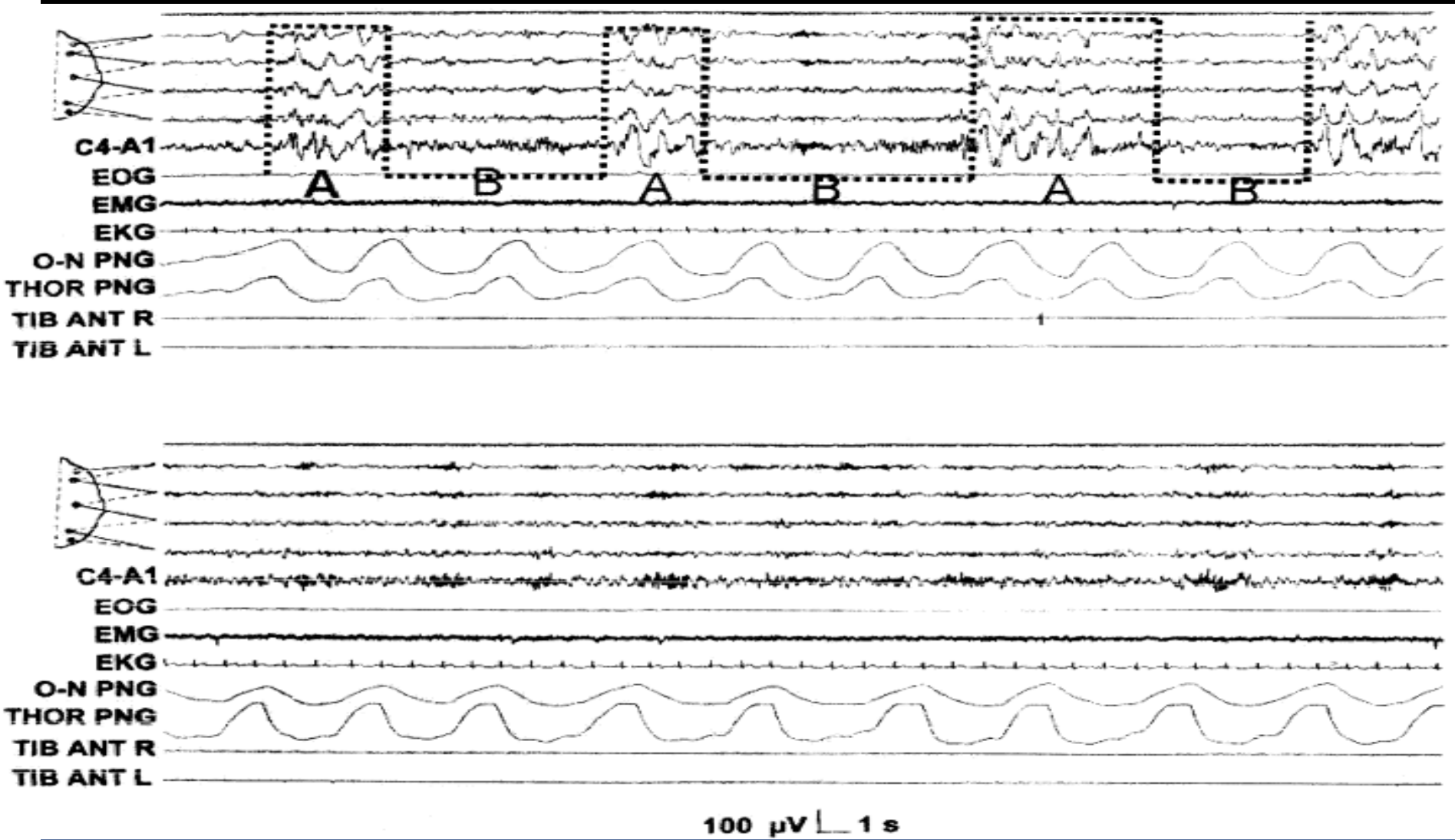
Arousals as elements weaved into the texture of sleep, taking part in regulation of sleep, ensuring reversibility of sleep ,

Micro Arousal (MA) are part of Normal Sleep and t not isolated events but periodic in nature , expressed in NREM sleep by the cyclic alternating pattern (CAP)

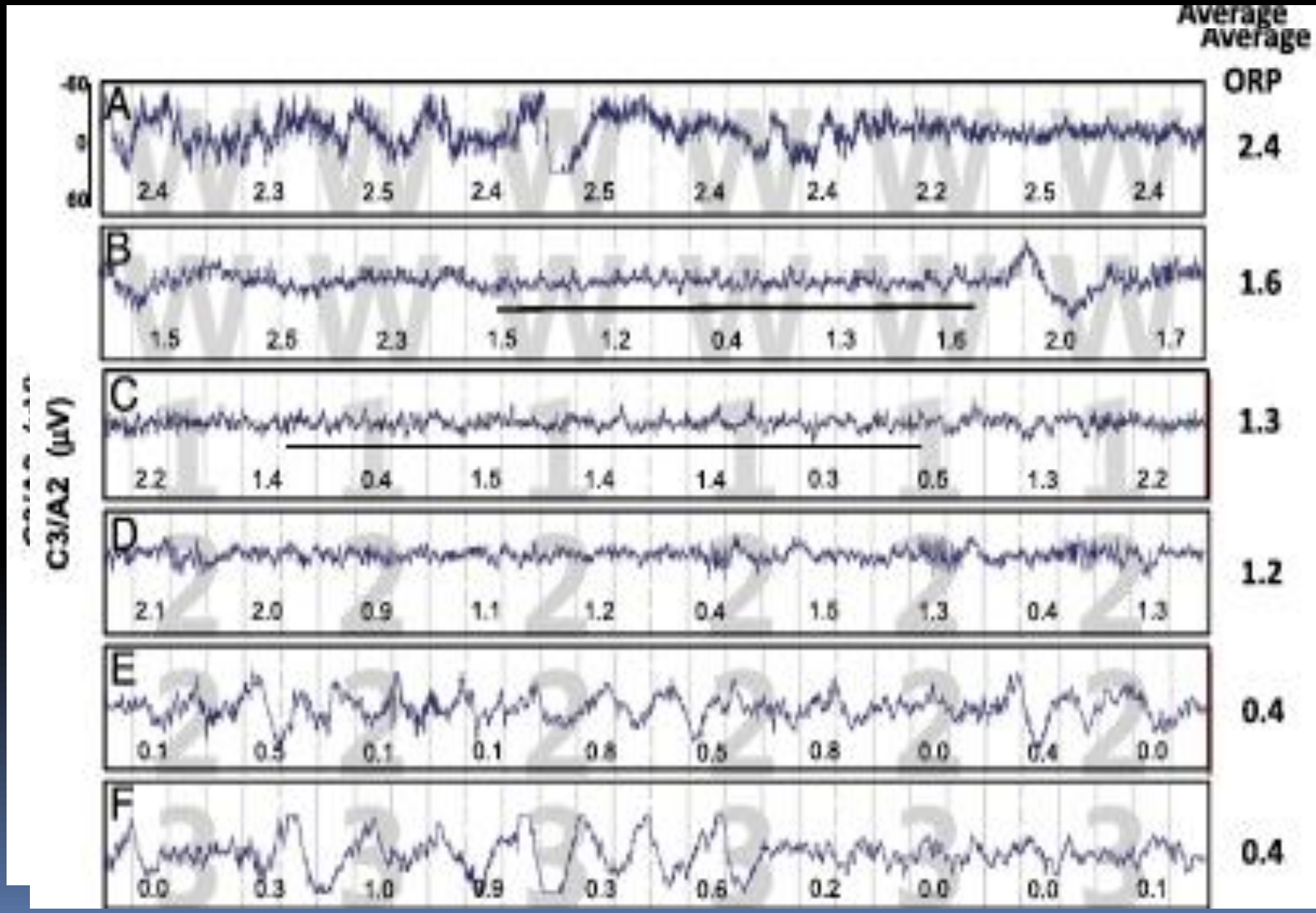
A: Fast rhythm low voltage classical EEG arousals are present across the ascending slope of cycles prevails during the last third of sleep

B: Slow rhythm high amplitude delta-like or K-complexes, mobilizing parallel anti-arousal swings, occuring more frequently across the descending part of sleep cycles and in the first cycles,

Example of cyclic alternating pattern (CAP) sequence (top) and non-CAP (bottom) in stage 2 NREM sleep



Variable vigilance/sleep depth within wakefulness and sleep stage



Classification of Arousals

The concept of cortical, subcortical and autonomic arousal

- Cortical Arousal: When the EEG compartment is involved by transient desynchronization patterns, regardless of the participation of the autonomic system or behavioral components, it was held as 'cortical arousal

- Sub cortical Arousals: When there is evidence of vegetative or behavioral activation associated with an EEG pattern different from conventional arousal the event was defined as 'subcortical arousal'

- Autonomic Arousal When an autonomic activation appears isolated or in conjunction with a respiratory event, but without any concomitant EEG sign, it is commonly defined as an 'autonomic arousa

Arousals Associated with Sleep Disorders

- The conventional definition of arousal includes a cluster of physiologic manifestations expressed by an activation of EEG rhythms, an increase of blood pressure and muscle tone and a variation of heart rate and Ventilation

- Sleep fragmentation which leads to impaired cognitive function?

- Relationship between arousal and or arousal Frequency and pathophysiological complications in sleep disorders

Arousals in OSA,, Insomnia , RLS-PLMS

B: Integral Part of Sleep- Sleep Disorders Pathophysiology

Scoring of arousal

The standard definition of arousal is "an abrupt shift in EEG to a higher frequency, including alpha, theta or beta, for at least 3 sec, with at least 10 sec of stable sleep preceding the change

EEG changes that meet this definition cover a wide range of visual appearances, ranging from changes that barely meet the scoring criteria, to very intense changes associated with high-amplitude beta waves

In clinical PSG arousals are scored as either present or absent without regard to there visual intensity

Arousal intensity varies and and may have an impact on HR, BP, Ventilation and Sleep Architect

Arousal Intensity: Visual scaling of intensity

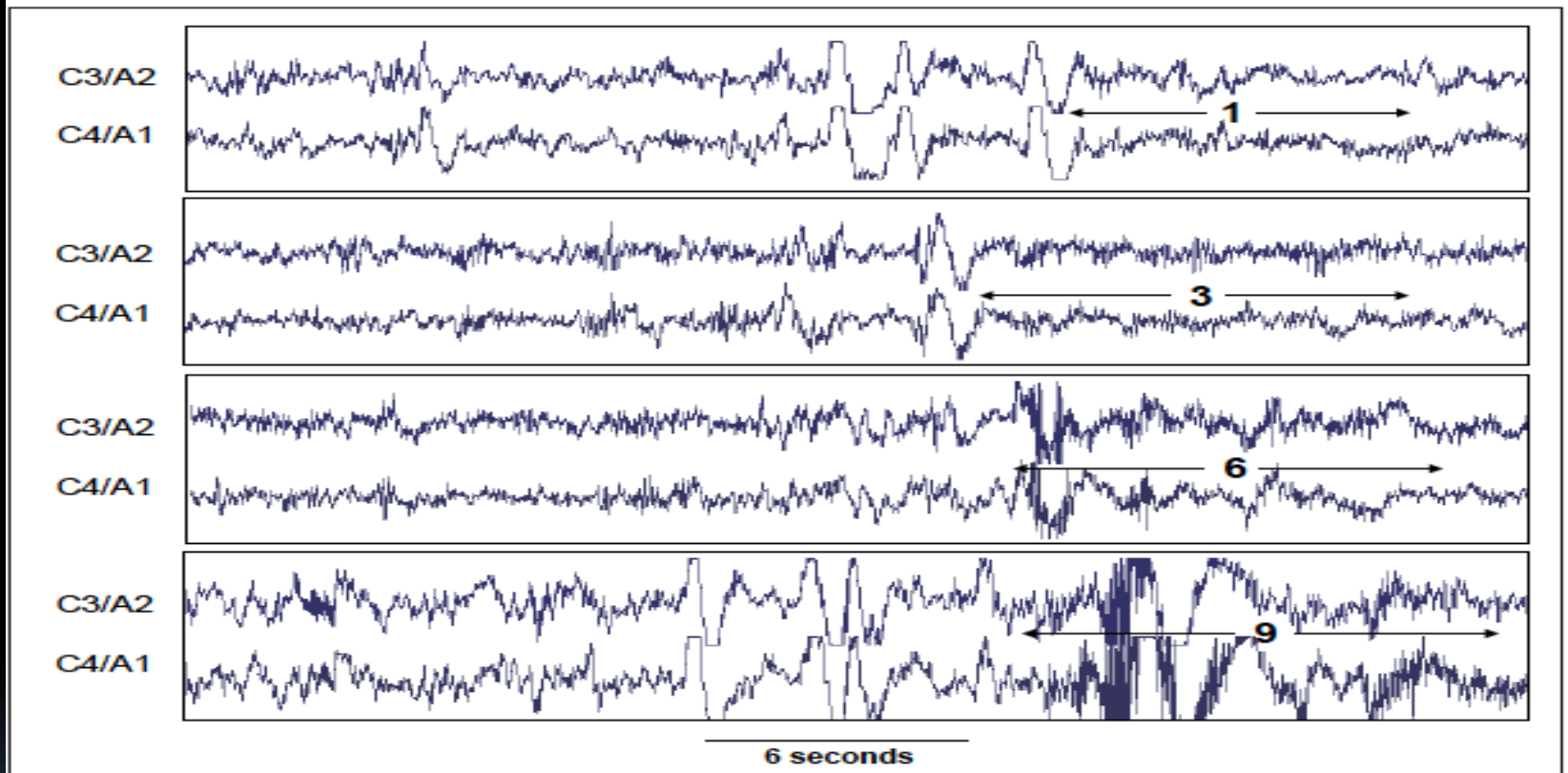


Figure 1—Examples of arousal with different intensity scales in the same patient. C3/A2 and C4/A1 are central electroencephalograms.

Examples of arousal with different intensity scales in the same patient.
C3/A2 and C4/A1 are central EEG

Variable vigilance/sleep depth within wakefulness and sleep stage

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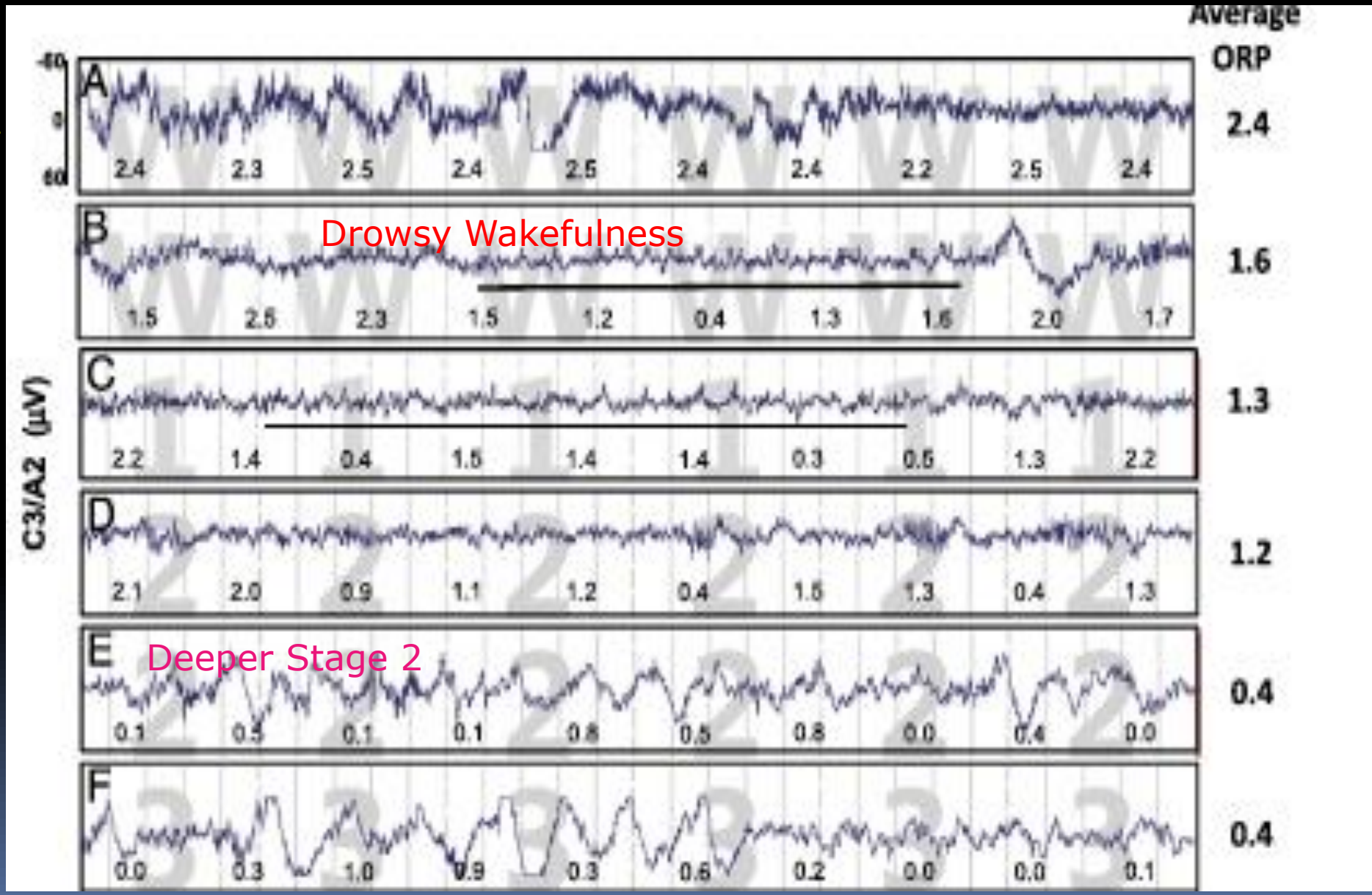


Clinical shortcomings with current scoring:

Severity of sleep fragmentation on polysomnography (PSG) is conventionally reported as the frequency of arousals, despite the fact that this index does not reliably predict which patients will experience clinical consequences of sleep disruption.

A normal sleep study in the face of sleep complaints may indicate either that the complaint represents a perception problem or that the criteria currently used to evaluate sleep quality are not sensitive enough to identify poor sleep

Is it possible that scoring the intensity of arousals may provide additional guidance into which patients with sleep disorders will develop cognitive and cardiovascular complications?

Evaluation of Arousal Intensity
Impact of Arousal Intensity

1: Measurement of arousal intensity

Visual analysis, Digital Analysis

2: Impact of Arousal Intensity

- Impact of Arousal on autonomic system HR and Blood pressure
- Impact of arousal on subsequent sleep architect (dynamics of sleep recovery following arousals i.e how quickly sleep deepens following arousal

Methodology : 1: Arousal Intensity Scaling, 2) HR

- Total 20 PSG files that contained more than 70 arousals and were free of arrhythmias (atrial fibrillation, frequent ectopic beats) were selected
- 3/20 files were **manually/** scored. Total of 271 arousals and were **visually** assigned intensity scale from 0-9. Scale 0 when the arousal was barely perceptible, and did not believe it met the minimum AASM criteria

- *Digital Arousal scaling was performed by standard signal processing techniques, utilizing wavelet transform (WT) and appropriate classifiers .*
- Wavelet analysis of C3/A2 and C4/A1 EEG signals was performed on each of the scaled arousals in the three training files
- A table containing the visually determined arousal intensity scale and various wavelet features for each of the 271 arousals in the three training files was generated.
- The scaling technique in the table was used to scale the intensity of all the arousal i.e. 2,695 arousals in 20 files

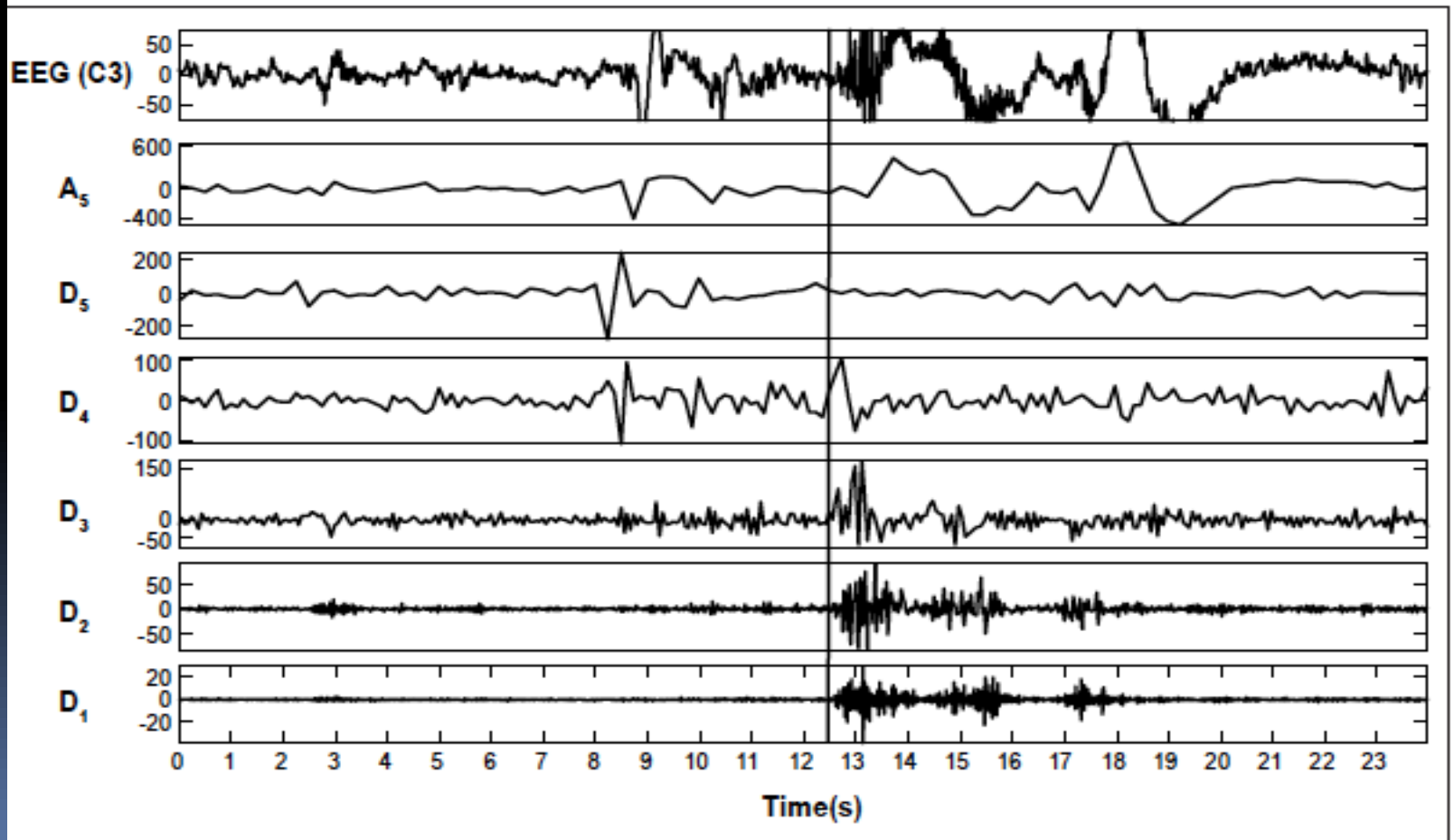
Changes on Heart Rate during Arousal

HR Measurement

- Beat-by-beat HR was measured and the highest value in the interval 2-12 sec preceding the arousal was used as baseline
- The highest HR in the interval [arousal onset to (arousal end +8 sec) was also measured and the difference from baseline

- HR (ΔHR) represented the change in HR associated with the arousal.

Arousal scaling was performed using wavelet transformation (WT).



Results:

- The average number of arousals examined per file was
- 134.8 ± 61.2, for a total of 2,695 arousals..
- Scale 3 arousals were the most frequent, accounting for 34.3% of all arousals examined.
- The frequency decreased progressively in either direction, reaching 2.1% for scale 1 and 3.4% for scale 9. Only one of 2,695 visually

- An important finding in this study is that the overall average arousal intensity varied considerably among subjects (

- As in the case of visual scaling, there was a highly significant correlation between arousal intensity and arousal duration in all files

- WT can duplicate the visual scaling of intensity

Changes in mean absolute amplitude (MABS) in different frequency ranges with different visually scored arousal intensities in the training file

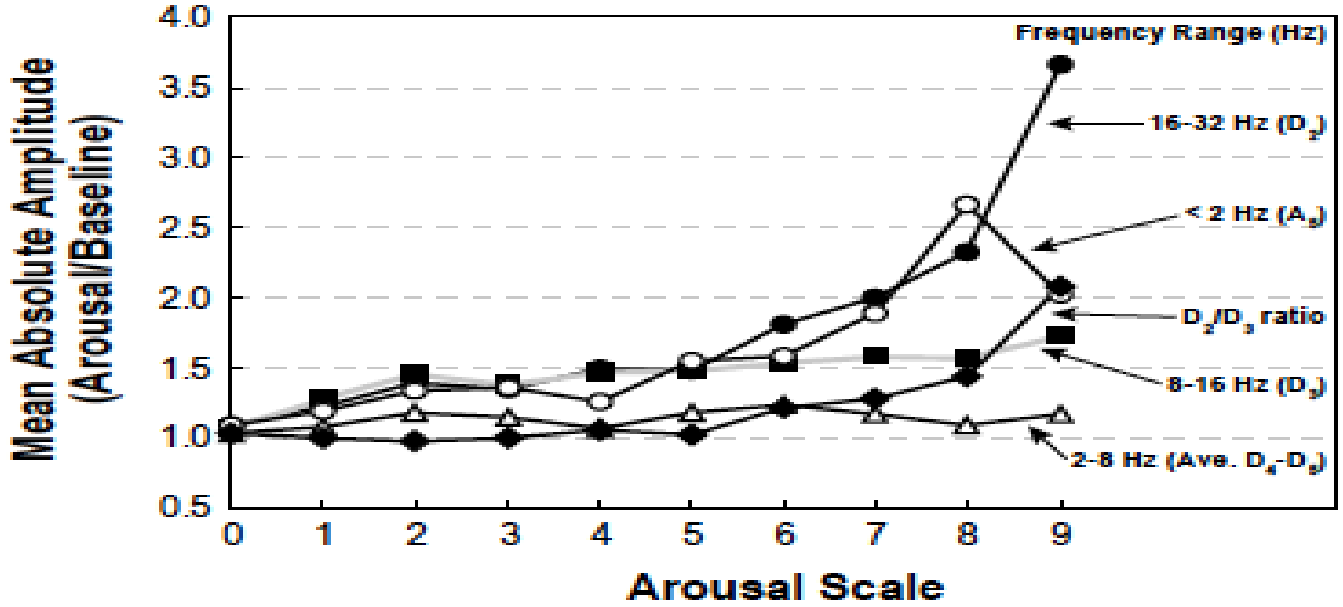


Figure 8—Changes in mean absolute amplitude (MABS) in different frequency ranges with different visually scored arousal intensities in the training file. The ratio of MABS (D_2) to MABS (D_3) is also shown (D_2/D_3) and this approximates the ratio of amplitude in the beta frequency range over the amplitude in the alpha frequency range. All values represent the change relative to prearousal baseline so that a value of 1.0 reflects no change from baseline.

Characteristic of Arousals in 20 patient

Table 2—Characteristics of arousals in different polysomnograph files

File	n	Average scale	Average duration	With movement			No movement		
				n	Scale	Range	n	Scale	Range
1	140	3.8	7.4	24	5.1	1-8	116	3.6	1-9
2	111	5.1	10.0	21	7.2	2-9	90	4.5	0-9
3	85	3.9	7.6	15	6.5	5-9	70	3.4	0-8
4	320	4.0	8.7	81	5.2	2-9	239	3.5	1-9
5	157	4.2	9.3	14	6.2	5-9	143	4.0	0-9
6	80	3.7	7.6	14	4.6	2-8	66	3.5	0-9
7	182	3.4	8.0	52	4.8	1-9	130	2.9	0-8
8	80	3.9	9.2	13	4.2	1-8	67	3.7	0-8
9	100	3.4	8.9	4	3.8	2-4	96	3.4	1-9
10	133	3.9	10.4	15	5.2	0-7	118	3.8	0-7
11	63	5.9	11.0	17	6.7	2-9	46	5.5	1-9
12	167	5.1	9.9	56	6.5	0-9	111	4.1	0-9
13	95	3.9	8.3	16	5.6	3-9	79	3.5	0-9
14	140	3.5	7.4	30	4.0	1-9	110	3.4	1-9
15	146	3.4	7.8	13	5.2	2-9	133	3.3	1-9
16	110	3.5	8.6	22	4.1	3-8	88	3.4	1-9
17	77	3.9	9.6	22	5.1	1-9	55	3.3	1-9
18	128	4.4	8.6	53	5.1	2-8	75	3.9	1-8
19	137	4.0	7.7	7	7.0	3-9	130	3.9	2-9
20	244	4.7	11.4	23	5.7	3-9	221	4.6	2-9
Mean	134.8	4.1	8.9	25.6	5.4		109.2	3.8	
SD	61.2	0.7	1.2	19.6	1.0		49.9	0.6	

Results

- Arousal vary greatly, not only in intensity, but also in the manner in which there is a "shift in EEG frequency".
- Some arousals may display primarily an increase in alpha rhythm whereas others display primarily an increase in beta rhythm. Often there is an increase in both rhythms, in slow waves, or a change in the primary rhythm from time to time during the same arousal

1: The intensity of arousals can be objectively quantified using the EEG signal's time and frequency characteristics

2: Arousal widely vary in intensity and movements are associated with higher intensity arousal intensity was also correlated with duration

3: Average arousal intensity varies considerably among subjects;

4: HR response to arousal appears to be most strongly related to arousal intensity;

5 Increase in HR for a given arousal intensity varies considerably among subjects

Scale 3 arousals were the most frequent, accounting for 34.3% of all arousals examined

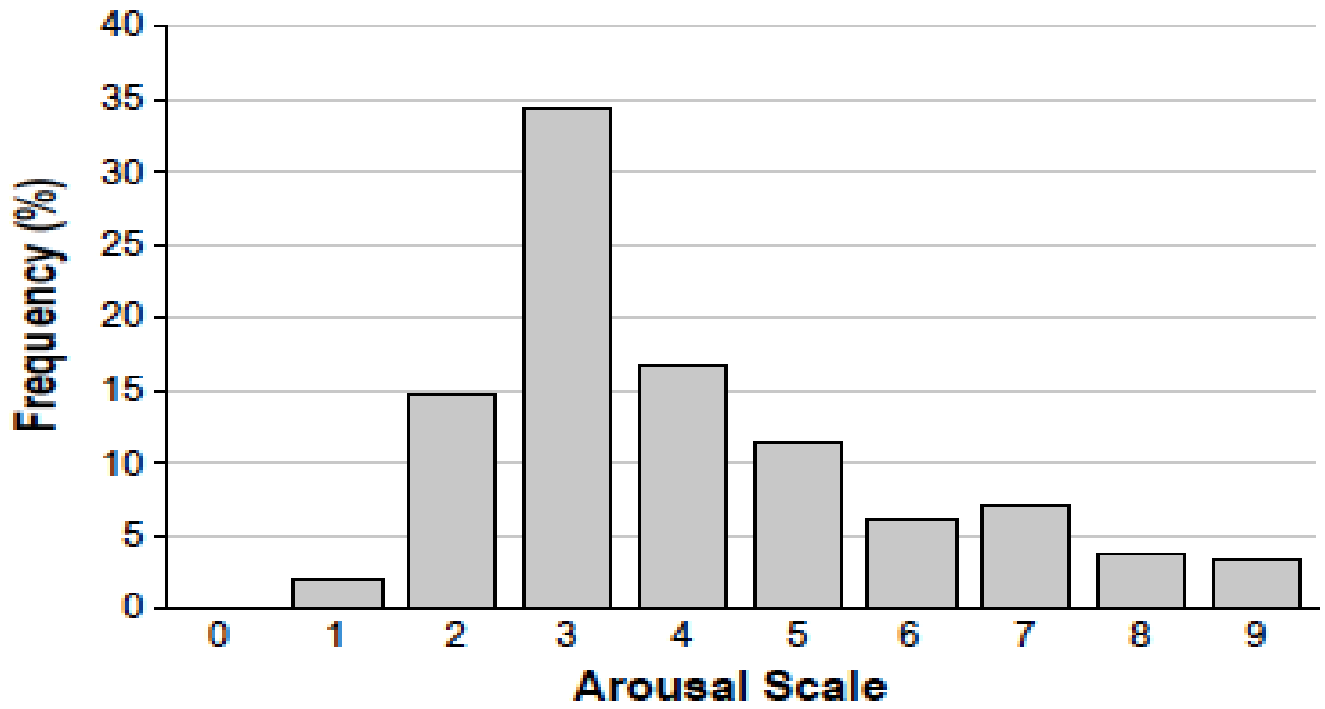


Figure 5—Frequency distribution of arousal intensity.

Azarbarzin A; Ostrowski M; Hanly P; Younes M. Relationship between arousal intensity and heart rate response to arousal. SLEEP2014;37(4):645-653.

AROUSAL AND HEART RATE RESPONSE

- Peak HR occurred on average 7.1 ± 0.9 sec after arousal onset
- The gain of the relationship between arousal intensity and change heart rate varied greatly among subjects, with ΔHR ranging from 3.1-11.7 min-1 at an arousal scale of 5
- Significant correlations were found between ΔHR and arousal intensity in all subjects
- Significant correlations were found between between ΔHR and arousal duration in 16 files,
- Significant correlations were found between ΔHR and the presence of arousal-related leg movement in 17 files.

Arousal Intensity and Heart Rate Response (EXAMAPLE OF A PATIENT FILE)

HR Measurement: Beat-by-beat HR was measured and the highest value in the interval 2-12 sec preceding the arousal was used as baseline HR. The 2 sec preceding arousal were avoided in baseline determination

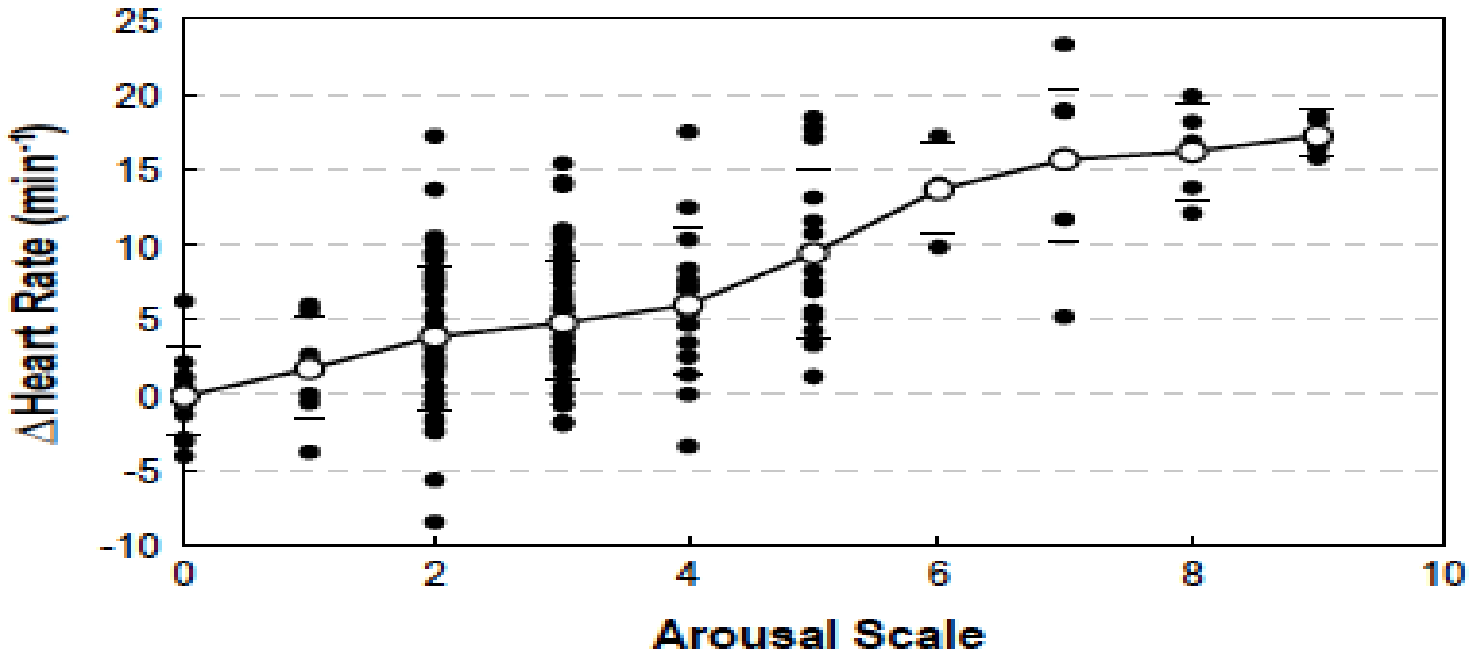


Figure 6—The change in heart rate with arousals of different intensities in a representative patient. Each dot represents one or more arousals. Horizontal bars are ± standard deviation. The solid line represents the average response.

Arousal Intensity and HR response

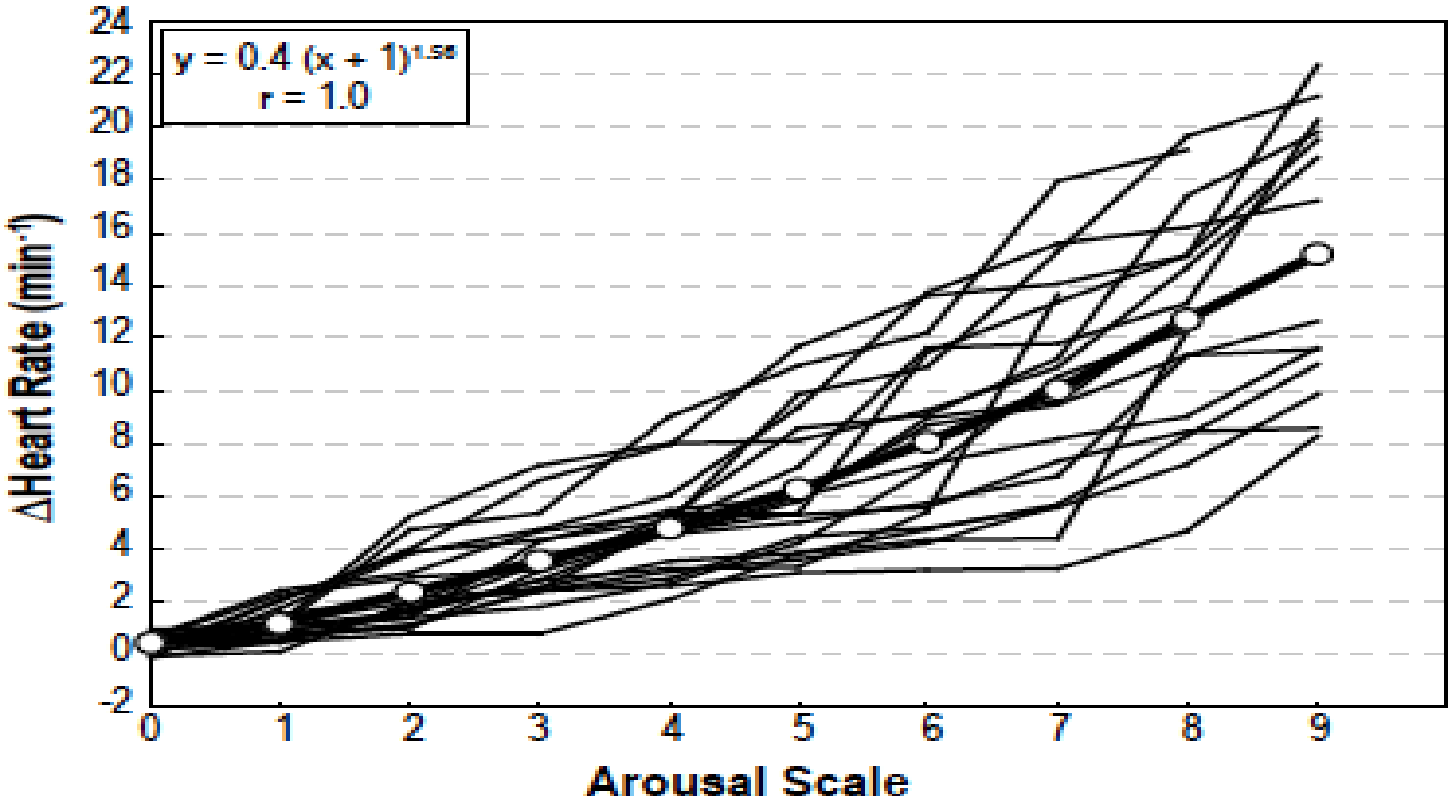


Figure 7—Average heart rate response to different arousal intensities in individual subjects and the overall average (open circles).

Results Summary

Average intensity was higher in arousals with movement than in those without movement.

Arousal scale was significantly correlated with arousal duration in all files. Arousal intensity reaches higher levels as the duration increases

ΔHR was strongly correlated with arousal intensity, and that duration and the presence of leg movements is secondary to arousal intensity

There was an excellent correlation between arousal intensity and ΔHR in each subject, but the slope of the relationship varied considerably among subjects For a mid-intensity arousal (scale 5), average increase in HR ranged 3.1-11.7 min1

Is it the arousal intensity per se responsible for ΔHR or it is due t he stimulus per se that cause the arousal?

Conclusions

- Arousal intensity, quantified by wavelet transform, is strongly associated with arousal-related change/increase HR,

- The most common arousal scale (scale 3) is associated with only small changes in HR and may be a large number of low intensity arousals may not be so clinically significant.

- The slope of the relationship between HR and arousal intensity varies in subjects may reflect a more labile cardiovascular response to arousal stimuli, and this may offer some predictive value for the development of cardiovascular complications

PSG Scoring: Future Research and Clinical implications

- Future PSG scoring: Visual scoring vs. Digital scoring or Combination
- Evaluation of Arousal Intensity and post arousal recovery of sleep EEG may better predict sleep fragmentation and quality of sleep
- We may have better understanding the link between arousal, arousal intensity and cardiovascular complications.
- Evaluation of factors that influence arousal intensity should be explored (Age, Sex background sleep architect, medication, co morbid conditions)

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Data Presented
Relationship between arousal intensity and heart rate response to arousal. SLEEP 2014;37(4):645-653. Azarbarzin A; Ostrowski M; Hanly P; Younes M.