ORIGINAL ARTICLE

Association of sleep related events and arousals during light sleep in healthy individuals

C Nayak[1,3], M Nagappa[1], S Sinha[1], M Philip[2], AB Taly[1]

[1]Department of Neurology, National Institute of Mental Health and Neurosciences (NIMHANS);
[2]Department of Biostatistics, National Institute of Mental Health and Neurosciences (NIMHANS);
[3]Department of Clinical Neurosciences, National Institute of Mental Health and Neurosciences (NIMHANS).

DOI No:

Indian J Sleep Med 2013; 8.3, 129-132

Abstract

Background: Few studies have assessed impact of sleep related physiological events on arousals.

Methods: Overnight PSG recording of 30 healthy volunteers were analysed for occurrence of various sleep events and arousals during light sleep.

Results: 864 arousals (N1=210; N2=654) were noted during light sleep in 30 patients. Forty-three arousals were de novo (N1=18; N2=25). The mean arousal per patient was 28.8±16.3 (median: 24; range: 9-84). In N1, sleep events associated with arousals included PLM- 157 (74.8%); roving eye movements- 92 (43.8%); vertex transients- 45 (21.4%); desaturation- 5 (2.4%); snore- 9 (4.3%); and apnea- 3 (1.3%). In N2, sleep events associated with arousals included sleep spindle- 570 (87.2%); PLM- 441 (67.4%); K complex- 226 (34.6%); snore - 85 (13%); vertex sharp transients- 57 (8.7%); desaturation - 5 (0.8%); and apnea - 28 (4.3%). The number of arousals in N1 and N2 that occurred de novo, and with single and multiple events were: a) N1 - de novo 18 (8.6%); Single event - 91 (43.3%) and multiple events – 101 (48.1%); b) N2: de novo – 25 (3.8%); single event - 129 (19.7%) and multiple event – 500 (76.5%).

Conclusions: In light sleep, 95.02% arousals were associated with physiological events viz. PLM, roving eye movements, and vertex sharp transients in N1 and sleep spindle, PLM, and K complexes in N2. Comparative studies in health and disease may enhance the understanding of arousal mechanisms.

Key Words: arousal; polysomnography; sleep

Introduction

According to the American Sleep Disorders Association (ASDA), Electroencephalographic (EEG) arousals are abrupt frequency shifts towards fast rhythms, mostly alpha and beta that shortly interrupt the continuity of the sleep stage background.[1] So far, arousals have been investigated in conditions of disturbed sleep. However, consolidated literature indicates that arousals are spontaneous manifestations

Correspondence Address
Dr. Sanjib Sinha, MD, DM
Additional Professor,
Department of Neurology, NIMHANS,
Hosur Road, Bengaluru – 560029
E-mail: sanjib_sinha2004@yahoo.co.in

of sleep even in the absence of sleep disturbance.[2]

The aim of this study was to study the relationship between arousals and various sleep related phasic events in normal healthy individuals during light sleep.

Materials and Methods

This observational analysis of PSG data of 30 healthy subjects (M=17, F=13; 18-35yrs of age) who volunteered to participate as 'controls' was carried out in the Department of Neurology, NIMHANS, Bengaluru. Overnight PSG recording was done (Sleepscan Vision Collection Software, version 2.03.05, Biologic Systems Corp, IL, USA) after obtaining a written informed consent from all participants using standard protocols. The parameters recorded included Electroencephalogram (EEG), Eye movements, electrocardiography, body position, chin and right anterior tibialis muscle EMG, oxygen saturation, thoraco-abdominal motion and oro-nasal flow. Sleep was staged in 30-second epochs using standard criteria. The PSG analysis was carried out according to AASM guidelines[3] which is based on R and K staging of sleep[4]. Various conventional sleep parameters, including TST, Sleep latency, etc. were calculated. In addition, the number of arousals occurring during the entire sleep period, as well as during NREM and REM sleep were noted.

An arousal was defined as an abrupt shift in EEG frequency, including alpha, theta /or frequencies higher than 16 Hz (but not spindles) lasting at least 3 sec, with at least 10 sec of stable sleep preceding the change in N1, N2, N3 and R; an arousal in REM had to be associated with an increase in chin EMG tone for at least 1 sec[1].

Sleep related events were considered to be **associated with arousals**, if they occurred 5 seconds before/after or simultaneously during the period of arousal. Arousals during sleep were classified as occurring in association with:- 1) a physiological sleep transient such as Vertex Sharp Transient (VST), 'K' complex, and/ or sleep spindles; 2) other events during light sleep such as roving eye movements (Fig 1A), periodic or isolated limb movements (Fig 1A, 1B), apneic spells (Fig 1B) and oxygen desaturation; or 3) 'de novo' when they occurred independent of any of the above events.

The level of spatial and temporal relationship of these arousals with sleep related phasic events during the various sleep stages was determined using chi-square

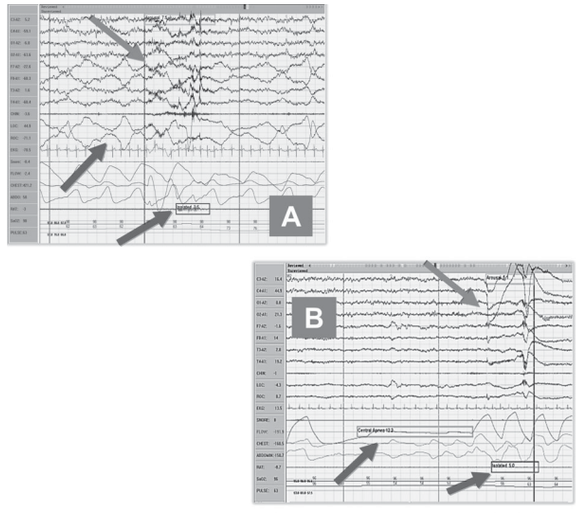

Figure 1: A)N1 arousal (Grey arrow) preceded by Roving eye movements and concomitant Isolated limb movement (Black arrows) in a healthy 21year old lady. B) N2 Respiratory Event Related Arousal (RERA) (Grey arrow) preceded by a central apnea and a concomitant isolated limb movement (Black arrows) in a healthy 17 year old boy.

contingency table analysis. We also classified arousals based on their association with no event, single event and multiple events using 'Kruskal-Wallis Test'. Finally, Multivariate Regression analysis was carried out to determine the level of significance of various sleep related events in their spatial and temporal association with the occurrence of spontaneous arousals.

Results

A total of 864 arousals (N1=210; N2=654) were noted in 30 patients during light sleep and the mean arousal per patient during light sleep was 28.8±16.3 (median: 24; range: 9-84).Of these 864 arousals, 43 (4.97%) occurred de novo, whereas 821(95.03%) occurred in association with a sleep related event (SRE). Spatial relationship of EEG arousals and SREs showed a statistically significant difference between N1 and N2 using chi-square contingency table analysisare summarised in Table 1.

Individually, statistical significant association was found between arousals and 3 sleep related events viz. Vertex sharp transients (<0.001), PLM's (0.045) and Snoring(<0.001) measured.

Of these 821 arousals associated with SREs,

Table 1: The de novo arousals and those occurring in association with various physiological events during sleep (Chi-square analysis)

		N1+N2	N1	N2	p Value
De novo		43	18 (8.57%)	25 (3.82%)	0.006
Event Assoc. Arousal	Total	821	192 (91.42%)	629 (96.17%)	
	Single	219	90 (46.87%)	129 (20.5%)	<0.001
	Multiple	602	102 (53.12%)	500 (79.5%)	
Vertex sharp transients		102	45 (21.4%)	57 (8.7%)	<0.001
Roving eye movements		92	92 (43.8%)	-	-
K complex		226	-	226 (34.6%)	-
Sleep Spindles		570	-	570 (87.2%)	-
Apnea		31	3 (1.3%)	28 (4.3%)	0.053
Desaturation		10	5 (2.4%)	5 (0.8%)	0.057
Periodic/ Isolated limb movements		598	157 (74.8%)	441 (67.4%)	0.045
Snore		945	9 (4.3%)	85 (13%)	<0.001
Total events		864	210	654	

219(25.34%) occurred in association with a single sleep related event and 629 (72.8%) were associated with multiple sleep related events.However there was no statistically significant difference between N1 and N2. Comparison of arousals among those who have no events, single and multiple events using Kruskal Wallis test is summarised in Table 2.

Table 2: Comparison of arousals among those who have no events, single and multiple events (Kruskal Wallis test)

		Arousals	p-value
N1	De novo	18	0.290
	Single	90	
	Multiple	102	
N2	De novo	25	0.307
	Single	129	
	Multiple	500	

In both N1 and N2, majority of Vertex sharp transients, K-complexes, Sleep Spindles and Snore occurred prior to the arousal, whereas, majority of Desaturations, Apneas and PLM/Isolated movements occurred during and/or following the arousal. Temporal relationship of EEG arousals and SREs has been summarized in Table 3.

In N1, Vertex sharp transient was the most important and statistically significant phasic event (p=0.032) associated with arousal, followed by PLM, Apnea, Roving eye movement, $SaO_2$and Snore, whereas, in N2, Apnea was the most important phasic event (p= 0.057) associated with arousal, followed by PLM, SaO_2, Sleep spindle, Vertex and Snore.Multivariate regression analysis indicating the importance of each event in its relationship with arousals during N1 and N2has been summarized in Table 4.

Table 3: The temporal relationship between arousals and various sleep related events in sleep

	Pre Arousal (≤ 5 s before)	During Arousal	Post Arousal (≤ 5 s after)
Vertex sharp transients			
N1	97.8%	8.8%	13.3%
N2	96.5%	0%	3.5%
K complexes			
N2	92.5%	8.8%	7.1%
Sleep spindles			
N2	93.3%	51.4%	46.7%
Roving eye movements			
N1	76.1%	31.5%	77.2%
Rapid eye movements			
R	71.7%	74.7%	17.2%
Desaturation			
N1	60%	60%	80%
N2	60%	100%	75%
Apnea			
N1	33.3%	66.7%	66.7%
N2	55.6%	77.8%	84%
PLM's			
N1	30.2%	100%	15.1%
N2	28.1%	96.8%	9.8%
Snore			
N1	100%	44.4%	0%
N2	84.7%	32.1%	33.3%

Table 4: Multivariate regression analysis indicating the importance of each event in its relationship with arousals

	VSTs	K complex	Roving eye movements	Spindles	SaO2	Apnea	Snore	PLM
N1	0.032	-	0.891	-	0.977	0.228	0.999	0.138
N2	0.369	0.466	-	0.269	0.184	0.057	0.643	0.085

Discussion and Conclusions

In our study, majority (95%) of the arousals was associated with sleep related events (SREs) and a significant association between arousals and Vertex transients, PLMs and Snore was observed in N2. However, in a study by Collard et al (1996), Movement Arousal Index (MAI) was distinctly increased in most patients with sleep apnea and snorers.[5]

Most of the arousals in N1 and N2 were associated with multiple events compared to de novo and single event (not statistically significant; Table 2) in our study, however, Fietz et al (1997) found that most of the arousals were associated with both respiratory events and limb movements rather than each event individually.[6]

A total of 568 arousals were associated with PLMs during light sleepin 30 patients in our study, however, a similar study in 10 patients with PLM and found that there were a total of 3916 phasic EEG arousals related to a total of 2614 leg movements.[7]

In our 30 normal subjects, we found that sleep related events causing arousals were more often associated with N2 than N1 (Table 2). However, in a study by Fietz et al (2003) on 38 patients with sleep apnea, majority ofrespiratory and movement related arousals occurred during N1.[6]

We noted that both in N1 and N2, majority of VSTs, KCs, sleep spindles and snore preceded the arousals, while desaturations, apneas and PLMs were seen during and following the arousals (Table 3). However in a similar study[7], they found that about 49.2% of EEG arousals occurred before, 30.6% simultaneously and 23.2% just after leg movements and another study[8] found that K Complex rate was significantly greater prior to the phases of transitory activation (PATs) in stage 2 or 3. K-complexes along with sleep spindles occurred less frequently preceding the PATs.

The most important sleep related event associated with arousals during N1 in our study was Vertex sharp transients, while in N2 it was Apnea.However, other studies found that respiratory related arousals were more commonly seen than movement relatedarousals; however, not every respiratory event seems to be the cause of an ASDA arousal.[6]

The important limitations of our study were sample size was small and analysis of sleep related events which were not associated with arousals was not performed.

A complex spatial and temporal relationship exists between arousals and various sleep related events, especially during N2. A significantly higher number of Vertex sharp transients, K complexes, Sleep spindles and Snoring prior to the period of EEG arousals among our healthy subjects suggested that they may probably be, either, arousing stimuli themselves, or may be mediated by a central/cerebral generator of arousals in response to an external or internal arousing stimulus. In contrast, a significantly higher number of desaturations and PLM's in our subjects during and following the period of EEG arousals suggested that they may probably be the clinical manifestation/ consequence of arousals. The generator may trigger arousals and in-turn the arousals may manifest as PLM's and/or Desaturations. Clarification of these interactions will require a more detailed analysis of these sleep related events. In addition, comparative studies in health and disease may further enhance our understanding of arousal mechanisms and unravel the border zone between physiological and pathological states.

References

1. **ASDA**: EEG arousals: scoring rules and examples: a preliminary report from theSleep Disorders Atlas Task Force of the American Sleep Disorders Association. *Sleep* 1992: 15: 173-184.
2. **Halasz P**, Kundra O, Rajna P, Pal I, Vargha M. Micro-arousals during nocturnal sleep. *Acta Physiol Acad Sci Hung* 1979: 54:1-12.
3. **Iber C**, Ancoli-Israel S, Chesson A, Quan S. The AASM manual for the scoring of sleep and associated events: rules, terminology and technical specifications 2007. Westchester, IL.
4. **Rechtschaffen A,** Kales A. A manual of standardized terminology, techniques, and scoring system for sleep stages of human subjects 1968. Bethesda, MD, National Institute of Neurological Disease and Blindness.
5. **Collard P,** Dury M, Delguste P, Aubert G, Rodenstein DO. Movement arousals and sleep-related disordered breathing in adults. *Am J Respir Crit Care Med* 1996: 154:454-459.
6. **Fietze, I.,** S. Quispe-Bravo, T. Hansch, J. Rottig, G. Baumann and C. Witt. Arousals and sleep stages in patients with obstructive sleep apnoea syndrome: Changes under nCPAP treatment. *J Sleep Res* 1997:6: 128-133
7. **Karadeniz D**, Ondze B, Besset A, Billiard M. EEG arousals and awakenings in relation with periodic leg movements during sleep. *J Sleep Res* 2000: 9 :273-277.
8. **Ehrhart J,** Ehrhart M, Muzet A, Schieber JP, Naitoh P. K-complexes and sleep spindles before transient activation during sleep. *Sleep* 1981: 4: 400-407.