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Abstract

*Background***:** Arousals are common, sudden and transient elevations of the vigilance level during normal sleep, but arousal-associated behaviors have not yet been studied.

Objective: We aimed to describe the duration as well as motor and autonomic patterns associated with arousals across sleep stages in normal subjects.

Methods: The spontaneous arousals of 25 healthy young adults were randomly analyzed on polysomnography with body- and face-oriented video cameras. The duration of the heart rate response as well as the frequency, amplitude, speed, body segment and semiology of associated movements were measured.

Results: Among 624 arousals (258 in N2, 140 in N3 and 226 in REM sleep), REM sleep arousals had the shortest duration, and N3 arousals were associated with greater heart rate acceleration. Movements and behaviors (mostly involving the head and neck, then the upper limbs, with rare eyes opening and no turning in bed) were frequent during arousals (69.4% during N2 sleep, 89.3% during N3 and 93.8% during REM sleep). Arousals more frequently included ample, prolonged and whole-body movements during N3 sleep and fast movements and facial expressions during REM sleep. During N2 arousals, chewing was the most prevalent behavior. Some movements resembled orientation and comfort behaviors (flexing/rotating the neck and trunk, scratching, pulling the sheets, rubbing the nose, yawning, smiling, frowning and speaking), whereas others resembled sleep-associated automatisms (swallowing, chewing).

*Conclusion***:** In contrast with previous assumptions, most arousals are associated with movements. The type of movements suggests that arousal is an intermediary state between wakefulness and sleep.

1. Introduction

Behind the sleep macroarchitecture, many different but repeated events occur during sleep, superimposed on the background activity and connecting the sleeping subject to the external world. They include autonomic reactions (e.g., brief episodes of tachycardia), K complexes, cyclic alternating patterns, arousals and awakenings [1-3]. They may be spontaneous or occur in reaction to environmental, physical or mental events. Arousals are defined by sudden and transient shifts in EEG frequency that are greater than the background frequency and lasting between 3 and 15 seconds [4]. Longer durations define awakenings. Because alpha EEG rhythms are common in rapid eye movement (REM) sleep, arousals in this stage should also include a concomitant increase in chin muscle tone [4].

Arousals are more frequent in the N2 stage of non-REM (NREM) sleep than in REM and N3 sleep [5]. Their frequency increases with age [6]. Arousals are characteristic of normal sleep, but they play a prominent role in sleep disorders. They contribute to fragmented sleep as a reaction to disturbing factors (including mainly noise, disturbed breathing and periodic leg movements) and to increased daytime sleepiness and reduced functional outcomes of sleep [3]. Per the first scoring rule, arousals are “transient and generally do not result in behavioral awakening” [7]. However, this last affirmation has not been formally studied through video studies. The motor behavior and semiology of arousal in normal subjects and across the different sleep stages have not been described. A precise description of movements and behaviors during arousals in normal sleep would be interesting to establish a hierarchy of motor arousals and help distinguish normal behaviors during arousals from the behaviors observed in NREM and REM sleep parasomnias [8, 9]. Therefore, this study aimed to describe and compare the motor (plus the autonomic) pattern profiles associated with arousal across sleep stages in healthy young adults.

2. Methods

2.1 Participants

Twenty-five healthy young adults were recruited by word of mouth for another study focusing on undisturbed sleep in normal subjects (clinicaltrial.gov: NCT03074578). Inclusion criteria were male or female sex, between 18 and 30 years old, good health, absence of sleep, physical and mental problems and drug intake. These criteria were assessed by interviews, scales and a physical examination performed one week before the sleep study by a sleep physician plus a psychologist. A regular sleep-wake schedule and the absence of sleep deprivation were recommended and verified on sleep logs for seven days prior to sleep monitoring. Participants signed an agreement (including the retrospective use of their data for studies other than the primary study) and were paid for taking part in the study. The study was approved by the local ethics committee and promoted by the Centre National de la Recherche Scientifique.

2.2 Video and sleep analysis

The video-polysomnography included three standard EEG channels, left and right electrooculography, chin (*mentalis*) and legs (left and right *tibialis anterior*) EMG, nasal pressure, naso-oral thermistors, tracheal microphone, chest and abdominal plethysmography, pulse oximetry, electrocardiogram, EEG-synchronized videos from two cameras (focused on the face and on the whole body) in an infrared light source and ambiance audio monitoring. The sleep stages, periodic leg movements, respiratory events and arousals were scored according to international criteria [4]. Twenty-five to 30 arousals (3 to 15 sec long) per subject were further analyzed (five to 10 arousals in each sleep stage). They were randomly selected after excluding those occurring during the N1 stage and those associated with periodic leg movements, neck myoclonus, ambient noises and respiratory events. The onset of arousal was defined as the first appearance of a visible alpha (8-12 Hz) EEG rhythm. Their duration was measured. ~~as~~ The associated heart rate (measured on the pulse wave) change was the difference between the maximal heart rate during arousal and the average basal heart rate during 10 s before arousal. In each spontaneous arousal, the corresponding video recording was carefully examined by a single scorer. She determined whether the eyes were open or not, if there were movements or behaviors, their amplitude and speed (qualitative measure, as previously described [8]), the body parts displaced in the movement (face and neck, torso, upper and lower limbs), and their types (turning in bed, chewing, scratching, raising the head or torso, facial movement, including emotional expressions or simple frowning, verbal utterances, …). The sequence between arousing and moving was measured in the full sample, and the exact time elapsed between arousing and moving was measured in 10% of the sample.

2.3. Statistical analysis

Continuous variables are presented as the mean ± standard deviation (SD), and categorical variables are presented as absolute frequency (%). The arousals were grouped by sleep stage. ANOVA was used to compare arousal characteristics across stages for quantitative dependent factors. Logistic regression was used for qualitative dependent factors. When the global level of significance of tests was lower than 0.05, a two-stage comparison was performed using a Bonferroni correction (significant *p* value < 0.001).

3. Results

3.1. Duration of the arousals and autonomic reaction

The 12 men and 13 women in the sample had a mean age of 22.5 years (18 to 26 years). The sleep efficiency, sleep onset and REM sleep latencies, percentage of N1, N2, N3 and REM sleep, arousals and awakenings, periodic leg movements and apnea-hypopnea indices were normal in all participants (Supplemental Table). A total of 624 spontaneous arousals were analyzed, including 258 in N2 sleep, 140 in N3 sleep and 226 in REM sleep. The arousals were shorter in REM sleep than in N2 and N3 sleep (Table 1). The heart rate change was greater when arousing from N3 sleep than from REM or N2 sleep. As many as 1311 behaviors or movements were observed during the 624 spontaneous arousals, and most (82.7%) of them were associated with movements (more often in N3 and REM sleep than in N2 sleep). Movements occurred after the onset of arousals, not before (Supplemental video-clip). Ample movements were more frequent during N3 arousals, and rapid movements were more frequent during REM sleep arousals than during other stages (Table 1). The heart rate change was higher during arousals associated with (16.2 ± 10.5 beats per min) than without (7.9 ± 6 beats per min, P < 0.001) movements, regardless of the sleep stage. In order of frequency, the head and neck moved more frequently upon arousals, then it was the upper limbs, whereas the lower limbs and trunk more rarely moved, with no further difference between sleep stages regarding this order of frequency.

3.2 *Type of movements during arousals*

The nature of movements and behaviors observed during arousals is described in Table 2 in descending order of frequency. No turning in bed was observed during arousals. Head rotation and arm movements were the most frequent types. During N2 arousals, chewing was more frequent, but head rotation, arm and leg movements and trunk rotation were less frequent here than during other sleep stages. During N3 arousals, arm movements, scratching oneself, head flexion and opening the eyes were more frequent than during other sleep stages, and yawning was more frequent than during N2 arousals. However, all healthy participants had fewer than two arousals in N3 associated with eye opening. During REM sleep arousals, facial expressions (frowning, smiling and contracting *orbicularis oris* muscles) predominated over other sleep stages arousals, and arm movements were more frequent than in N2 sleep.

4. Discussion

The characterization of movements and behaviors associated with more than 600 arousals in N2, N3 and REM sleep using a double camera yielded several new results. In contrast with the rarity of arousal-associated movements mentioned in the pioneering rules for scoring arousals [7], movements and behaviors (mostly involving the head, neck and upper limbs) were frequent during arousals, especially during N3 and REM sleep. REM sleep arousals had the shortest duration and contained the most rapid movements and more facial expressions, whereas N3 arousals yielded the highest sympathetic activation and contained frequent sequences of head and arm movements (including scratching oneself) and eye openings.

Video-polysomnography has developed significantly over the last 30 years, possibly explaining why the movements and behaviors associated with arousals have been previously underreported [7]. Movement arousals were previously described in the Rechstchaffen and Kales manual of sleep scoring (EMG increase plus a change in another channel) but were not quantified or characterized [10]. This characterization requires examining the real-time concomitant videos (body and face) of each arousal, which is time-consuming. Routine scorers may subjectively recognize these numerous comfort movements made by sleepers during arousals as “normal”.

The maximal heart rate acceleration (approximately 12–15 beats per minute) during arousals is one of the autonomic markers of transient elevations of sympathetic tone. It was expected during spontaneous EEG arousals and reached values close to those demonstrated in healthy subjects [11-13]. The heart rate maximal response was higher during N3 than N2 and REM sleep-associated arousals, whereas the opposite (lowest maximal heart rate) was found during arousals evoked by noise [11, 13]. These findings might possibly be linked to the major step between N3 sleep (a stage associated with low, stable and regular heart rate and predominant parasympathetic tone) and wakefulness (a stage with both sympathetic and parasympathetic tones).

The patterns of movements upon arousal mostly involved first the head and neck and then arm movements, suggesting a general, coordinated orientation behavior. In contrast, rare sleepers occasionally opened their eyes during arousals. Therefore, brainstem arousal systems may trigger a cephalic reflex response, even in the absence of external stimulation and without the need for eye opening to establish a connection to the external world. If eye opening was mainly seen (15%) during N3 arousals, it was isolated, never reaching the cutoff of two N3 arousals with eye opening that we previously demonstrated as sensitive and specific for differentiating healthy subjects from those with arousal disorders [8]. Alternatively, the movements observed during arousals may correspond with comfort, automatic movements, as suggested by scratching oneself and changing the position of a body segment (head, arm, leg). Swallowing and pushing/pulling the sheets were, however, rare behaviors, and turning in bed (to the supine, side or prone position) was absent during arousals, suggesting that this last behavior requires a longer time (in this case corresponding with an awakening). Rubbing the nose, which may be triggered by sensing the nasal pressure canula during polysomnography, was, however, rare. Chewing occurred during one-third of arousals, although none of the participants suffered from sleep bruxism. In normal sleepers, as many as 60% exhibit rhythmic masticatory motor activities (detected using masseter muscle electromyography) in the absence of teeth grinding [14]. Such automatic movements (which seem devoid of practical utility in the absence of food during the night) may correspond with the release of brainstem pattern generators relieved from the inhibition from higher cortical structures [15]. They nicely indicate that arousals are not equivalent to fully established wakefulness (during which automatic chewing movements are rare). In contrast, yawning, opening the eyes, displaying exploratory behavior and verbalizing were exceptional, possibly corresponding with elaborate behaviors more typical of awakenings than of arousals. Facial expressions were rare (4% of arousals contained frowning, smiles or contractions of the *orbicularis oris* muscle which did not correspond with emotional expressions) but more frequent (8.7% of arousals) in REM sleep. This result parallels previous findings indicating that smiles and frowning occur more frequently during REM than NREM sleep [16, 17], although they here occurred upon arousal, not during sleep. Whether they correspond with briefly enacted dreaming behaviors (when emotions are more frequent during REM than NREM sleep mentation [18]) cannot be demonstrated here in the absence of recalled information from the sleeper. Taken together, these results suggest that arousal is not only a construct in a manual of coding, but may be conceptualized as an intermediary stage between sleep and wakefulness because it includes behaviors that are close to wakefulness behaviors (flexing/rotating the neck and trunk, scratching oneself [19], pulling the sheets, rubbing the nose, yawning, opening the eyes, smiling, frowning and speaking) and behaviors that are close to sleep-associated automatic behaviors (swallowing, which is normal during sleep and prevents saliva aspiration [20], chewing, smiling and frowning).

Because this study is limited to healthy young subjects, the first night in a sleep laboratory (without adaptation night) and spontaneous arousals, the results are restricted to these conditions. Additionally, some elements (speed and amplitude of movements) were subjectively analyzed in the absence of kinematics techniques, such as motion capture.

The new concept of arousal as an intermediary state between sleep and wakefulness may explain why some movement disorders are exacerbated during arousal [21, 22]. The automatic analysis of 3D video during the night or even simple wrist monitors may be developed in the future to monitor normal sleep and diagnose and follow up parasomnia and other movement disorders during sleep. The manual analysis of arousal-associated movements across sleep stages, as performed here, may be useful for this purpose.

References

[1] Halasz P. Hierarchy of micro-arousals and the microstructure of sleep. Neurophysiol Clin 1998;28:461-75.

[2] Halasz P, Terzano M, Parrino L, Bódizs R. The nature of arousal in sleep. J Sleep Res 2004;13:1-23.

[3] Bonnet M, Doghramji K, Roehrs T, Stepanski E, Sheldon S, Walters A, et al. The scoring of arousal in sleep: reliability, validity, and alternatives. J Clin Sleep Med 2007;3:133-45.

[4] Berry R, Brooks R, Gamaldo C, Harding S, Marcus C, Vaughn B, et al. The AASM manual for the scoring of sleep and associated events. Rules, Terminology and Technical Specifications. Version 2.1. Westchester, IL: American Academy of Sleep Medecine; 2014

[5] Boselli M, Parrino L, Smerieri A, Terzano M. Effect of age on EEG arousals in normal sleep. Sleep 1998;21:361-7.

[6] Mathur R, Douglas N. Frequency of EEG arousals from nocturnal sleep in normal subjects. Sleep 1995;18:330-3.

[7] American Sleep Disorders Association. EEG arousals: Scoring rules and examples. Sleep 1992;15:174-84.

[8] Barros A, Uguccioni G, Salkin-Goux V, Leu-Semenescu S, Dodet P, Arnulf I. Simple behavioral criteria for the diagnosis of disorders of arousal. J Clin Sleep Med 2020;16:121-8.

[9] Oudiette D, Leu-Semenescu S, Roze E, Vidailhet M, De Cock VC, Golmard JL, et al. A motor signature of REM sleep behavior disorder. Mov Disord 2012;27:428-31.

[10] Rechstchaffen A, Kales A. A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Los Angeles: UCLA Brain Information Service/Brain Research Institute; 1968

[11] Griefahn B, Bröde P, Marks A, Basner M. Autonomic arousals related to traffic noise during sleep. Sleep 2008;31:569-77.

[12] Kato T, Montplaisir J, Lavigne G. Experimentally induced arousals during sleep: a cross-modality matching paradigm. J Sleep Res 2004;13:229-38.

[13] Tassi P, Saremi M, Schimchowitsch S, Eschenlauer A, Rohmer O, Muzet A. Cardiovascular responses to railway noise during sleep in young and middle-aged adults. Eur J Appl Physiol 2010;108:671-80.

[14] Lavigne G, Rompré P, Poirier G, et al. Rhythmic masticatory muscle activity during sleep in human. J Dent Res 2001;80:443-8.

[15] Tassinari CA, Rubboli G, Gardella E, Cantalupo G, Calandra-Buonaura G, Vedovello M, et al. Central pattern generators for a common semiology in fronto-limbic seizures and in parasomnias. A neuroethologic approach. Neurol Sci 2005;26 Suppl 3:s225-32.

[16] Cle M, Maranci JB, Weyn Banningh S, Lanfranchi J, Vidailhet M, Arnulf I. Smiling asleep: A study of happy emotional expressions during adult sleep. J Sleep Res 2019;28:e12814.

[17] Maranci JB, Aussel A, Vidailhet M, Arnulf I. Grumpy face during adult sleep: A clue to negative emotion during sleep? J Sleep Res 2021;e13369.

[18] Siclari F, Valli K, Arnulf I. Dreams and nightmares in healthy adults and in patients with sleep and neurological disorders. Lancet Neurol 2020;19:849-59.

[19] Aoki T, Kushimoto H, Hishikawa Y, et al. Nocturnal scratching and its relationship to the disturbed sleep of itchy subjects. Clin Exp Dermatol 1991;16:268-72.

[20] Pinto A, Yanai M, Nakagawa T, Sekizawa K, Sasaki H. Swallowing reflex in the night. Lancet 1994;344:820-1.

[21] Meneret A, Roze E, Maranci JB, Dodet P, Doummar D, Riant F, et al. Sleep in ADCY5-Related Dyskinesia: Prolonged Awakenings Caused by Abnormal Movements. J Clin Sleep Med 2019;15:1021-9.

[22] Neutel D, Tchikviladze M, Charles P, Leu-Semenescu S, Roze E, Durr A, et al. Nocturnal agitation in Huntington disease is caused by arousal-related abnormal

movements rather than by rapid eye movement sleep behavior disorder. Sleep medicine 2015;16:754-9.

Conflict of interest

This is a surrogate study of NCT03074578 (clinicaltrial.gov) promoted by Centre National de la Recherche Scientifique (CNRS), France. The authors have no conflicts of interest related to the study. The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link:..

Appendix: Supplementary material

Supplementary data to this article can be found online at …

Legend of the video-clip

This video-clip illustrates an arousal in stage N2 in a healthy volunteer (who accepted her face to be shown). The video-polysomnography shows the EEG alpha rhythm started a few milliseconds before a head movement (EOG: 2 first pink channels; EEG: 3 further channels including F3-A2, C3-A2, O3-A2; Chin EMG: last channel).

Table 1- The duration, autonomic reaction and frequency of movements and behaviors associated with spontaneous arousals across sleep stages in 25 healthy young adults.

Sleep stage	All	N2 sleep	N3 sleep	REM sleep	P*
Arousals, no.	624	258	140	226	NA
Duration, sec	8.6 ± 3.6	8.3 ± 6.1	11.6 ± 3.5	7.4 ± 3.3[b,c]	< 0.0001
Heart rate change, bpm	14.7 ± 10.3	12.9 ± 8.8	19.6 ± 11.9[a,c]	13.8 ± 10	< 0.0001
Heart rate change >30 bpm, % of arousals	7.1	4.3	12.9	6.6	0.262
Movement/behavior during arousals, % with	82.7	69.4[a,b]	89.3	93.8	< 0.0001
Ample movements	18.1	8.9	36.4[a,c]	17.3	< 0.0001
Rapid movements	23.9	5.4	7.2	55.3[b,c]	< 0.0001
Body part involved, % of movements/behaviors					
Head or neck	53.1	59.6	49.5	51.2	NA
Torso	8.2	5	10.3	8.7	NA
Upper limb	28.1	26.5	31.2	26.5	NA
Lower limb	10.7	8.9	9	13.6	NA
Time from arousal onset to movement onset, sec	1.6 ± 1.6	1.7 ± 1.4	2.1 ± 1.4	1.6 ± 2.0	0.55

*ANOVA for quantitative dependent factors and logistic regression for qualitative dependent factors. Post hoc test: p<0.001 for a difference between [a] N2 and N3, [b] N2 and REM, [c] N3 and REM.

Table 2 – Type of movements and behaviors observed during arousals across sleep stages in healthy young subjects

Sleep	Total	N2	N3	REM	P*
Head rotation	46	29.5[a,b]	61.4	55.3	< 0.0001
Arm movement	36.7	24	55.7[a,c]	39.4[b]	< 0.0001
Chewing	36.4	43.8[b]	34.3	29.2	0.0002
Leg movement	22.4	13.2[a,b]	27.9	29.6	< 0.0001
Scratching	14.6	11.6	25[a,c]	11.5	< 0.0001
Trunk rotation	11.5	3.5[a,b]	25	12.4	< 0.0001
Swallowing	8.2	5.8	8.6	6.2	NA
Head flexion	6.6	3.9	18.6[a,c]	6.6	< 0.0001
Trunk flexion	5.6	3.9	7.1	6.6	0.01
Eyes opening	5.5	2.7	15[a,c]	2.7	< 0.0001
Facial expressions	4.2	1.2	2.9	8.4[b,c]	< 0.0001
Pushing the sheets	4	2.3	7.1	4	0.03
Rubbing the nose	3.7	1.6	9.3	2.7	0.0008
Yawning	3.2	0.4	8.6[a]	3.1	< 0.0001
Exploratory behavior	1	0	4.3	0	NA
Verbalization	0.6	1.4	0	0	NA

*ANOVA for quantitative dependent factors and logistic regression for qualitative dependent factors. Post hoc test: p<0.001 for a difference between [a] N2 and N3, [b] N2 and REM, [c] N3 and REM.

Supplemental Table – Clinical and polysomnographic characteristics in healthy young subjects

Variable	No.
Gender, female %	52
Age, y	22.5 ± 2.5
Polysomnographic measures	
Total sleep time, min	423.9 ± 29.9
Sleep efficiency, %	92.6 ± 6.2
Latency to, min	
Sleep onset	21.2 ± 28.6
REM sleep	104.0 ± 45.3
Sleep stages, % of total sleep time	
N1	2.7 ± 1.8
N2	51.2 ± 7.8
N3	26.2 ± 4.5
REM	19.9 ± 5.3
Sleep fragmentation, event/h of sleep	
Arousal index	8.8 ± 6.1
Periodic leg movements	0.2 ± 1.1
Apnea/hypopnea	0.3 ± 0.4

mean ± standard deviation (SD)

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Apnea/hypopnea	0.3 ± 0.4

mean ± standard deviation (SD)