

# Are confusional arousals pathological?

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## ABSTRACT

**Objective:** The objective of this study was to determine the extent that confusional arousals (CAs) are associated with mental disorders and psychotropic medications.

**Methods:** Cross-sectional study conducted with a representative sample of 19,136 noninstitutionalized individuals of the US general population aged 18 years or older. The study was performed using the Sleep-EVAL expert system and investigated sleeping habits; health; and sleep, mental, and medical conditions (*DSM-IV-TR*, *ICSD-II*, *ICD-10*).

**Results:** A total of 15.2% (95% confidence interval 14.6%–15.8%) ( $n = 2,421$ ) of the sample reported episodes of CAs in the previous year; 8.6% had complete or partial amnesia of the episodes and 14.8% had CAs and nocturnal wandering episodes. Eighty-four percent of CAs were associated with sleep/mental disorders or psychotropic drugs. Sleep disorders were present for 70.8% of CAs. Individuals with a circadian rhythm sleep disorder or a long sleep duration ( $\geq 9$  hours) were at higher risk of CAs. Mental disorders were observed in 37.4% of CAs. The highest odds were observed in individuals with bipolar disorders or panic disorder. Use of psychotropic medication was reported by 31.3% of CAs: mainly antidepressant medications. After eliminating possible causes and associated conditions, only 0.9% of the sample had CA disorder.

**Conclusions:** CAs are highly prevalent in the general population. They are often reported allegedly as a consequence of the treatment of sleep disorders. For the majority of subjects experiencing CAs, no medications were used, but among those who were using medications, antidepressants were most common. Sleep and/or mental disorders were important factors for CAs independent of the use of any medication. **Neurology® 2014;83:834–841**

## GLOSSARY

**AOR** = adjusted odds ratio; **CA** = confusional arousal; **DSM-IV-TR** = *Diagnostic and Statistical Manual of Mental Disorders, 4th edition, Text Revision*; **ICD-10** = *International Classification of Diseases, 10th revision*; **ICSD-II** = *International Classification of Sleep Disorders, 2nd edition*; **OR** = odds ratio.

Confusional arousals (CAs), also known as sleep drunkenness or severe sleep inertia, as defined in *ICSD-II* “consist of mental confusion or confusional behavior during or following arousals from sleep, typically from slow-wave sleep in the first part of the night, but also upon attempted awakening from sleep in the morning.”<sup>1</sup> The disorder is accompanied by temporospatial confusion, inappropriate behavior, diminished mentation, and memory impairment. Complete or partial amnesia of the episodes can be present. An episode can be triggered by a forced awakening.

CAs have received little attention in epidemiologic studies. Laberge et al.<sup>2</sup> have estimated that approximately 17% of children between 3 and 13 years of age experience occasional or frequent episodes. In one general population study, their prevalence was estimated at 4.2%, decreasing from 6.1% in the 15 to 24 age group to 3.3% in the 25 to 34 age group and stabilizing around 2% after age 35 years.<sup>3</sup> No other figure exists for comparative purposes.

Precipitant factors of CAs include sleep deprivation, use of hypnotics or tranquilizers before bedtime, or a sudden awakening from sleep.<sup>3–7</sup> The role of alcohol, at least in sleepwalking, has been questioned.<sup>8</sup>

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Supplemental data  
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This study assessed the prevalence of CAs in the US general population and evaluated the importance of medication consumption, sleep, and mental disorders associated with CAs.

**METHODS Sample.** Fifteen states were selected to represent the US population based on the number of inhabitants and geographical area: Arizona, California, Colorado, Florida, Idaho, Missouri, New York, North Carolina, North Dakota, Oregon, Pennsylvania, South Dakota, Texas, Washington, and Wyoming. The final sample included 19,136 individuals representative of the general population of these states (138 million). Of 19,136 eligible adults, 15,929 completed interviews were obtained, providing an 83.2% cooperation rate using CASRO (Council of American Survey Research Organizations) standards.

**Procedures.** First, telephone numbers were retrieved in proportion to the population size of each county in the represented states. Telephone numbers were randomly selected within each state using a computerized residential phone book. Second, during the telephone contact, the Kish method<sup>9</sup> was used to select one respondent per household. This method allowed for the selection of a respondent based on age and sex to maintain a sample representative of these 2 parameters.

Interviewers explained the goals of the study to potential participants and requested verbal consent before conducting the interview. The participants had the option of calling the principal investigator if they wanted further information.

**Standard protocol approvals, registrations, and patient consents.** The study was approved by the Stanford University institutional review board.

Subjects who declined to participate or who gave up before completing half the interview were classified as refusals. Excluded from the study were subjects who were not fluent in English or Spanish, who had a hearing or speech impairment, or who had an illness (such as dementia, Alzheimer disease, or a terminal disease) that precluded being interviewed. The interviews lasted on average 62.1 ( $\pm 32.2$ ) minutes.

**Instrument.** The Sleep-EVAL knowledge-based expert system was used in this study to conduct the interviews.<sup>10,11</sup> Each interview began with a series of questions asked of all the participants. Questions were read aloud by the interviewer as they appeared on the screen. These questions were either closed-ended (e.g., yes/no, 5-point scale, multiple choice) or open-ended (e.g., duration of symptoms, description of illness).

Once this information was collected, the system began the diagnostic exploration of mental and sleep disorders. Concurrent diagnoses are allowed in accordance with the *DSM-IV-TR*<sup>12</sup> and the *ICSD-II*.<sup>1</sup> The differential process is based on a series of key rules allowing or prohibiting the co-occurrence of 2 diagnoses (for further information, see supplemental data and table e-1 on the *Neurology*<sup>®</sup> Web site at [Neurology.org](http://Neurology.org)). The decision about the presence of a symptom is based on the interviewee's responses rather than on the interviewer's judgment. This approach has proven to yield better agreement between lay interviewers and psychiatrists on the diagnosis of minor psychiatric disorders.<sup>13</sup> The system has been tested in various contexts, in clinical psychiatry and sleep disorders clinics.<sup>14-17</sup> In psychiatry, overall kappa between psychiatrists and the system was 0.71<sup>15</sup>; kappas have ranged from 0.44 (schizophrenia disorders) to 0.78 (major depressive disorder). Agreement for insomnia diagnoses was obtained in 96.9% of cases ( $\kappa$  0.78). Overall agreement on any breathing-related sleep disorder was 96.9% ( $\kappa$  0.94).<sup>14,16</sup> For

excessive sleepiness as a symptom, kappas between Sleep-EVAL and 3 sleep specialists ranged from 0.62 to 0.70 with an overall sensitivity of 98.3% and a specificity of 62.5%. For narcolepsy with cataplexy, kappas between sleep specialists on the presence of narcolepsy ranged from 0.83 to 0.93 while kappas between Sleep-EVAL and each sleep specialist were 0.89, 0.93, and 1.0.<sup>17</sup>

**Variables.** Information gathered related to CAs included:

- Frequency of CA episodes (>1 time/wk; 2-5 times/mo; 1 time/mo; <1 time/mo; <1 time/y; never)
- Length of an episode
- Duration

Participants were also assessed on:

- Frequency and duration of other parasomnias (sleepwalking, sleep terrors, violent behaviors during sleep, and hypnagogic and hypnopompic hallucinations)
- Medications, which were grouped according to their drug class and approved label

Sleep disorder diagnoses were assessed according to *DSM-IV-TR* and *ICSD-II* classifications (see figure e-1 for CAs decision tree). Mental disorders were evaluated using the *DSM-IV-TR* classification.

The *ICSD-II* criteria<sup>1</sup> for CAs (p. 140) include the following: (1) recurrent mental confusion or confusional behavior that occurs during an arousal or awakening from nocturnal sleep or a daytime nap, and (2) the disturbance is not better explained by another sleep disorder, medical or neurologic disorder, mental disorder, medication use, or substance use disorder.

**Analyses.** A weighting procedure was applied to correct for disparities in the geographical, age, and sex distributions between the sample and the populations of different states. Results were based on weighted *n* values and percentages. Logistic regressions were used to compute the odds ratios (ORs) associated with CAs. Reported differences were significant at the  $\leq 0.01$  level (determined using the Holm-Bonferroni method for multiple comparisons).<sup>18</sup> SPSS version 20 (IBM Corp., Armonk, NY) was used to perform statistical analyses.

**RESULTS** From 19,136 solicited individuals, data from 15,929 participants, aged 18 to 102 years, were included in the analyses. Fifty-nine percent were living in areas with a population density of >200 inhabitants per square mile. Women represented 51.3% of the sample.

Nearly 40% of the sample was working on a daytime schedule; shift work (i.e., working outside regular daytime hours) represented approximately 20% of the sample.

**Prevalence.** A total of 15.2% (95% confidence interval 14.6%–15.8%) (*n* = 2,421) of the sample reported CA episodes in the previous year. CAs occurred as frequently in men as in women but decreased with age (table 1). More than half of them (53.8%) reported at least one episode per week; an additional 24.7% reported 2 to 5 episodes per month, and 21.6% had 1 to 12 episodes in the previous year.

CAs were present for less than 6 months in 11.5% of cases; 6.2% had them for 6 to 12 months, 25.5% for 1 to 5 years, and 56.2% for more than 5 years.

**Table 1** Prevalence of confusional arousals by age groups, sex, and occupation

	No.	% (95% CI)
<b>Sex</b>		
Male	7,755	15.3 (14.4–16.1)
Female	8,174	15.0 (14.3–15.9)
<b>Age groups, y</b>		
18–44	4,978	22.5 (21.3–23.7) <sup>a</sup>
45–64	8,230	13.4 (12.6–14.1)
≥65	2,721	7.2 (6.2–8.2)
<b>Occupation</b>		
Daytime work	6,321	14.5 (13.6–15.4) <sup>a</sup>
Shift work	3,168	17.6 (16.2–18.9)
Unemployed	634	22.8 (19.3–26.2)
Not working	2,095	16.4 (14.6–18.1)
Student	1,017	25.0 (22.2–27.7)
Retired	2,694	7.7 (6.7–8.7) <sup>a</sup>

Abbreviation: CI = confidence interval.

<sup>a</sup> $p < 0.001$ .

Duration of CAs was associated with their frequency: individuals with at least one episode of CAs per week were more likely to have them for at least 5 years (72.3%) compared to those with episodes occurring 2 to 5 times/mo (56.4%;  $p < 0.01$ ).

Episodes of CAs were brief for 37.6% of participants who reported a duration of less than 5 minutes; 32.3% said it lasted between 5 and 15 minutes and 30.1% reported episodes lasting 15 minutes or more. Episodes were triggered when suddenly awakened by someone or something in 33.7% of CA cases. Being disoriented upon awakening (subject not knowing where they are or what period of the day it is) was reported by 57.0%. Another 34.4% of subjects with CA recounted difficulty talking or thinking clearly upon awakening. Experiencing inappropriate behaviors (such as answering the phone when the alarm clock rings) was mentioned by 19.9% of participants.

Among participants with CA, 36.4% had sleep-related hallucinations (hypnagogic or hypnopompic) and 14.8% ( $n = 350$ ) reported episodes of nocturnal wandering. Nearly half of these nocturnal wandering episodes (46.2%) were accompanied by violent behaviors during sleep. Complete or partial amnesia of the episode was reported by 8.6% ( $n = 207$ ) of individuals with CAs.

**Sleep disorders.** As many as 70.8% of individuals with CAs had a dyssomnia (disorders of initiating or maintaining sleep or of excessive sleepiness characterized by a disturbance in the amount, quality, or timing of sleep) and 20.9% had another parasomnia (undesirable

physical events or experiences occurring during sleep onset, within sleep, or during arousals from sleep). Logistic regressions were performed to determine factors associated with the presence of CAs.

As seen in table 2, individuals with excessive sleepiness symptoms, circadian rhythm sleep disorder, obstructive sleep apnea syndrome, or insomnia disorder were significantly more likely to have CAs. Hypersomnia disorder and restless legs syndrome were also associated with CAs. The odds considerably decreased after adjusting for age, sex, and use of psychotropic medication. One of the main changes was for shorter sleep duration, which was no longer significant after adjusting the model.

**Mental disorders.** Similar analyses were undertaken to examine the associations between mental disorders and CAs. We found that 37.4% of individuals with CAs also had a mental disorder. Many mental disorders were not significantly associated with CAs, such as simple phobia, psychotic, eating, and adjustment disorders.

Agoraphobia, obsessive-compulsive, and social anxiety disorders were significant only in bivariate model. Individuals with major depressive, bipolar, or dysthymic disorder were more likely to report CAs. Similarly, alcohol abuse/dependence, panic disorder, posttraumatic stress disorder, and generalized anxiety disorder were significantly associated with CAs (table 3). Odds ratios considerably decreased when the models were adjusted for age, sex, and psychotropic use.

**Medications.** Of the individuals with CAs, 31.3% were taking a psychotropic drug for sleep or mental disorders. As seen in table 4, individuals taking any kind of antidepressant medication (selective serotonin reuptake inhibitor, serotonin–norepinephrine reuptake inhibitor, tricyclic, tetracyclic, other antidepressants) were more likely to report CAs. Anxiolytics, hypnotics, and other types of psychotropics (antipsychotics, anticonvulsants, etc.) were significant only in bivariate analyses.

**Medical conditions.** Of the 16 most frequently reported medical conditions, 3 were significantly associated with CAs after adjusting for age and sex. Individuals with diseases of the digestive system (adjusted OR [AOR]: 1.5 [1.2–1.9];  $p < 0.0001$ ), those with a cerebrovascular disease (AOR: 1.7 [1.2–2.4];  $p = 0.003$ ), and subjects with upper respiratory tract diseases (AOR: 1.3 [1.1–1.5];  $p = 0.001$ ) were more likely to report CAs than the remainder of the sample. Diseases of the CNS were found in comparable proportions among subjects with CAs (1.3%) and the remainder of the sample (1.1%).

Overall, CAs were accompanied by a sleep disorder, a mental disorder, or the use of psychotropic drugs in 84.0% of cases. The breakdown is shown

**Table 2** Sleep factors associated with confusional arousals

	Prevalence, %	Crude OR (95% CI)	AOR (95% CI)
<b>Sleep duration, h:min</b>			
<6:00	19.5	1.58 (1.37-1.81) <sup>a</sup>	0.94 (0.81-1.10)
6:00-6:59	17.1	1.36 (1.20-1.54) <sup>a</sup>	1.14 (1.00-1.29)
7:00-8:59	12.8	1.00	1.00
≥9:00	15.1	1.37 (1.11-1.69) <sup>b</sup>	2.40 (1.41-4.09) <sup>a</sup>
<b>Excessive sleepiness</b>			
Absence	11.4	1.00	1.00
Presence	25.9	2.72 (2.47-2.98) <sup>a</sup>	1.89 (1.68-2.13) <sup>a</sup>
<b>Circadian rhythm sleep disorder</b>			
Absence	12.8	1.00	1.00
Presence	36.4	3.87 (3.24-4.65) <sup>a</sup>	2.85 (2.33-3.48) <sup>a</sup>
<b>Obstructive sleep apnea syndrome</b>			
Absence	14.6	1.00	1.00
Presence	28.0	2.27 (1.88-2.74) <sup>a</sup>	1.79 (1.44-2.22) <sup>a</sup>
<b>Restless legs syndrome</b>			
Absence	14.6	1.00	1.00
Presence	28.4	2.31 (1.91-2.81) <sup>a</sup>	1.61 (1.26-2.06) <sup>a</sup>
<b>Insomnia disorder</b>			
Absence	13.8	1.00	1.00
Presence	31.8	2.91 (2.55-3.34) <sup>a</sup>	1.87 (1.55-2.25) <sup>a</sup>
<b>Hypersomnia disorder</b>			
Absence	15.0	1.00	1.00
Presence	43.8	4.42 (2.90-6.73) <sup>a</sup>	2.40 (1.41-4.09) <sup>a</sup>

Abbreviations: AOR = adjusted odds ratio; CI = confidence interval; OR = odds ratio.

AOR was adjusted for age, sex, and use of psychotropic medication.

<sup>a</sup> $p < 0.001$ .

<sup>b</sup> $p < 0.01$ .

in figure 1. Individuals with CAs and amnesia of the episode (93.8%) or nocturnal wanderings (94.1%) nearly always had an associated sleep or mental disorder or were using psychotropic drugs.

Having a dyssomnia increased the likelihood of having CAs by nearly 3 times (17.0% vs 7.1%; OR: 2.69 [2.61-3.31]) and having a parasomnia by 3.25 (2.86-3.69; 29.6% vs 11.5%). Similarly, the presence of a mental disorder increased the likelihood of having CAs by 2.84 (2.54-3.19; 23.5% vs 9.7%), while the use of any psychotropic drug increased the odds of having CAs by 1.98 (1.78-2.21; 20.0% vs 11.2%).

The 2.0% of the sample who had CAs but no sleep or mental disorders and not using psychotropic drugs had fewer CA episodes (57.6%). The prevalence of CA disorders, without known cause or associated condition, was 0.8% [0.7%-0.9%] in the sample.

**Does complete or partial amnesia of CA episodes or nocturnal wandering episodes change the associations?** Compared to individuals with CAs without amnesia, those with amnesia were more likely to have a long sleep

duration (13.6% vs 5.6%; OR: 3.17 [1.86-5.40];  $p < 0.001$ ), and more frequently reported excessive sleepiness symptoms (60.7% vs 42.5%; OR: 2.13 [1.53-2.97];  $p < 0.001$ ) or circadian rhythm sleep disorder (23.5% vs 10.1%; OR: 2.40 [1.61-3.59];  $p < 0.001$ ). Individuals who had CAs with or without nocturnal wanderings were comparable for sleep disorders.

For mental disorders, when comparing presence/absence of amnesia of the episodes, 3 disorders were more frequently observed among individuals with CAs accompanied by amnesia of the episodes compared to those without amnesia: major depressive disorder (22.8% vs 11.7%; OR: 2.02 [1.31-3.10];  $p = 0.001$ ), bipolar disorders (8.7% vs 3.7%; OR: 2.70 [1.46-4.99];  $p = 0.002$ ), and panic disorder (25.1% vs 7.8%; OR: 3.41 [2.26-5.14];  $p < 0.001$ ). A comparison of participants with or without nocturnal wanderings revealed that individuals with CAs and a major depressive disorder (OR: 1.76 [1.10-2.82]) or panic disorder (OR: 2.25 [1.41-3.61]) were more likely to have episodes of nocturnal wanderings.

**Table 3** Mental disorders associated with confusional arousals

	Prevalence, %	Crude OR (95% CI)	AOR (95% CI)
<b>Alcohol abuse/dependence</b>			
Absence	14.8	1.00	1.00
Presence	24.5	1.87 (1.53-2.28) <sup>a</sup>	1.58 (1.25-2.00) <sup>a</sup>
<b>Major depressive disorder</b>			
Absence	13.4	1.00	1.00
Presence	32.0	3.04 (2.58-3.59) <sup>a</sup>	1.82 (1.49-2.24) <sup>a</sup>
<b>Dysthymic disorder</b>			
Absence	14.1	1.00	1.00
Presence	47.4	5.48 (3.91-7.70) <sup>a</sup>	1.87 (1.24-2.83) <sup>b</sup>
<b>Bipolar disorders</b>			
Absence	14.1	1.00	1.00
Presence	42.3	4.46 (3.29-6.05) <sup>a</sup>	3.19 (2.26-4.49) <sup>a</sup>
<b>Agoraphobia</b>			
Absence	14.4	1.00	1.00
Presence	26.1	2.10 (1.44-3.06) <sup>a</sup>	NS
<b>Generalized anxiety disorder</b>			
Absence	14.1	1.00	1.00
Presence	38.9	3.87 (2.88-5.19) <sup>a</sup>	1.78 (1.27-2.51) <sup>a</sup>
<b>Obsessive-compulsive disorder</b>			
Absence	14.4	1.00	1.00
Presence	31.2	2.70 (1.80-4.07) <sup>a</sup>	NS
<b>Panic disorder</b>			
Absence	13.6	1.00	1.00
Presence	40.4	4.31 (3.53-5.26) <sup>a</sup>	2.57 (2.03-3.25) <sup>a</sup>
<b>Posttraumatic stress disorder</b>			
Absence	13.9	1.00	1.00
Presence	30.1	2.66 (2.17-3.26) <sup>a</sup>	1.52 (1.21-1.91) <sup>a</sup>
<b>Social anxiety disorder</b>			
Absence	14.0	1.00	1.00
Presence	19.3	1.47 (1.25-1.72) <sup>a</sup>	NS

Abbreviations: AOR = adjusted odds ratio; CI = confidence interval; NS = not significant; OR = odds ratio. AOR was adjusted for age, sex, and use of psychotropic medication.

<sup>a</sup> $p < 0.001$ .

<sup>b</sup> $p < 0.01$ .

Psychotropic drug use was not significantly associated with presence or absence of nocturnal wanderings or of amnesia of the episodes in CAs.

**DISCUSSION** This epidemiologic study representative of the US general population examined prevalence and risk factors associated with CAs. We found that 15.2% of the sample had episodes of CAs.

CAs have received considerably less attention than sleepwalking even though the consequences can be equally serious.<sup>19</sup> In animals, sudden awakenings by an external stimulus from non-REM sleep provoke a

reduction of the prepulse inhibition of the startle reflex that is not observed in spontaneous arousals. This mechanism has a protective role for the survival of the animal, which needs to respond quickly to potential threats when it is suddenly aroused.<sup>20</sup> A similar protective mechanism probably exists in humans. Therefore, techniques used for sudden awakening in the morning (e.g., alarm clock, telephone ringing) can trigger this reaction and provoke CAs.

Sleep deprivation has also been linked with CAs.<sup>3</sup> In our sample, nearly 20% of the subjects were getting less than 6 hours of sleep per night. Short sleep

**Table 4** Psychotropic medications associated with confusional arousals

	Prevalence, %	Crude OR (95% CI)	AOR (95% CI)
<b>Anxiolytic</b>			
Absence	14.7	1.00	1.00
Presence	24.6	1.88 (1.52-2.34) <sup>a</sup>	NS
<b>Hypnotic</b>			
Absence	14.9	1.00	1.00
Presence	24.2	1.83 (1.41-2.36) <sup>a</sup>	NS
<b>SSRI antidepressant</b>			
Absence	14.3	1.00	1.00
Presence	25.5	2.05 (1.75-2.40) <sup>a</sup>	1.92 (1.60-2.31) <sup>a</sup>
<b>SNRI antidepressant</b>			
Absence	14.9	1.00	1.00
Presence	26.5	2.06 (1.48-2.86) <sup>a</sup>	1.86 (1.27-2.71) <sup>a</sup>
<b>Tricyclic antidepressant</b>			
Absence	15.0	1.00	1.00
Presence	26.4	2.04 (1.36-3.07) <sup>a</sup>	2.14 (1.34-3.41) <sup>a</sup>
<b>Tetracyclic antidepressant</b>			
Absence	14.9	1.00	1.00
Presence	28.3	2.24 (1.54-3.26) <sup>a</sup>	2.06 (1.35-3.14) <sup>a</sup>
<b>Other type of antidepressant</b>			
Absence	14.9	1.00	1.00
Presence	27.4	2.15 (1.51-3.06) <sup>a</sup>	1.74 (1.16-2.61) <sup>b</sup>
<b>Other psychotropics</b>			
Absence	14.9	1.00	1.00
Presence	23.6	1.75 (1.27-2.42) <sup>a</sup>	NS

Abbreviations: AOR = adjusted odds ratio; CI = confidence interval; SNRI = serotonin-norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

AOR was adjusted for age and sex.

<sup>a</sup> $p < 0.001$ .

<sup>b</sup> $p < 0.01$ .

duration was associated with several sleep disorders, including insomnia disorders, obstructive sleep apnea syndrome, and circadian rhythm sleep disorder.

In our study, individuals reporting CAs presented with the following specific characteristics:

- Episode duration was short, 15 minutes or less for 69.9%. Although it was not possible to measure the duration of CAs with laboratory tests, studies that used cognitive tests such as the Memory and Search Test or the Descending Subtraction Test to measure the effects of CAs have shown that effects dissipate within 30 minutes for most cases.<sup>21,22</sup>
- Chronicity: For most individuals, CAs were chronic, occurring repeatedly for more than 1 year (81.7%). Chronicity was associated with frequency of the episodes: subjects with at least one episode per week were more likely to have them for at least 5 years (72.3%).

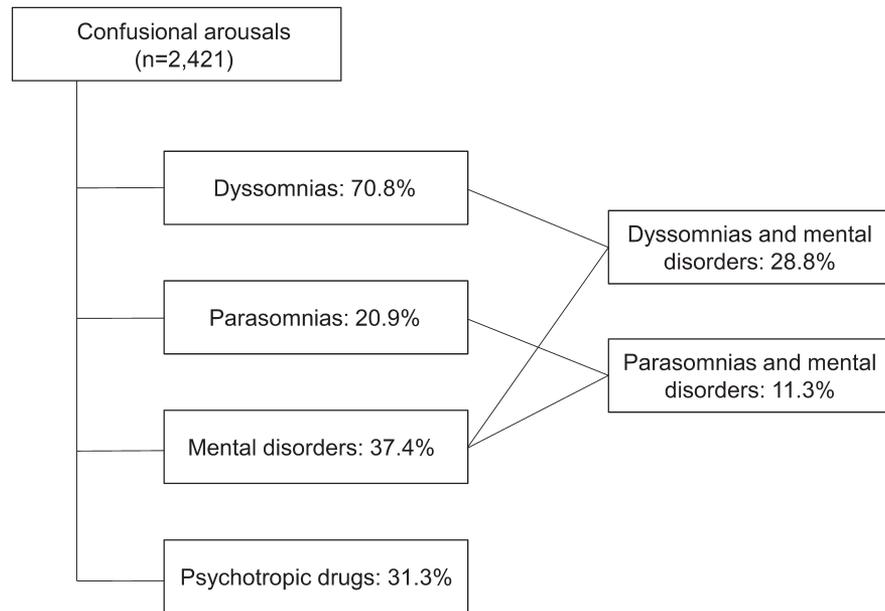
- Other symptom associations: 36.4% of participants had sleep-related hallucinations (hypnagogic or hypnopompic) and 14.8% also reported episodes of nocturnal wanderings; 7% of CA episodes were accompanied by nocturnal wanderings and violent behaviors during sleep.

It should be kept in mind that our results are based on subjective reports. Because this was an epidemiologic study, we did not conduct laboratory testing with respondents to confirm diagnoses. CAs, however, do not require polysomnographic recordings to confirm the diagnosis. Given the absence of objective measures of CAs, and the fact that complete or partial amnesia can be present during an episode and mental confusion is always present, it is likely that CAs were misreported, especially among participants living alone. Nonetheless, our data provide critical information regarding this understudied sleep disorder.

Several issues deserve attention:

1. CAs can be followed by complete or partial amnesia of the episode. In our study, the presence of amnesia increased the risk of some mental disorders, notably, mood and panic disorders. Amnesia was also accompanied by a greater likelihood of subjects taking selective serotonin reuptake inhibitor antidepressants. Regardless of the presence of amnesia, CAs were highly comorbid with several mental disorders. Amnesia is not a distinct trait related to severity. It is therefore not surprising that the latest *ICSD* classification has dropped this criterion.
2. CAs can be accompanied by episodes of nocturnal wanderings (sleepwalking or other kinds of automatic behaviors during sleep). Again, although the presence of nocturnal wanderings increased the risk of some mental disorders (mood disorders, panic disorder, and alcohol abuse/dependence), the association with several mental disorders remained strong even in the absence of nocturnal wanderings.
3. CAs were associated with sleep apnea. It is possible that hypoxemia occurring in sleep apnea provokes an episode when an awakening occurs close to the apneic event. Another important effect on sleep produced by obstructive sleep apnea syndrome is the increase of arousal and microarousal during sleep, which in some cases provokes waking neurobehavioral deficits.<sup>23</sup> A similar mechanism could be present for individuals with upper respiratory tract diseases. However, research is needed to understand the link between upper respiratory tract diseases and CAs.
4. The highest odds for CAs were observed in individuals with circadian rhythm sleep disorder and

**Figure 1** Association between confusional arousals and dyssomnias, parasomnias, mental disorders, and psychotropic drugs



in those with long sleep duration ( $\geq 9$  hours). Shift work disorder, a circadian rhythm sleep disorder, has been reported to be highly associated with CAs.<sup>3</sup> CAs have been rarely studied in the context of sleep or mental disorders.

5. Hypnotics and anxiolytics were not related to CA episodes in our study.<sup>24</sup>
6. CA as a parasomnia without a known cause or associated condition is rare. This occurred in only 0.9% of the sample.

A general assumption about CAs is that they are not pathological. This assumption is supported by the high prevalence of the disorder in the general population and the apparent benignity of its consequences. It is not yet considered a disorder in the *DSM-V* classification, probably because it has received little attention from the scientific community. However, including CA as a sleep disorder in the major classifications would increase awareness among physicians and patients and contribute to its identification, research, and treatment.

Our study shows that underestimating the importance of CA leads to a misunderstanding of the disorder and its effects. The majority of subjects experiencing CAs were not using any medication, and among those who were, antidepressants were most common. Sleep and/or mental disorders were important factors for CAs independent of the use of any medication.

#### AUTHOR CONTRIBUTIONS

Maurice M. Ohayon: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for

conduct of research and will give final approval, acquisition of data, statistical analysis, study supervision. Mark Mahowald: drafting/revising the manuscript, accepts responsibility for conduct of research and will give final approval. Damien Leger: study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval.

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#### DISCLOSURE

M. Ohayon was supported by the Arrillaga Foundation. M. Mahowald and D. Leger report no disclosures relevant to the manuscript. Go to [Neurology.org](http://Neurology.org) for full disclosures.

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