CLINICAL REVIEW

Assessment and treatment of nocturnal panic attacks

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Summary
Nocturnal panic (NP), waking from sleep in a state of panic, is a common occurrence among patients with panic disorder, with 44–71% reporting at least one such attack. NP is a non-REM event that is distinct from sleep terrors, sleep apnea, nightmares or dream-induced arousals. This review outlines recent advances in the characterization of NP, as well as current approaches to the assessment and treatment of NP. In contrast to earlier work, more recent studies suggest that patients with NP do not differ from patients without NP on sleep architecture, sleep physiology, self-reported sleep quality and severity of panic disorder. However, more precise measurement of physiological precipitants and features is warranted.

Assessment of NP focuses on ruling out other explanations for NP, with differential diagnosis based on interviews, sleep polysomnography and ambulatory recording of sleep. Psychological treatment (cognitive-behavioral therapy) targets misappraisals of anxiety sensations, hyperventilatory response, and conditioned reactions to internal, physical cues. Recent evidence supports the efficacy of this approach, however, controlled studies on pharmacological agents in the treatment of NP are lacking. Research is needed to examine the effects of combined cognitive-behavioral therapy and medications, compared to medication alone in the treatment of NP.

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Phenomenon of nocturnal panic

Definition and characteristics

Nocturnal panic (NP) refers to waking from sleep in a state of panic, where panic is defined as an abrupt and discrete period of intense fear or discomfort, accompanied by cognitive and physical symptoms of arousal. These include tachycardia, sweating, shortness of breath, chest pressure, chocking sensations, dizziness or lightheadedness, depersonalization or derealization, stomach discomfort, and fears of dying or going crazy. A full panic attack (in contrast to a limited symptom attack) is defined by endorsement of four or more symptoms. The symptom profile of NPs does not differ significantly from panic attacks that occur during wakeful states. NP does not refer to waking from sleep and panicking after a lapse of waking time, or night-time arousals induced by nightmares (described below) or environmental stimuli.
(such as unexpected noises). Instead, NP is an abrupt waking from sleep in a state of panic without an obvious trigger. NP is most often experienced by individuals with panic disorder, an anxiety disorder characterized by unexpected panic attacks, and persistent apprehension regarding their recurrence or changes in lifestyle as a result of their occurrence. Thus, most patients with NP experience panic attacks during wakeful states as well, although a small subset predominantly experience NPs.3 The only other anxiety disorder in which NPs have been documented is posttraumatic stress disorder (described below). Most patients report that NP occurs between one and three hours after sleep onset, and only occasionally occurs more than once per night.2 NPs typically last 2-8 min,3 and return to sleep is usually difficult. Patients are able to vividly recall their NPs.2

Although epidemiological studies have not been conducted, surveys of select clinical groups suggest that NP is relatively common among panic disorder patients, with 44-71% reporting experienced NP at least once.2,4-6 From the largest survey to date, 58% of 1166 definite or probable panic disorder patients reported having experienced NP at least once, and 30-45% endured NP repeatedly.3 Our sample of 51 patients who reported repeatedly enduring NP averaged 11.4 NPs in the last month.7 Many patients who suffer NP frequently become fearful of sleep and attempt to delay sleep onset. Avoidance of sleep may result in chronic sleep deprivation, in turn precipitating more NPs.3 Although not yet directly investigated, NPs may be exacerbated by medication withdrawal, particularly withdrawal from benzodiazepines. Three to 5% of non-clinical populations self-report NPs8,9 although these figures may be inflated, given that estimates of prevalence are quite sensitive to specific questioning procedures,10 and self-report surveys tend to yield higher estimates than interview procedures. There are no reported data regarding ethnic or cultural differences in nocturnal panic, although sleep-paralysis is more common in African-American than Caucasian individuals.11

Sleep architecture

NP is a non-REM event, usually occurring in late Stage II or early Stage III sleep, in the absence of electroencephalographic abnormalities.12-16 In particular, NPs seem to develop during the transition from Stage II to Stage III.13 That is, some EEG slowing precedes NPs that emerge from Stage II, while NPs from Stage III are preceded by a maximum of only 2 min of Stage III sleep.3,16

In a methodologically rigorous, albeit small, polysomnography study of a second night following an initial adaptation night, eight panic disorder patients with NP and eight controls did not differ on measures of sleep latency, total sleep time, total duration of wakemings, percent awakenings, sleep efficiency, number of awakenings, REM latency, number of REM periods, REM efficiency, duration and percent of Stage 1, Stage 2, Stage 3, Stage 4 and REM sleep, or number and index of micro-awakenings.14 Previous reports of increased sleep latency, decreased sleep time, decreased sleep efficiency16 and less stage 4 sleep12 in NP patients were confounded by absence of an adaptation night and overall brief medication washout durations.

Distinction from other sleep disorders

NP is distinct from sleep terrors that occur mostly from Stage IV sleep (vs Stages II-III), and are followed by a quick return to sleep without recall of the event.18,19 NP is also distinct from sleep apnea that occurs mostly from Stages I, II and REM sleep20 and often occurs repeatedly during the night, compared to the typical single occurrence per night for NP. Moreover, respiratory cessation has not been detected prior to episodes of NP,12 although different results may emerge with more precise measurement of upper airway resistance (i.e., PES esophageal pressure through nasal gastric tubes: American Academy of Sleep Medicine, 1999).

A subset of apneic individuals meet criteria for panic disorder;21 NP may be triggered by apnea, or apneic episodes and NP may be experienced independently in these individuals. The absence of electroencephalographic abnormalities distinguishes NP from nocturnal seizures. In contrast to sleep paralysis, NP is not associated with inability to perform voluntary movements; instead patients typically sit up and/or get out of bed. The major distinction between nightmares and NP is the stage of sleep from which they occur; NP is a non-REM event. Also, according to EEG data, panic disorder patients are accurate in their discrimination between dream-induced anxiety and NPs, even though both are associated with autonomic activation.3,13

Persons with posttraumatic stress disorder (PTSD) mostly connect their awakenings to specific trauma-related dreams and images. Nonetheless, a substantial proportion of their self-monitored and laboratory recorded arousals from sleep occur in the absence of dreams.22 Conceivably, the latter reflect a psychophysiological conditioned response to REM sleep as a result of nightmares.
Reported sleep quality

Patients with NP report more insomnia than panic disorder patients without NP. We conducted a comprehensive assessment of sleep and sleep history, using daily ratings of sleepiness for every waking hour for 1 week using the Stanford Sleepiness Scale, a daily sleep log each morning for 1 week to record total hours of sleep, estimated time taken to fall asleep, and number of wakenings during the night, and the Sleep Questionnaire and Assessment of Wakefulness in 51 panic disorder patients with NP versus 41 who never experienced NP. NP patients self-reported more severe past and current sleeping difficulties in general, and more frequent past and current difficulties with sleep onset, than panic disorder patients who never experienced NP. However, these self-reports were not validated by ongoing daily logs, which did not differentiate between the two groups. Since ongoing monitoring yields more accurate data than retrospective judgments, the reported difficulty with sleep onset by NP patients is probably representative of an anxious bias in their judgments of sleep-related behaviors. Also, there was no evidence for more reported sleep disturbance due to environmental interruptions (e.g., heat, noise) or physical discomfort (e.g., shortness of breath, snoring, sweating), disorders of arousal (e.g., sleep walking or talking), or dream activity (including vivid dreams and nightmares) in the NP group. A recent report of strong correlations between nightmare frequency and frequency of NPs is limited by retrospective recall of NP and nightmare frequency and questionable diagnoses of NP.

Sleep physiology

Respiratory dysregulation possibly contributes to NP. For example, NP may result from extreme hypercapnia, as a result of carbon dioxide sensitivity in central medullary carbon dioxide receptors at times of increases in partial pressure of carbon dioxide during sleep. Conversely, Ley (1988) suggested that NP results from chronic hyperventilation, in which reduced levels of carbon dioxide, and eventual insufficiency in plasma bicarbonate levels and increased blood alkalinity create a state of vulnerability to ventilatory irregularities during sleep. Extant empirical data have failed to support either hypothesis. First, patients with NP do not exhibit patterns of chronic hyperventilation or hypersensitivity to carbon dioxide or hyperventilation challenges in laboratory conditions relative to patients who never experience NP. Second, Hauri et al. (1989) found no evidence for hyperventilation or dysregulated respiratory drive prior to NP, although this study was limited to only four subjects. In a larger sample, we found no evidence for respiratory differences (rate and volume) during sleep of panic disorder patients with NP versus panic disorder patients without NP (Aikins & Craske, in submission). However, further research is indicated since more precise measurement of upper airway resistance using PES esophageal pressure through nasal gastric tubes may yield different results.

Panic disorder patients show more movement time during sleep, especially large body movements, than non-anxious controls. On the other hand, there is some evidence to suggest that patients with NP show a depression of movement time, leading Uhde (1994) to speculate that increased movement during sleep may confer a degree of compensatory protection against NP. However, we did not find differences in gross body activity (recorded from a triaxial piezo-resistive accelerometer mounted on a wrist strap) or leg movement during sleep between panic disorder patients with and without NP, although in both groups leg movement was higher than for non-anxious controls (Aikins & Craske, in submission). More study is needed before firm conclusions can be drawn regarding differences in the extent and type of movement during sleep in NP relative to patients without NP.

Higher total heart period variability during non-REM sleep was found in panic disorder patients with NP compared to patients without NP, but results were confounded by various methodological limitations. In another study, we found no differences in indices of heart rate variability between the same two groups (Aikins & Craske, in submission), with both exhibiting lower heart rate variability and higher heart rate on average throughout sleep than non-anxious controls. However, cardiac symptomatology may be a salient precipitant to NP in patients with mitral valve prolapse; a higher percentage of patients with NP have a prior diagnosis of mitral valve prolapse relative to other panic disorder patients. Thus, further study regarding the role of cardiac symptoms in NP is warranted.

Several studies have evaluated reactivity to pharmacological challenges during sleep. For example, NPs were induced by administration of caffeine during delta sleep. Also, CCK-4 induced NPs in four of nine healthy controls when infused during delta sleep. Similarly, pentagastrin (a synthetic analog of CCK-4) infused during the transition from Stage II to Stage III or early Stage III sleep induced panic in four of seven patients with...
social phobia or panic disorder who had previously demonstrated pentagastrin-induced wake panic attacks. The finding that panic was induced without observing a transitional lightening of sleep prior to waking was interpreted as evidence that cognitive processing dependent on lightening of sleep stage is not a pre-requisite for NP. But other studies (discussed below) support the notion that cognitive factors may play an important role in NP.

**Psychosocial variables**

It is conceivable that NP represents the more severe end of the panic disorder continuum, especially since patients with NP report history of more psychopathology, \(^34\) and higher rates of suicidal ideation \(^35\) than panic disorder patients without NP. However, these studies failed to comprehensively evaluate NP or rule out other sleep conditions. In our relatively large sample, in which other sleep disorders were ruled out using polysomnography and sleep history analyses, we found no evidence for patients with NP to be more severe in terms of panic disorder, psychological comorbidity, anxious and depressive symptoms, interference with functioning, or interpersonal functioning.\(^7\)

On the other hand, there is evidence for panic disorder patients with NP to show a specific elevated emotional reactivity (measured psychologically and subjectively) to conditions that resemble sleep, including meditative relaxation\(^36\) and hypnotic imagery \(^37\) relative to panic disorder patients without NP. In contrast, the two groups do not differ in their reactivity to other panicogenic challenges, including hyperventilation and cardiac tracking.\(^36\) These laboratory findings confirm earlier self report findings in which NP patients cited relaxation and fatigue as more likely triggers of panic attacks than did patients without NP.\(^16\) Moreover, NP patients endorse more feelings of discomfort in relation to relaxation and ‘letting go’ (Reactions to Relaxation and Arousal).\(^38\) We have suggested that fears of loss of vigilance (states involving diminution of awareness) contribute to distress in sleep and sleep-like states,\(^37,39\) although additional research is needed to determine whether such fears represent a vulnerability to NP or are simply the consequence of NP.

In addition, our work on reactivity to signals of arousal during sleep suggests that specific misappraisals of physiological events during sleep may contribute to NP.\(^40,41\) Before sleep, discernible biofeedback audio signals were ostensibly calibrated for each patient to reflect changes in their physiological (i.e., heart rate, skin temperature, sweat gland activity) state. During stages II and III of sleep, an ascending decibel series (35–80 db, 2 s duration, 3 min inter-trial intervals) of audio signals was experimentally induced; for some participants these were the same as the biofeedback signals calibrated prior to sleep, whereas a control group received a distinctly different set of audio signals not previously associated with their own physiology.\(^40\) Panic disorder patients with recurrent NPs who, before sleep, were led to believe that changes in their physiology would be indicative of ‘abnormal-abnormality’ failed to achieve as deep sleep, woke with more distress and endorsed more panic attacks in response to the audio signals previously associated with their physiological state than patients who were led to believe that such changes were ‘normal’ or patients who were presented with a distinctly different signal unrelated to their physiological arousal. Thus, replicating our earlier findings,\(^41\) individuals who were reassured that episodes of physiological arousal during sleep were safe and expected were less fearful of signals of such arousal than individuals who were not reassured and who did not expect episodes of arousal to occur. These findings support the role of cognitive factors in NP.

We propose that, like day time panic attacks,\(^42,43\) NPs are triggered by changes in physiological state during sleep through a process of interoceptive conditioning, whereby low-level somatic sensations of arousal or anxiety become conditional stimuli\(^44\) so that early somatic components of the anxiety response come to elicit anxiety or panic. An extensive body of experimental literature attests to the robustness of interoceptive conditioning.\(^45\) In addition, interoceptive conditional responses are not dependent on conscious awareness of triggering cues,\(^46\) such that, once acquired, these responses can be elicited under anesthesia, even in humans.\(^46\) Consequently, changes in relevant bodily functions that are not consciously recognized due to sleep or sleep-like states may elicit conditional fear due to previous pairings with panic. The role of precipitating physiological events has received some support from reports of short muscle twitches, increased EEG frequency, body movements, breathing irregularities, and increases in heart rate and skin conductance in the minutes and seconds preceding panic attacks.\(^5,12,16\) It may be necessary for these physiological events to co-occur with sleep Stages II or III, as one shifts from semi-vigilance to
non-vigilance; a shift that may be particularly anxiety-provoking for NP individuals.

Assessment of nocturnal panic attacks

Sleep disorder assessment

The primary goal of a sleep assessment is to rule out other explanations for NPs, such as sleep apnea, night terrors, periodic movements, seizures, stage IV night terrors, non-restorative sleep, sleep hallucinogenesis, and sleep paralysis. These differentiations can be made by an adequate interview regarding current and past sleep functioning, sleep polysomnography in a sleep laboratory, and ambulatory recording of sleep features in the natural environment.

Importantly, the gold standard for measuring upper airway resistance (PES esophageal pressure through nasal gastric tubes; American Academy of Sleep Medicine, 1999), data from which is yet to be reported in NP patients, is likely to be very difficult for anxious patients to tolerate. Snoring without apneas, easily detected via a microphone on the trachea, also are important to measure since they can contribute to the Respiratory Arousal Index with sleep disturbance and probable increase in sympathetic tone. Also, occurrences of NP are recorded infrequently in the sleep laboratory setting, probably because laboratories provide a sense of safety and lessen fear responding overall. Indeed, all sleep-related disorders of arousal (e.g., nightmares and sleep walking) tend to occur less often in laboratory settings. 19 Thus, a polysomnographic recording will be most effectively targeted at ruling out other sleep disorders rather than measuring the physiology of NPs.

Ambulatory monitoring devices have been utilized in numerous studies 47 to continuously record physiological information and event marking for prolonged intervals, up to 60 h. Patients are asked to avoid vigorous physical activity, sexual activity, and alcohol, caffeine and drug use. The equipment is usually attached by a trained technician who checks calibration, electrode impedances and instructs patients in the use of the event marker to press for every wakening during the course of the recording. By the second night of ambulatory recording, most patients indicate that the ambulatory sleep equipment is relatively unobtrusive and had little perceived effect on their sleep (Aikins & Craske, in submission). Although ambulatory recording is less costly than sleep laboratory polysomnograms, and more likely to capture the physiology associated with naturally occurring NPs, ambulatory devices are generally less precise in measuring various physiological parameters. On the other hand, given that there is no evidence for physiological dysregularities in NP, precision in physiological measurement may be less relevant to clinical decision making than it is to research studies; ambulatory devices should be sufficient for differentiating NP from other sleep disorders such as sleep apnea, nocturnal seizures, periodic movements, non-restorative sleep and so on.

Since nocturnal panickers do not differ from panic disorder patients who never experience NP in terms of daily monitoring of sleep related behaviors (using instruments such as the Stanford Sleepiness Scale 24 or daily logs of total hours of sleep, estimated time to fall asleep, number of awakenings etc), such scales may provide very little differential diagnostic information.

Mental health assessment

The goal of this assessment is to establish whether the NPs are symptomatic of an anxiety disorder or any other psychological disorder for that matter. Semi-structured diagnostic interviews are considered the most reliable and valid means of diagnosing anxiety disorders. For example, the Anxiety Disorders Interview Schedule-IV (ADIS-IV 46) covers all anxiety disorders, mood disorders, somatoform disorders, and screens for psychosis and substance related disorders, with high inter-rater reliability. 49 Also, the SCID interview 50 is another state-of-the-art semi-structured interview that facilitates reliable diagnoses of anxiety disorders and mood disorders using the criteria of the DSM-IV. Both interviews require adequately trained diagnosticians. In the absence of such instruments and interviewers, a trained clinician can conduct a mental health assessment to establish the presence of anxiety disorders, mood disorders, substance use related disorders and so on. In addition, the interviewer/clinician will establish whether the NPs are symptomatic of panic disorder (i.e., repeated panic attacks, most likely to be occurring during the day as well, and associated with excessive anxiety and worry about their recurrence during the day and out of sleep) or posttraumatic stress disorder (i.e., emotional reactivity to reminders of trauma, avoidance of trauma, and physiological hyperarousal following traumatization). The interviewer will also assess the relationship between NPs and substance use and/or drug withdrawals. Another important differential is between...
NP and sleep disturbance characteristic of generalized anxiety disorder, that includes insomnia as well as occasional waking in a restless, ‘unsettled’ state, followed by a period of worry and eventual panic. By virtue of being delayed rather than immediate upon waking, the latter is not considered a true NP.

**Nocturnal panic assessment**

We have developed an interviewer administered Nocturnal Panic Screen (see Appendix A) in which NPs are defined as abrupt surges of arousal that are felt immediately upon waking from sleep and are not attributable to frightening dreams, external interruptions, or other sleep disorders. Additional useful descriptive information includes the estimated frequency of NPs over the past month, estimated time of onset of NP, behavioral changes as a result of NP (e.g., avoidance of sleep, sleep medications, sleep with TV, air conditioner or lights on), and anticipatory anxiety about sleep and NP.

Also, patients can self-monitor episodes of waking during the night in terms of time, panic symptoms and intensity, and perceived precipitants (see Appendix B) as a way of gathering more accurate descriptive information. A recommended assessment plan is provided below (see Practice points).

**Psychological treatment for nocturnal panic attacks**

Cognitive-behavioral therapy (CBT) for nocturnal panic NP is used to treat both daytime and NP attacks, incorporating psychological approaches originally developed for daytime panic attacks, as well as novel techniques targeting nocturnal panic attacks.

The therapy targets the panic attacks themselves as well as chronic apprehension over recurrence of panic attacks and consists of 11, 60-min sessions. Initial sessions focus on education about panic attacks with emphasis on providing patients with accurate information regarding the physiological aspects of the flight/flight response in relation to both daytime and nocturnal panic attacks. Patients are informed that anxiety is a natural process that evolved to protect humans by activating the body in the event of actual danger and thus, anxiety symptoms are not in themselves dangerous. For NP attacks, emphasis is given to the harmless nature of normal physiological fluctuations that occur during sleep.

The cognitive-behavioral model of panic attacks is discussed at length. For daytime panic attacks, patients are taught how misappraisals of physiological arousal related to anxiety (e.g., rapid heartbeat) as a sign of catastrophe (e.g., heart attack) lead to heightened arousal which in turn reinforces the original maladaptive belief, resulting in a spiral of continued, increased arousal culminating in a panic attack. Because the symptoms of physiological arousal are feared, situations or triggers that become associated with arousal (e.g., exercise) are avoided. Continued avoidance of internal sensations of anxiety and/or external places (e.g., the mall) or activities (e.g., driving), which become associated with panic attacks, prevents patients from learning disconfirming evidence that sensations are not harmful. The model is also applied to the occurrence of NP attacks. Patients are taught that a heightened sensitivity to sensations of anxiety leads them to notice subtle fluctuations in physiology during sleep and because the sensations are feared, arousal is further increased, leading to panic out of sleep. Common misappraisals of arousal sensations during sleep include increased risk of cardiac arrest during sleep, suffocation during sleep, and various culturally based beliefs such as pressure on the chest as a sign of being possessed by demons or a sign of near death. To address these misappraisals, patients are informed that natural physiological changes (e.g., muscle twitches, difficulty breathing) that occur during sleep are benign and that heightened arousal during sleep may be due to several explanations such as increased anxiety and stress during the day, use of stimulants before sleep, dreams that induce arousal, and anxious anticipation before sleep. The role of overbreathing (i.e., hyperventilation) in precipitating feared sensations is discussed using detailed written materials outlining the biochemical changes in the body resulting from hyperventilation. Breathing retraining is then taught as a coping technique especially for such symptoms associated with overbreathing. Patients are instructed to breathe smoothly and evenly through the diaphragm rather than take shallow breaths from the chest. A meditative component is also introduced: patients are taught to count their in-breaths and when they breathe out, to silently say the word ‘relax.’ In addition to practicing during the day, to assist with night-time arousal, practice of breathing exercises is encouraged prior to sleep and upon each wakening.

Cognitive restructuring directly targets misappraisals of bodily sensations as threatening or dangerous. Specific thoughts are categorized as probability overestimations (i.e., inflating the
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likelihood of a negative outcome) and/or catastrophizations (i.e., blowing events out of proportion; viewing them as disastrous and unmanageable). Panicogenic thoughts are questioned using an empirical, hypothesis-testing approach (i.e., ‘What is the evidence for…?’). Therapists assist patients in examining realistic probabilities (e.g., ‘What is the actual likelihood of suffocating during sleep?’), gathering data (e.g., patients’ medical status), exploring alternative explanations (e.g., attributing heart rate accelerations to normal sleep-related changes in physiology or to anxiety), and examining realistic consequences and concrete strategies for dealing with events should they occur (e.g., “How bad would it really be if I woke up panicking? How would I cope if it happened?”). Interoceptive exposure is then introduced. During exposure, patients repeatedly induce physical sensations associated with panic attacks to weaken or disrupt the associations between specific internal cues and panic reactions. In addition to typical interoceptive inductions (e.g., voluntary hyperventilation, spinning) used to treat daytime panic attacks, patients practice deep relaxation (a panic-trigger for NP patients3), ‘buzzer arousal inductions’ from a sleeping state (e.g., setting the alarm to go off at various times during the night), sleeping in hot, stuffy conditions and other inductions tailored to NP.

Naturalistic exposure exercises (e.g., drinking coffee, exercise) that induce feared sensations are then introduced within the therapy session and patients are encouraged to practice such exposures at home. In addition, maladaptive behaviors specific to NP (e.g., lights or television to facilitate sleep, delayed sleep onset) are targeted by generating a hierarchy of behaviors to be modified, ranked from least to most difficult to change. Then, patients are encouraged to gradually modify behaviors, beginning with the least difficult (e.g., sleep with television off) with the aid of cognitive restructuring and breathing retraining to manage anxiety and distress. With each session, patients continue to the next item on the hierarchy. Also, basic sleep hygiene guidelines are instituted to modify poor sleep habits (e.g., inconsistent sleep schedule, foods and alcohol before sleep), because onset-insomnia and sleep deprivation may contribute to NP recurrence.

Existing research indicates that CBT for panic disorder is highly effective, with 85–100% of treatment completers panic-free by the end of treatment, and effects lasting up to 2 years.53–55 Recent findings show that CBT specifically tailored for NP for patients who endure NP repeatedly leads to marked reductions in the severity of panic disorder, including the frequency of daytime and nocturnal attacks, with treatment gains persisting at 9 month follow-up. Symptom improvement was also accompanied by reductions in subjective and heart rate reactivity to laboratory stressors, as well as lowered heart rate and leg movement and increased cardiac variability during sleep when assessed immediately and 9 months following treatment completion.52 An area for future study concerns the generalizability of CBT for NP to other related conditions. As noted above, persons with posttraumatic stress disorder (PTSD) are also vulnerable to NP attacks, distinct from nightmare induced arousals.56 Thus, it may be that CBT for NP would be an effective agent for controlling NP attacks in persons with PTSD. On the other hand, cognitive-behavioral approaches for PTSD may be sufficient to control all symptoms of PTSD, including NP attacks. These possibilities, however, have not yet been subject to empirical test.

Pharmacological treatment of nocturnal panic attacks

Pharmacological approaches to NP have received relatively little attention. Published reports have been limited to uncontrolled single-case pharmacological trials.15,57 Daytime panic attacks are typically treated with benzodiazepines (alprazolam, clonazepam) or antidepressants (tricyclics, selective serotonin reuptake inhibitors),58 and these psychotropics are clearly more effective than drug placebos.59 In an early study, Lesser and colleagues (1985)15 reported cessation of daytime and NP panic attacks in a 36-year-old woman following treatment with alprazolam (maximum dose 5 mg), although the length of follow-up was not reported. Mellman and Uhde (1990)57 reported that in 12 patients with NP attacks, seven patients showed marked improvement (i.e., absence of nocturnal panic attacks over 3–12 months of follow-up) with tricyclic antidepressant therapy. An additional patient had a partial response (i.e., reduced frequency and intensity of attacks) to low-dose alprazolam; one patient spontaneously remitted and three patients refused medication or were unavailable to follow-up.57 Although these reports are promising, double-blind, placebo-controlled studies are needed to establish the efficacy of pharmacological agents in the treatment of NP.
Research agenda

Future studies should examine the following.

1. Physiological precipitants to and characteristics of NP, including more precise measurement of upper airway resistance such as PES esophageal pressure through nasal gastric tubes.
2. Occurrence of NP in relation to medication and non-prescription drug withdrawals, and other emotional disorders such as depression or substance use related disorders; and in relation to different cultural and ethnic groups.
3. Whether cognitive-behavioral therapy (CBT) for NP attacks effectively controls such attacks in persons with posttraumatic stress disorder (PTSD) or is CBT for PTSD sufficient to alleviate NP attacks in these individuals.
4. The efficacy of pharmacological agents used to treat daytime panic attacks applied to the treatment of NP attacks, as demonstrated by placebo-controlled trials.
5. Comparison of CBT for NP in combination with medication to medication alone in the treatment of NP attacks.

Summary

Nocturnal panic (NP) is relatively common among patients with panic disorder, with 30-45% of patients enduring repeated nocturnal panic attacks. \(^3\) NP is a non-REM event that typically occurs during transition from Stage II to Stage III, \(^13\) and is thus distinct from sleep terrors, sleep apnea, nightmares or dream-induced arousals. The extent to which respiratory dysregulation contributes to NP remains unclear. Although there is no existing evidence of hyperventilation or dysregulated respiratory drive prior to NP, studies using more precise measurement of upper airway resistance using PES esophageal pressure through gastric tubes have yet to be conducted and may yield different results. Recent work suggests that NP patients do not differ from panic disorder patients without NP in sleep physiology, sleep quality, or psychosocial aspects (e.g., panic disorder severity). \(^7\) These findings, however, require confirmation in future studies.

The assessment of NP focuses on ruling out alternative explanations for NP (e.g., seizures, apnea, other emotional disorder). Differential diagnosis is made on the basis of interviews (see Appendix A), sleep polysomnography in a sleep laboratory and ambulatory recording of sleep in the natural environment. Psychological treatment for NP is based on recent work demonstrating that cognitive factors, such as expectations about arousal during sleep, predict increased distress and panic attacks out of sleep. \(^40\) NP is thus conceptualized as triggered by interoceptive conditioning, whereby fluctuations in normal bodily sensations that are not consciously recognized due to sleep, elicit conditional fear due to prior pairings with panic.

Cognitive-behavioral therapy (CBT) targets both daytime and nocturnal panic attacks as well as chronic apprehension over their recurrence, with emphasis given to the benign nature of normal physiological fluctuations during sleep. Breathing retraining is taught as coping technique especially for symptoms associated with overbreathing, and patients practice interoceptive inductions tailored to NP (e.g., deep relaxation, ‘buzzer arousal inductions’ from a sleeping state). Maladaptive behaviors specific to NP (e.g., television to facilitate sleep) are targeted, as are poor sleep habits, because onset-insomnia often accompanies NP and may contribute to its recurrence. \(^3\) Recent evidence suggests that relative to wait list control, CBT for NP leads to substantial reductions in the frequency and severity of daytime and nocturnal panic attacks, and these gains persisted at 9 month follow-up. \(^52\)
Pharmacological treatment of NP has not yet been subject to rigorous empirical testing. Although uncontrolled trials suggest that agents typically used to treat daytime panic attacks (e.g., benzodiazepines; antidepressants) can ameliorate NP, future double-blind, placebo-controlled trials are required to establish the efficacy of these agents. Additional work is also needed to compare treatment outcome for CBT for NP in combination with pharmacological agents to use of these agents alone. Finally, given that individuals with posttraumatic stress disorder (PTSD) are vulnerable to nocturnal panic attacks, further study is required to establish whether CBT for NP is effective for nocturnal panic attacks in persons with PTSD, or whether CBT for PTSD is sufficient to control NP attacks in these individuals.

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Appendix A

Nocturnal Panic Screen

1. Have you ever experienced a sudden rush of intense fear or dread from a sleeping state? That is, have you ever woken out of sleep feeling fearful, for no apparent reason (i.e., no nightmares that you could recall and no loud noises or interruptions that woke you)? Do not include times that you panic after being awake for some time.

   YES ____ NO ____

If NO do not continue. If YES, ask for an example to ensure the subject is referring to nocturnal panic attacks, and continue with question 2.

2. How many panic attacks out of a sleeping state have you had in the past month? List the number for each week over the last month.

   First week # ________
   Second week # ________
   Third week # ________
   Fourth week # ________

3. When was your most recent panic attack from a sleeping state?

   # of days/months ago ________

4. Rate each of the following symptoms that are typically present during your most recent panic attacks that have occurred from a sleeping state, using the following scale:

   0-------------------1-------------------2-------------------3-------------------4
   Not at all        Mild       Moderate       Strong        Extreme

   Shortness of breath or smothering sensations ________
   Pounding or racing heart ________
   Tight or painful chest ________
   Dizziness, unsteadiness or faintness ________
   Trembling or shaking ________
   Sweating ________
   Choking sensations ________
   Hot flashes or cold chills ________
   Nausea or abdominal distress ________
   Numbness or tingling ________
   Detached or unreal feelings ________
   Fears of going crazy ________
5. Have you ever experienced four or more of the above listed symptoms, at one time, during a panic attack that occurs out of a sleeping state?

YES _______ NO _______

6. When did you first experience a panic attack out of a sleeping state for no apparent reason?

_______ # years/months ago

7. Have you ever worried about experiencing another panic attack out of a sleeping state?

YES _______ NO _______

If YES, from when ______________ to when ______________

8. What do you typically do when you experience a sudden rush or intense fear or dread from a sleeping state?

_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________
_________________________________________________________________

Appendix B

WAKING RECORD

Name________________ Date_______ Time________

With: Spouse_____ Friend_____ Alone_____ Other________________

Reason for waking: Nightmare_____ Noise/Environment Interruption_____ 
Physical Discomfort_____ No Reason_____
Other________________

Did you wake abruptly out of sleep? Yes_____ No_____

Did you feel physical sensations such as a racing heart or shortness of breath as soon as you awoke? Yes_____ No_____

Did you feel strong fear or dread as soon as you woke? Yes_____ No_____

Did you panic as soon as you woke? Yes_____ No_____

What was your maximum anxiety level when you woke? (circle on the scale)

0------------1------------2------------3------------4------------5------------6------------7------------8

None Mild Moderate Strong Extreme
Please rate how intensely you felt each of the following physical sensations when you woke. Use the following intensity scale:

<table>
<thead>
<tr>
<th></th>
<th>None</th>
<th>Mild</th>
<th>Moderate</th>
<th>Strong</th>
<th>Extreme</th>
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</thead>
<tbody>
<tr>
<td>Pounding or racing heart</td>
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<tr>
<td>Nausea or abdominal distress</td>
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<tr>
<td>Sense of unreality/detachment</td>
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<td>Tight or painful chest</td>
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<tr>
<td>Numbness, tingling or pricking</td>
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<tr>
<td>Shortness of breath, or difficulty breathing</td>
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<tr>
<td>Dizziness, unsteadiness, faintness</td>
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<tr>
<td>Trembling or shaking</td>
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<td>Hot flashes or cold chills</td>
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<tr>
<td>Sweating</td>
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<tr>
<td>Fear of dying</td>
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<td>Choking sensations</td>
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<tr>
<td>Fear of going crazy</td>
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<td>Choking sensations</td>
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<tr>
<td>Fear of losing control</td>
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</table>

References


Glossary

CBT: cognitive-behavioral therapy
NP: nocturnal panic
PES: esophageal pressure study
PTSD: posttraumatic stress disorder