



CLINICAL REVIEW

Assessment and treatment of nocturnal panic attacks

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KEYWORDS

Nocturnal panic;
Panic disorder;
Panic attacks;
Ambulatory monitoring;
Cognitive-behavioral therapy;
Posttraumatic stress disorder

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.¹ These include tachycardia, sweating, shortness of breath, chest pressure, choking 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.^{2,3} 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

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(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% report having 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 NPs,^{8,9} 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 awakenings, 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 sleep¹⁷ in NP patients were confounded by absence of an adaptation night and overly 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.

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Reported sleep quality

Patients with NP report more insomnia than panic disorder patients without NP.^{16,23} 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,²⁴ a daily sleep log each morning for 1 week to record total hours of sleep, estimated time taken to fall asleep, and number of awakenings during the night, and the Sleep Questionnaire and Assessment of Wakefulness²⁵ in 51 panic disorder patients with NP versus 41 who never experienced NP.⁷ 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,²⁶ 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 NPs²⁷ 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.¹⁶ Conversely, Ley (1988)²⁸ 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.²⁹ Second, Hauri

et al. (1989)¹³ 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.^{13,16,30} On the other hand, there is some evidence to suggest that patients with NP show a depression of movement time, leading Uhde (1994)³ 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,¹⁷ 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.³ 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.³¹ Also, CCK-4 induced NPs in four of nine healthy controls when infused during delta sleep.³² 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

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337 social phobia or panic disorder who had previously
338 demonstrated pentagastrin-induced wake panic
339 attacks.³³ The finding that panic was induced
340 without observing a transitional lightening of
341 sleep prior to waking was interpreted as evidence
342 that cognitive processing dependent on lightening
343 of sleep stage is not a pre-requisite for NP. But
344 other studies (discussed below) support the
345 notion that cognitive factors may play an important
346 role in NP.

347 **Psychosocial variables**

350 It is conceivable that NP represents the more
351 severe end of the panic disorder continuum,
352 especially since patients with NP report history of
353 more psychopathology,³⁴ and higher rates of
354 suicidal ideation³⁵ than panic disorder patients
355 without NP. However, these studies failed to
356 comprehensively evaluate NP or rule out other
357 sleep conditions. In our relatively large sample, in
358 which other sleep disorders were ruled out using
359 polysomnography and sleep history analyses, we
360 found no evidence for patients with NP to be more
361 severe in terms of panic disorder, psychological
362 comorbidity, anxious and depressive symptoms,
363 interference with functioning, or interpersonal
364 functioning.⁷

366 On the other hand, there is evidence for panic
367 disorder patients with NP to show a specific
368 elevated emotional reactivity (measured physio-
369 logically and subjectively) to conditions that
370 resemble sleep, including meditative relaxation³⁶
371 and hypnotic imagery³⁷ relative to panic disorder
372 patients without NP. In contrast, the two groups
373 do not differ in their reactivity to other panico-
374 genic challenges, including hyperventilation and
375 cardiac tracking.³⁶ These laboratory findings con-
376 firm earlier self report findings in which NP
377 patients cited relaxation and fatigue as more
378 likely triggers of panic attacks than did patients
379 without NP.¹⁶ Moreover, NP patients endorse more
380 feelings of discomfort in relation to relaxation and
381 'letting go' (Reactions to Relaxation and Arou-
382 sal³⁸).³⁶ We have suggested that fears of loss of
383 vigilance (states involving diminution of aware-
384 ness) contribute to distress in sleep and sleep-like
385 states,^{37,39} although additional research is needed
386 to determine whether such fears represent a
387 vulnerability to NP or are simply the consequence
388 of NP.

389 In addition, our work on reactivity to signals of
390 arousal during sleep suggests that specific misap-
391 praisals of physiological events during sleep may
392 contribute to NP.^{40,41} Before sleep, discernible

biofeedback audio signals were ostensibly cali-
brated 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 physio-
logy.⁴⁰ Panic disorder patients with recurrent NPs
who, before sleep, were led to believe that changes
in their physiology would be indicative of 'abnorm-
abnormality' failed to achieve as deep sleep, woke
with more distress and endorsed more panic attacks
in response to the audio signals previously associ-
ated 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 physio-
logical 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 interocep-
tive conditioning, whereby low-level somatic sen-
sations of arousal or anxiety become conditional
stimuli⁴⁴ 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 con-
ditioning.⁴⁵ In addition, interoceptive conditional
responses are not dependent on conscious aware-
ness of triggering cues,⁴⁴ 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 panicky awa-
kenings.^{6,12,16} It may be necessary for these
physiological events to co-occur with sleep Stages
II or III, as one shifts from semi-vigilance to

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449 non-vigilance; a shift that may be particularly
450 anxiety-provoking for NP individuals.

451 Assessment of nocturnal panic attacks

452 Sleep disorder assessment

453 The primary goal of a sleep assessment is to rule out
454 other explanations for NPs, such as sleep apnea,
455 night terrors, periodic movements, seizures, stage
456 IV night terrors, non-restorative sleep, sleep hallu-
457 cinogenesis, and sleep paralysis. These differen-
458 tiations can be made by an adequate interview
459 regarding current and past sleep functioning, sleep
460 polysomnography in a sleep laboratory, and ambu-
461 latory recording of sleep features in the natural
462 environment.

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

484 Ambulatory monitoring devices have been uti-
485 lized in numerous studies⁴⁷ to continuously record
486 physiological information and event marking for
487 prolonged intervals, up to 60 h. Patients are asked
488 to avoid vigorous physical activity, sexual activity,
489 and alcohol, caffeine and drug use. The equipment
490 is usually attached by a trained technician who
491 checks calibration, electrode impedances and
492 instructs patients in the use of the event marker
493 to press for every waking during the course of the
494 recording. By the second night of ambulatory
495 recording, most patients indicate that the ambu-
496 latory sleep equipment is relatively unobtrusive and
497 had little perceived effect on their sleep (Aikins &
498 Craske, in submission). Although ambulatory
499 recording is less costly than sleep laboratory

500 polysomnograms, and more likely to capture the
501 physiology associated with naturally occurring NPs,
502 ambulatory devices are generally less precise in
503 measuring various physiological parameters. On the
504 other hand, given that there is no evidence for
505 physiological dysregularities in NP, precision in
506 physiological measurement may be less relevant
507 to clinical decision making than it is to research
508 studies; ambulatory devices should be sufficient for
509 differentiating NP from other sleep disorders such
510 as sleep apnea, nocturnal seizures, periodic move-
511 ments, non-restorative sleep and so on.

512 Since nocturnal panickers do not differ from
513 panic disorder patients who never experience NP in
514 terms of daily monitoring of sleep related behaviors
515 (using instruments such as the Stanford Sleepiness
516 Scale²⁴ or daily logs of total hours of sleep,
517 estimated time to fall asleep, number of awaken-
518 ings etc), such scales may provide very little
519 differential diagnostic information.

520 Mental health assessment

521 The goal of this assessment is to establish whether
522 the NPs are symptomatic of an anxiety disorder or
523 any other psychological disorder for that matter.
524 Semi-structured diagnostic interviews are con-
525 sidered the most reliable and valid means of
526 diagnosing anxiety disorders. For example, the
527 Anxiety Disorders Interview Schedule-IV (ADIS-
528 IV;⁴⁸ covers all anxiety disorders, mood disorders,
529 somatoform disorders, and screens for psychosis
530 and substance related disorders, with high inter-
531 rater reliability.⁴⁹ Also, the SCID interview⁵⁰ is
532 another state-of-the-art semi-structured interview
533 that facilitates reliable diagnoses of anxiety dis-
534 orders and mood disorders using the criteria of the
535 DSM-IV. Both interviews require adequately trained
536 diagnosticians. In the absence of such instruments
537 and interviewers, a trained clinician can conduct a
538 mental health assessment to establish the presence
539 of anxiety disorders, mood disorders, substance use
540 related disorders and so on. In addition, the
541 interviewer/clinician will establish whether the
542 NPs are symptomatic of panic disorder (i.e.,
543 repeated panic attacks, most likely to be occurring
544 during the day as well, and associated with
545 excessive anxiety and worry about their recurrence
546 during the day and out of sleep) or posttraumatic
547 stress disorder (i.e., emotional reactivity to remin-
548 ders of trauma, avoidance of trauma, and physio-
549 logical hyperarousal following traumatization). The
550 interviewer will also assess the relationship
551 between NPs and substance use and/or drug with-
552 drawals. Another important differential is between
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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,⁵¹ as well as novel techniques targeting nocturnal panic attacks.⁵² 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 fight/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 waking.

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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673 likelihood of a negative outcome) and/or catastro-
674 phizations (i.e., blowing events out of proportion;
675 viewing them as disastrous and unmanageable).
676 Panicogenic thoughts are questioned using an
677 empirical, hypothesis-testing approach (i.e.,
678 'What is the evidence for...?). Therapists assist
679 patients in examining realistic probabilities (e.g.,
680 'What is the actual likelihood of suffocating during
681 sleep?'), gathering data (e.g., patients' medical
682 status), exploring alternative explanations (e.g.,
683 attributing heart rate accelerations to normal
684 sleep-related changes in physiology or to anxiety),
685 and examining realistic consequences and concrete
686 strategies for dealing with events should they occur
687 (e.g., 'How bad would it really be if I woke up
688 panicking? How would I cope if it happened?').
689 Interoceptive exposure is then introduced. During
690 exposure, patients repeatedly induce physical
691 sensations associated with panic attacks to weaken
692 or disrupt the associations between specific
693 internal cues and panic reactions. In addition to
694 typical interoceptive inductions (e.g., voluntary
695 hyperventilation, spinning) used to treat daytime
696 panic attacks, patients practice deep relaxation
697 (a panic-trigger for NP patients³), 'buzzer arousal
698 inductions' from a sleeping state (e.g., setting the
699 alarm to go off at various times during the night),
700 sleeping in hot, stuffy conditions and other induc-
701 tions tailored to NP.

702 Naturalistic exposure exercises (e.g., drinking
703 coffee, exercise) that induce feared sensations
704 are then introduced within the therapy session
705 and patients are encouraged to practice such
706 exposures at home. In addition, maladaptive
707 behaviors specific to NP (e.g., lights or television
708 to facilitate sleep, delayed sleep onset) are
709 targeted by generating a hierarchy of behaviors
710 to be modified, ranked from least to most
711 difficult to change. Then, patients are encour-
712 aged to gradually modify behaviors, beginning
713 with the least difficult (e.g., sleep with television
714 off) with the aid of cognitive restructuring and
715 breathing retraining to manage anxiety and
716 distress. With each session, patients continue to
717 the next item on the hierarchy. Also, basic sleep
718 hygiene guidelines are instituted to modify poor
719 sleep habits (e.g., inconsistent sleep schedule,
720 foods and alcohol before sleep), because onset-
721 insomnia and sleep deprivation may contribute to
722 NP recurrence.³

723 Existing research indicates that CBT for panic
724 disorder is highly effective, with 85-100% of treat-
725 ment completers panic-free by the end of treat-
726 ment, and effects lasting up to 2 years.⁵³⁻⁵⁵ Recent
727 findings show that CBT specifically tailored for NP
728 for patients who endure NP repeatedly leads to

729 marked reductions in the severity of panic disorder,
730 including the frequency of daytime and nocturnal
731 attacks, with treatment gains persisting at 9 month
732 follow-up. Symptom improvement was also
733 accompanied by reductions in subjective and
734 heart rate reactivity to laboratory stressors, as
735 well as lowered heart rate and leg movement and
736 increased cardiac variability during sleep when
737 assessed immediately and 9 months following
738 treatment completion.⁵² An area for future study
739 concerns the generalizability of CBT for NP to other
740 related conditions. As noted above, persons with
741 posttraumatic stress disorder (PTSD) are also
742 vulnerable to NP attacks, distinct from nightmare
743 induced arousals.⁵⁶ Thus, it may be that CBT for NP
744 would be an effective agent for controlling NP
745 attacks in persons with PTSD. On the other hand,
746 cognitive-behavioral approaches for PTSD may be
747 sufficient to control all symptoms of PTSD, includ-
748 ing NP attacks. These possibilities, however, have
749 not yet been subject to empirical test.
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751 Pharmacological treatment of nocturnal 752 panic attacks

753 Pharmacological approaches to NP have received
754 relatively little attention. Published reports have
755 been limited to uncontrolled single-case pharma-
756 cological trials.^{15,57} Daytime panic attacks are
757 typically treated with benzodiazepines (alprazo-
758 lam, clonazepam) or antidepressants (tricyclics,
759 selective serotonin reuptake inhibitors),⁵⁸ and
760 these psychotropics are clearly more effective
761 than drug placebos.⁵⁹ In an early study, Lesser
762 and colleagues (1985)¹⁵ reported cessation of
763 daytime and NP panic attacks in a 36-year-old
764 woman following treatment with alprazolam
765 (maximum dose 5 mg), although the length of
766 follow-up was not reported. Mellman and Uhde
767 (1990)⁵⁷ reported that in 12 patients with NP
768 attacks, seven patients showed marked improve-
769 ment (i.e., absence of nocturnal panic attacks
770 over 3-12 months of follow-up) with tricyclic
771 antidepressant therapy. An additional patient had
772 a partial response (i.e., reduced frequency and
773 intensity of attacks) to low-dose alprazolam; one
774 patient spontaneously remitted and three
775 patients refused medication or were unavailable
776 to follow-up.⁵⁷ Although these reports are prom-
777 ising, double-blind, placebo-controlled studies
778 are needed to establish the efficacy of pharma-
779 cological agents in the treatment of NP.
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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.

Practice points

The assessment of NPs should include the following steps:

1. Differential diagnosis of NP from other sleep disorders, using an interview of sleep history and current functioning, and if advisable, an ambulatory recording of sleep EEG and physiology or a full sleep laboratory polysomnography recording.
2. Differential diagnosis of NP from other emotional disorders, using semi-structured diagnostic interviews consistent with DSM-IV criteria by trained interviewers, or a complete mental health diagnostic assessment by a clinician experienced with anxiety disorders.
3. Interviewer-administered Nocturnal Panic Screen (see Appendix A).
4. Self-monitoring of sleep awakenings (see Appendix B).

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

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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 _____

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1009 Fears of losing control _____ 1065
 1010 Fears of dying _____ 1066

1011 5. Have you ever experienced four or more of the above listed symptoms, at 1067
 1012 one time, during a panic attack that occurs out of a **sleeping** state? 1068
 1013 1069

1014 YES _____ NO _____ 1070
 1015 1071

1016 6. When did you first experience a panic attack out of a **sleeping** state for no 1072
 1017 **apparent reason?** 1073
 1018 1074

1019 _____ # years/months ago 1075
 1020 1076

1021 7. Have you ever worried about experiencing another panic attack out of a 1077
 1022 sleeping state? 1078
 1023 1079

1024 YES _____ NO _____ 1080
 1025 1081

1026 If YES, from when _____ to when _____ 1082
 1027 1083

1028 8. What do you **typically do** when you experience a sudden rush or intense 1084
 1029 fear or dread from a sleeping state? 1085
 1030 1086

1031 _____ 1087
 1032 _____ 1088
 1033 _____ 1089
 1034 _____ 1090
 1035 _____ 1091
 1036 _____ 1092

1037 **Appendix B** 1093
 1038 1094

1039 **WAKING RECORD** 1095
 1040 1096

1041 Name _____ Date _____ Time _____ 1097
 1042 1098

1043 With: Spouse _____ Friend _____ Alone _____ Other _____ 1099
 1044 1100

1045 Reason for waking: Nightmare _____ Noise/Environment Interruption _____ 1101
 1046 1102

1047 Physical Discomfort _____ No Reason _____ 1103
 1048 1104

1049 Other _____ 1105
 1050 1106

1051 Did you wake abruptly out of sleep? Yes _____ No _____ 1107
 1052 1108

1053 Did you feel physical sensations such as a racing heart or shortness of breath as 1109
 1054 soon as you awoke? Yes _____ No _____ 1110

1055 1111

1056 Did you feel strong fear or dread as soon as you woke? Yes _____ No _____ 1112
 1057 1113

1058 Did you panic as soon as you woke? Yes _____ No _____ 1114
 1059 1115

1060 What was your maximum anxiety level when you woke? (circle on the scale) 1116
 1061 1117

1062 0-----1-----2-----3-----4-----5-----6-----7-----8 1118

1063 None Mild Moderate Strong Extreme 1119
 1064 1120

Please rate how intensely you felt each of the following physical sensations when you woke. Use the following intensity scale:

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

None Mild Moderate Strong Extreme

Pounding or racing heart	_____	Nausea or abdominal distress	_____
Tight or painful chest	_____	Sense of unreality/detachment	_____
Shortness of breath, or difficulty breathing	_____	Numbness, tingling or prickling	_____
Trembling or shaking	_____	Dizziness, unsteadiness, faintness	_____
Sweating	_____	Hot flashes or cold chills	_____
Choking sensations	_____	Fear of dying	_____
		Fear of going crazy	_____
		Fear of losing control	_____

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Glossary

CBT: cognitive-behavioral therapy

NP: nocturnal panic

PES: esophageal pressure study

PTSD: posttraumatic stress disorder

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