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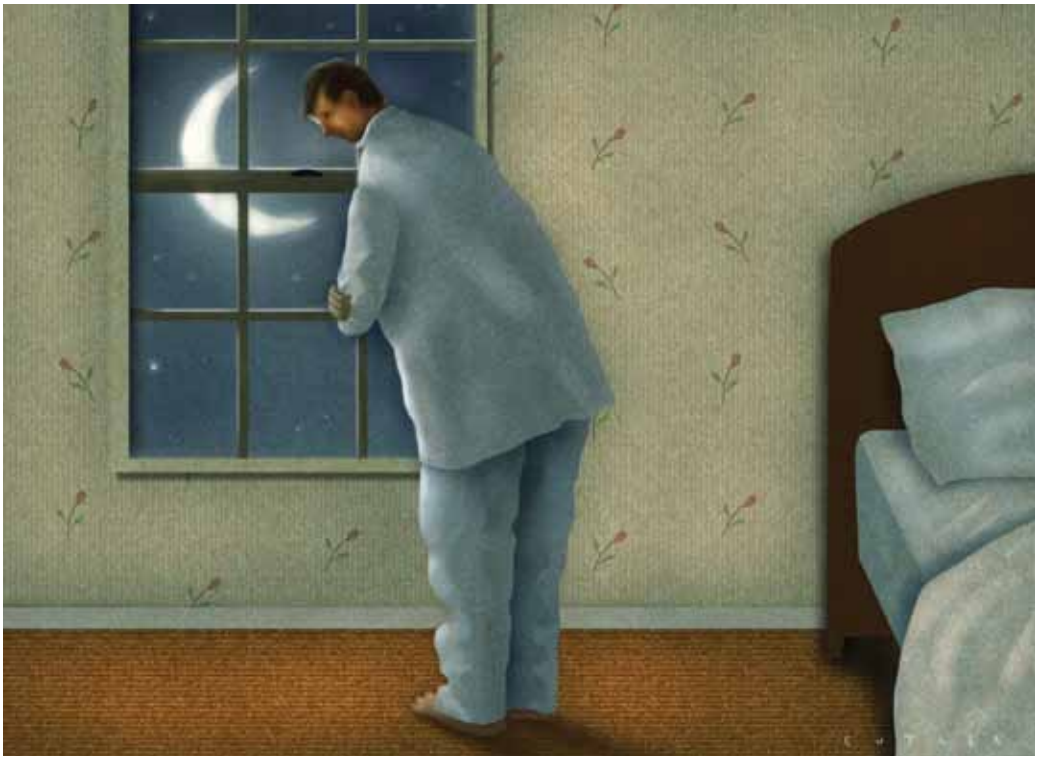
Sleep dysfunction, diabetes, and pain: A troublesome triad

PLUS

- Assessing suicide risk in patients with chronic pain and depression
- Biofeedback: A way to regain some control over pain



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FEATURE ARTICLE

Assessing suicide risk in patients with chronic pain and depression

Do you know the red flags for depression and suicide risk in your chronic pain patients? Read on.

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Illustration: Steve Denino

Nearly one-half of all patients seen in primary care experience persistent pain,[1] and major depressive disorder (MDD) is a common comorbidity with chronic pain. Patients with MDD are significantly more likely to report chronic pain, as compared with those without MDD (66% vs 43%).[2] Because access to mental health services and pain clinics is often limited, primary care physicians provide most pain and mental health care to this patient population.[3]

Although managing chronic pain with MDD can be challenging, a key to timely intervention is to be cognizant of the warning signs that a patient is becoming physically and emotionally less stable. For example, MDD and risk factors for suicidal ideation are highly likely when a patient reports increased pain, sleep disruption, or deterioration in function or grooming.

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CASE A spiral of pain and depression

Mr. G, age 49, sustained a back injury while working as an automobile mechanic. He developed low back pain and chronic lower extremity radiculopathy. His pain did not respond to conservative measures or to a lumbar laminectomy. Over time, as his pain progressed, he underwent a 2-level lumbar fusion and an extension of the fusion.

He was followed in a pain management center, but his pain did not respond to multiple interventions. He was placed on a regimen of low-dose opioid analgesics, antidepressants, muscle relaxants, and sleeping aids. Eventually he was referred back to his primary care physician, who continued to monitor his care and prescribe his medications. Because of his pain, Mr. G was unable to return to the job he'd held for 23 years. He started receiving Social Security disability benefits, and his wife returned to full-time employment.

Before his injury, Mr. G had enjoyed traveling with his wife and 3 children, hunting, and restoring vintage automobiles. He discontinued these hobbies and became increasingly isolated from his family and friends. He felt hopeless and without a sense of purpose. He considered himself a burden to his wife.

As his depression worsened Mr. G was seen by a psychiatrist, who increased his antidepressant dosage. Mr. G also developed a sleep disorder that did not respond to trials of various hypnotics and other sleeping aids. One evening his wife found him nonresponsive and called 911. He was dead on arrival at the emergency room from a polypharmacy overdose.

Commentary: *This case illustrates that despite a clinician's best efforts and best practices in treating depression in patients with chronic pain, an individual's despondence may be irrevocable, and in some cases suicide is unavoidable. Being cognizant of emerging signs of suicidal ideation in this vulnerable patient population—such as sleep disturbance, isolation, and having no daily purpose—can alert a clinician to the potential of suicide and prompt early intervention.*

Evidence links pain with suicidal thoughts

Compared with the general population, individuals with chronic pain have a significantly higher prevalence of depression (20.2% vs 9.3%), posttraumatic stress disorder (10.7% vs 3.3%), and any anxiety disorder (35.1% vs 18.1%), according to data from the National Comorbidity Survey.[4] Other studies show that people such as Mr. G (see "Case: A spiral of pain and depression," above) who experience chronic pain are more likely to develop depression than those without pain,[5] and suicidal ideation is highly comorbid with chronic pain.[6-16]

Risk factors for suicidal ideation include being unemployed or disabled, poor sleep quality, self-perceived mental health status, pain-related sense of helplessness, and a history of using illicit drugs, according to a survey by Racine et al.[16] Among 88 patients the researchers surveyed at several pain clinics, 24% reported active or passive suicidal ideation. Similarly, a survey of 153 individuals with chronic noncancer pain found passive suicidal ideation in 19%, active ideation in 13%, a plan for suicide in 5%, and a past suicide attempt in 5%. Drug overdose was the most commonly reported method for attempting suicide.[10]

Patients with chronic pain are twice as likely as nonpain controls to commit suicide, according to a systematic review by Tang and Crane.[15] General risk factors they identified include family history of suicide, previous suicide attempts, female gender, and comorbid depression. Pain-specific risk factors include location (low back and widespread pain), intensity (high), duration, and concomitant insomnia.

Three risk factors—history of sexual/physical abuse, family history of depression, and being socially withdrawn—were predictive of suicidal ideation in patients referred from a community health system to a behaviorally based pain program.[17] In this sample of 466 patients, 28% reported suicidal ideation.

10 WARNING SIGNS THAT A PAIN PATIENT MAY BE THINKING OF SUICIDE[15-19,35]

1. Screening score indicates moderate or more severe depression
2. Increased pain intensity or duration
3. Poor sleep quality
4. Social isolation and withdrawal
5. Deterioration in function or grooming
6. Pain-related sense of helplessness
7. Catastrophizing
8. Feelings of being a burden or liability to others
9. Drug screen reveals absence of prescribed opioids, suggestive of hoarding medications
10. Unwillingness to contract for safety

TABLE 1
Factors shown to increase suicide risk in patients with chronic pain[15-21,25]

General risk factors	Pain-specific risk factors
Unemployed/disabled	Pain location (low back, generalized)
Poor sleep quality	High pain intensity
History of illicit drug use	Pain duration
Family history of suicide	Pre-pain history of depression
Previous suicide attempts	Pain etiology (CRPS, fibromyalgia)
Concomitant mental health history (especially depression)	Catastrophizing
Social isolation	Pain-related helplessness
Family history of depression	History of sexual or physical abuse
Hopelessness	Burdensomeness ("I am a burden")

CRPS, complex regional pain syndrome.

Catastrophizing[18] and feelings of being a burden[19] also are associated with suicidal ideation in the pain population. Studies of patients with complex regional pain syndrome (CRPS) or fibromyalgia have shown particularly high rates of suicidal ideation (74% and 48%, respectively).[20,21]

Interpersonal theory of suicidal ideation

How does a person with chronic pain develop suicidal ideation? A prevailing model, called the interpersonal theory of suicide,[22,23] proposes that suicidal thoughts or desire arise from the confluence of 2 factors:

- thwarted belongingness (unfulfilled need for social interaction or connectedness) and
- perceived burdensomeness (perceiving oneself as a burden or liability to others).

Suicidal desire progresses to lethal action when an individual habituates to the fear of the potential pain of self-harm. Patients with debilitating pain often become isolated and perceive that they are unable to contribute to their family or society ("I am a burden"). Over time, they may become numb to their emotional and physical pain, which increases the risk of suicide.

Opioid use is another contributing factor, as the rate of "unintentional" opioid-related fatalities is related to the dosage of prescribed opioids.[24] A notable number of these overdoses most likely are suicides.

Based on this model, the risk of suicide is high in a person who perceives no purpose in life, becomes isolated from family and friends, and is on a high-dose opioid or is abusing opioids.

Suicide risk factors and screening

In the chronic pain population, risk factors for suicide may be general or pain-specific (TABLE 1).[15-21,25] Individuals with the following risk factors may be particularly vulnerable to suicide:

- inability to return to gainful employment
- isolation and feelings of burdensomeness
- loss of important family and social roles
- recent or current substance use disorder
- depression.

Depression screening. A number of screening tools for depression have sufficient validity and reliability.[26-34] Given the high prevalence of depression in the pain population, depression screening should be conducted at every office visit. Be aware that these screening tools have poor predictive value for suicide. Instead, they can provide important information to prompt an open discussion with the patient and explore more subtle signs of suicide risk (such as burdensomeness or isolation).

The Beck Depression Inventory (BDI)[26] and the Profile of Mood States (POMS)[27] are most appropriate for measuring emotional functioning in the chronic pain population, according to Initiative on Methods, Measurements and Pain Assessment in Clinical Trials (IMMPACT) recommendations.[28] The BDI is a 21-item, self-

TABLE 2
Self-report depression screening tools

Tool name	Number of items	Time to complete (min)	Access
Beck Depression Inventory-II[26]	21	5-10	Proprietary
Beck Depression Inventory–Fast Screen for Medical Patients[29]	7	<5	Proprietary
Profile of Mood States, 2nd Edition[27] Full-length version (POMS 2-A)	65	10-15	Proprietary
POMS 2 Short version	35	5-10	
Zung Self-rating Depression Scale[30]	20	10	Free
Center for Epidemiologic Studies Depression scale (CES-D): Full version[31]	20	5-10	Free
CES-D Short version	10	5	
Patient Health Questionnaire[33] PHQ-9 (full diagnosis of depression)	9	5	Free
PHQ-2 (short screen)[34]	2	<5	

report measure of the severity of depression symptoms assessed over the past week. The POMS evaluates 6 mood states—including depression, anxiety, and anger—considered most relevant in pain. The Beck Depression Inventory–Fast Screen for Medical Patients (BDI-FS)[29] is a 7-item assessment of depression in the medical population that excludes somatic symptoms, possibly more accurately assessing depression in the pain population.

Other assessment tools for depression include the Zung Self-rating Depression Scale[30]; the Center for Epidemiologic Studies Depression Scale, with both a short and full version[31]; and the Patient Health Questionnaire (PHQ), derived from the Primary Care Evaluation of Mental Disorders.[32] The PHQ has 2 versions for depression:

- PHQ-9 measures 9 symptoms of depression based on the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, text revision (DSM-IV TR)[33]
- PHQ-2, a 2-item screening tool.[34]

The PHQ-2 can be used to screen for depression, but the PHQ-9 is required to render the diagnosis of depressive disorder.

For a busy primary care practice, select an assessment tool that matches the financial resources, time to complete, and ease of interpretation of your clinic structure (TABLE 2).[26,27,29,30,31,33,34] These tools can help document the severity of depression, presence of suicidal ideation, and efficacy of prescribed treatments such as antidepressant therapy. Many of these scales can be easily integrated into the electronic health record.

Proactive care and intervention

Routine care strategies. To reduce the risk of suicidal ideation, target potential mediators of pain and suicide such as inadequate pain control, poor pain coping skills, and sleep disorders. To reduce isolation and promote a sense of belonging and purpose, strongly encourage patients to structure out-of-house time and to be productive in some manner, such as volunteering in the community.

When possible, co-treat these complex patients with a team consisting of psychiatrists, psychologists or other mental health clinicians, and pain physicians. Maintain an active list of crisis centers and local behavioral health practitioners and the type of insurance they accept.

If a patient begins to display signs of distress, set a low threshold to evaluate and treat depression with antidepressants and referral to mental health services. Maintain an

open, nonjudgmental dialogue with the patient in discussing the risk of suicide and the importance of adhering to treatment. Strengthening the clinician-patient relationship will provide ongoing opportunity to effectively monitor, intervene, and promote improvement in quality of life.

For outpatients receiving opioids as part of the treatment strategy, prescribe the opioids in small amounts with family members dispensing the medications. Perform frequent urine drug screenings to ensure that they are using their opioids appropriately and not hoarding them for a suicide attempt.[35]

Low or high risk of suicide? With the clinical evaluation of risk factors and depression screening results, an individual's suicide risk can be estimated as low or high, based on various factors, including:

- specific plans for suicide
- means (access to guns, lethal supply of medications)
- history of suicide attempts
- level of social support
- effectiveness of coping skills
- relationship with the health care provider (does the patient communicate emotional status and life stressors?)
- willingness to contract for safety (a written compact stating that if they become seriously suicidal with plans and intent, they will call 911, go the local emergency department, and contact your office).

Patients with chronic depression and chronic suicidal ideation, but no active suicide plans, have the potential to become acutely suicidal when facing new stressors.

Patients with chronic depression and chronic suicidal ideation, but no active suicide plans, have the potential to become acutely suicidal when facing new stressors (eg, divorce, financial losses, poorly controlled pain). Maintain these patients under psychiatric and psychological care as part of the overall pain management strategy, with ongoing mental health screening and close monitoring of medication use—particularly opioids and benzodiazepines.

If a patient's screening score indicates moderate or more severe depression, referral to local behavioral health specialists is indicated. Where qualified behavioral health specialists are scarce, the Substance Abuse and Mental Health Services Administration Web site (http://findtreatment.samhsa.gov) may help you locate mental health and substance abuse treatment services in or near your community.[36]

If a patient admits to an acute suicidal ideation, is unwilling to contract, and has a plan for suicide, inpatient admission is warranted.

Telehealth resources. Because local access to mental health services can be limited, interest in the use of telecommunication technologies is growing. The term "telehealth" includes telemedicine, which has been extremely effective in the long-distance diagnosis and treatment of medical and mental health problems, including pain.[37,38] Internet-based cognitive-behavioral therapy for pain and substance abuse disorders[39,40] and smartphone applications[41-43] have shown mixed results in the pain community but have the potential for providing needed services to individuals unable to directly access mental health care.

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FEATURE ARTICLE

Biofeedback: A way to regain some control over pain

Integrating biofeedback into a patient's treatment plan can ease pain and improve quality of life.

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Photo: Courtesy of Eugénie Pabst, PsyD, Chicago, Ill

American life is fast-paced, busy, and focused on productivity. In that rush, it's easy to lose touch with the body's physical responses and psychological reactions to the stress of daily living. The headache that starts during an early morning meeting or while hunched over a computer can cause the neck and shoulders to tense, breathing to become shallow, and heart rate to speed up. In an hour or so, those unchecked physical reactions can lead to pain symptoms.

Biofeedback can help a person increase awareness of—and even prevent—typical stress responses like muscle tension. It is especially beneficial, however, for patients who have more significant physical, mental, or emotional stressors, such as a traumatic injury, difficulty sleeping, challenges brought on by stroke, anxiety, depression, and many types of chronic pain, including low back pain, chronic headaches/

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migraines, fibromyalgia, and musculoskeletal pain.[1-6] Chronic pain patients may experience a downward spiral as their body reacts to stress and pain in ways that exacerbate their condition.

Biofeedback can stop this spiral by helping patients better recognize, understand, and control their physical, mental, and emotional responses.[7]

A valuable component of an interdisciplinary approach

Chronic pain creates complex biopsychosocial sequelae, and a traditional biomedical approach often doesn't address all of the pain patient's problems.[8] The limitations of a single-treatment approach can frustrate patients, and many move from one physician to another searching for pain relief. It's important to let patients know that there is no "magic" treatment, medication, or surgery for chronic pain. Believing that there is a such a single treatment can lead to decreased confidence, understanding, and motivation, as well as feelings of hopelessness, deteriorating emotional well-being, and an overall decrease of a patient's internal locus of control.[9] In addition, research shows that "how well patients manage chronic pain depends more on what they do for themselves rather than what is done to them; most of the 'work/change' of chronic pain management is done by the patient."[10]

It is critical to develop an interdisciplinary therapeutic team for managing patients with chronic pain. Compared with conventional medical treatments, an interdisciplinary team approach is more effective in reducing medication use, emotional distress, health care utilization, and iatrogenic consequences. It is also more effective in getting people back to work and closing disability claims.[11-13]

How biofeedback can help, who it can benefit

Many physicians view biofeedback and psychological services as a last-resort therapeutic option. Patients may be resistant, too, interpreting a referral to mean that "it's all in my head" or "because you think I'm crazy." But there is considerable evidence that supports the use of biofeedback as a nonpharmacologic therapy for chronic pain; patients with low back pain, chronic migraines, musculoskeletal pain, and other pain conditions have experienced reduced pain intensity and frequency with biofeedback training.[1-6]

Keep in mind that biofeedback is not a quick fix, but rather an investment in living with better health and recovery. Based on my experience in working with chronic pain patients, you should consider referring for biofeedback therapy when a patient:

- has consistently high pain complaints
- has pain that worsens despite treatment
- discontinues physical therapy because it causes too much pain
- exhibits signs of substance abuse, including misuse of medication
- progressively reduces activity
- has poor emotional regulation
- demonstrates exaggerated or inconsistent pain behaviors
- has a history of "shopping" for doctors or medication
- has a history of trauma or abuse.

For more on the referral process, see "Finding a biofeedback practitioner" on page S15.

The first visit

The first visit with a biofeedback practitioner involves an evaluation. In clinical practice, biofeedback evaluations are generally scheduled for 60 to 90 minutes, depending on the level of complication. The evaluation is similar to a basic psychological evaluation. In addition to obtaining the patient's history, identifying the reason for treatment, and assessing the patient's motivation, the biofeedback specialist involves the patient in the development of a treatment plan and goals.

Depending on the evaluation results and the patient's needs, the biofeedback therapist will schedule treatment sessions for once or twice a week, with each session lasting about 50 to 60 minutes. Based on my clinical experience, patients usually complete treatment in 12 to 24 sessions; about 30% of patients will later return for additional treatment, or "booster sessions."

Patients who return for further treatment often need support, encouragement, and feedback to assist them with tuning up the effectiveness of their home program, which was developed during the initial treatment phase. Typically, patients require 3 to 5 booster sessions. (For an example of how one of my patients combined a home-based program with professionally supervised biofeedback training, see "Case—The benefits of biofeedback: One patient's story," on page S16.)

Biofeedback is not a quick fix, but rather an investment in living with better health.

TABLE
Types of biofeedback modalities used in pain management*

Modality	Description†	Placement
Brainwave	Brainwave biofeedback uses scalp sensors to monitor the brain's electrical activity using an electroencephalograph Used to treat attention-deficit hyperactivity disorder, alcoholism/substance abuse, epilepsy, headache, and traumatic brain injury	
Breathing	Respiratory feedback uses bands placed around the abdomen and chest to monitor breathing pattern and respiration rate Used to treat anxiety, asthma, chronic obstructive pulmonary disease, high blood pressure, and unexplained abdominal pain	
Heart rate	Heart rate biofeedback uses finger or earlobe sensors with a photoplethysmograph or sensors placed on the chest and lower torso (or on the wrists) using an electrocardiograph to measure both heart rate and heart rate variability Used to treat asthma, depression, high blood pressure, and unexplained abdominal pain	
Muscle	Muscle biofeedback uses sensors placed over skeletal muscles with an electromyograph to monitor the electrical activity that causes skeletal muscle contraction Used to treat anxiety; asthma; cerebral palsy; fecal and urinary incontinence; headache; high blood pressure; pain involving the lower back, pelvic muscles, and temporomandibular joint; and paralysis and muscle weakness due to peripheral nerve injury and stroke	
Sweat gland	Sweat gland biofeedback uses sensors placed around the fingers or on the palm and wrist with an electrodermograph to monitor changes in skin moisture produced by sweating Used to treat excessive sweating and high blood pressure	
Temperature	Temperature biofeedback uses sensors placed on the hands or feet with a feedback thermometer to measure blood flow to the skin Used to treat headache, high blood pressure, Raynaud's disease, and swelling	

*Biofeedback can also play an important role in treating pelvic muscle dysfunction (eg, fecal and urinary incontinence, pelvic pain); a discussion of these disorders is beyond the scope of this article.

†Each modality can also be used to teach optimal performance.

Source: Reprinted, with permission, from: Overview of biofeedback. Biofeedback Certification International Alliance Web site. Available at: http://www.bcia.org/i4a/pages/index.cfm?pageid=3524. Accessed January 28, 2014.

What treatment entails

Biofeedback works like a complicated mirror that allows the brain and body to make adjustments to improve homeostasis. Biofeedback can be used to monitor heart rate, blood pressure, muscle tension, skin temperature, sweat response, breathing, brain waves, and more (TABLE). To identify the appropriate biofeedback modality for a particular patient, the therapist considers the patient's symptoms, emotional regulation, cognitive functioning, and past experiences and traumas. Modalities may be used alone—or in combination.

Various devices are used to measure change in the area of focus, and the data are then provided back to the patient. These devices include the following:

Scalp sensors can detect brainwave activity through electroencephalography (EEG). Therapists have used EEG biofeedback to treat headache, alcoholism, epilepsy, and a host of other disorders.

Bands placed around the patient's abdomen and chest can detect changes in respiratory rate and have been used to manage anxiety, hypertension, unexplained abdominal

FINDING A BIOFEEDBACK PRACTITIONER

Two useful Web sites can help you locate biofeedback practitioners in your area. They are **www.bcia.org**, from the Biofeedback Certification International Alliance (BCIA), and **www.aapb.org**, from the Association for Applied Psychophysiology and Biofeedback. Both sites provide a "find the practitioner" search tool.

Licensing. Many state licensing boards include the practice of biofeedback within the purview of psychologists, physical therapists, nurses, physicians, social workers, and other professionals. Licensure, however, doesn't mean that the license holder has training or experience in providing biofeedback; certification by the BCIA does.

The BCIA offers various levels of certification in biofeedback, neurofeedback, and pelvic muscle dysfunction biofeedback. Certification programs are based on prerequisite educational degrees, anatomy/physiology course work, didactic course work in biofeedback, clinical training or mentoring to learn skills application, and a certification exam.

pain, and other disorders, while earlobe and finger sensors, in conjunction with electrocardiograph sensors on the chest and lower torso, have been used in the treatment of asthma, depression, and hypertension.

Muscle sensors and an electromyograph (EMG) monitor the electrical activity that causes skeletal muscle contraction. Muscle biofeedback has been used for managing low back pain, anxiety, cerebral palsy, and incontinence.

Additional biofeedback devices, including those that provide sweat gland and temperature data, also have their place in the therapist's armamentarium.

How biofeedback helps to relieve muscle tension

If a patient needs to focus on relaxing her shoulder muscles to reduce pain, EMG sensors would be placed on her shoulders above the areas identified as most likely involved with the experience of pain and/or tension. (See the photo on page S12.) These sensors send information gathered from the body to the therapist's computer to analyze the information—in this case, muscle tension. The patient then receives feedback about this information through various cues.

For instance, information about muscle tension may be translated into a tone or beep that varies in pitch depending on the intensity of the tension, or music may start playing when muscles start to relax and stop when muscles tense. For visual cues, a monitor may show a flower opening when muscles are relaxing, or lines may move across a graph to indicate changes.

Visual markers or tactile aids can be used to further increase the patient's body awareness and help to facilitate change. For example, placing medical tape on the body can generate a pulling sensation when maladaptive muscle tension or posture changes occur. Placing an object—a cell phone, book, or hand—on the individual's abdomen can raise awareness of diaphragm breathing. Positioning reference points, such as dot-shaped stickers or the therapist's hands, on the shoulders or other area while the patient views him- or herself in a mirror or on a video monitor can enhance awareness of asymmetry, body mechanics, or posture.

Each form of feedback enables physical observations to become more apparent to the patient, which in turn improves mind-body awareness.

During the biofeedback session, the therapist guides the patient in mental exercises and relaxation techniques to achieve the therapeutic goal, such as muscle relaxation. The biofeedback monitor enables the patient to see (or hear) the changes that occur in response to being stressed or relaxed.

Breaking the chronic pain cycle

Biofeedback can help patients improve how they manage pain by guiding them in more effective use of nonpharmacologic techniques.[12] For example, while a patient may already know that breathing from the diaphragm is beneficial, biofeedback can document just how effectively—or ineffectively—he or she is breathing. The patient can then use the feedback to mindfully adjust breathing.

In addition to becoming aware of how the body is functioning, patients must learn how to truly relax. While elusive, this requires one to incorporate 3 states of relaxation—mental, physical, and emotional—to implement the type of changes needed to improve health and well-being.

Armed with better awareness and control, patients can more easily recognize and change functional patterns to prevent or mitigate chronic pain.[14]

True relaxation involves mental, physical, and emotional processes.

CASE The benefits of biofeedback: One patient's story

Jane M, 35 years old, slipped and fell on a wet floor. In addition to bruising her right hip and shoulder, she ruptured a disc in her cervical spine. The single-level fusion surgery that followed contributed to the development of unremitting chronic pain.

Over 2 years, her normal daily functioning eroded despite more than 100 physical therapy sessions, several sets of cervical injections, and a number of medications. When it was clear she was not a candidate for additional surgery, Ms. M's doctor recommended psychological counseling and/or biofeedback treatment.

What did the evaluation reveal?

Despite first resisting the suggestion, Ms. M eventually agreed. Her initial heart rate variability assessment indicated that her autonomic nervous system was not effectively autoregulating. As more data were obtained and behaviors were observed, her therapist recognized that overactive sympathetic arousal was causing an ongoing state of "flight or fight." The overactivity of the sympathetic system prevented her body from shifting to a parasympathetic-dominated relaxed state, which was needed to allow healing and recovery. It was likely that the limited flexibility of the autonomic nervous system contributed to her struggles with increasing pain, lack of progress in physical therapy, and poor responses during other treatment attempts.

Learning proper breathing technique. During the first 8 biofeedback sessions, Ms. M learned to use diaphragm breathing and breathing awareness to facilitate the relaxation response. Her heart rate decreased from the mid to high 90s to the low 80s/high 70s. When she first attempted to achieve the relaxation response, her average respiratory rate was 20 to 24 breaths per minute; as she developed improved slow-paced breathing skills, her average breath rate was 6 to 8 breaths per minute (6 breaths per minute, plus or minus one, is the general goal to maximize the potential benefits from the various breathing exercises).

Addressing muscle tension. Once Ms. M began to develop a solid foundation of improved autoregulation and enhanced mind-body awareness, the treatment plan addressed her continued struggles with severe muscle tension and chronic neck pain. She had bilateral pain that radiated up and down her neck nearly parallel with the spine, as well as severe burning and aching pain in her right shoulder with occasional sharp/stabbing episodes.

Finding the best program

Based on Ms. M's symptoms and the lack of improvement despite some positive gains, her therapist recommended a surface electromyography (sEMG) assessment. In muscle tension-based biofeedback, the therapist places electrodes above targeted muscles and measures the intensity of muscle activity in microvolts (μV) (microvolt intensity increases when a muscle activates and decreases when it relaxes). Four stages of tension levels are measured while the patient is at rest and engaged in controlled activation of specific muscle groups.

During sEMG assessment, the patient is guided through a structured protocol based on the muscles being reviewed. Ms. M's findings indicated that she had mild-to-moderate tension levels in the cervical paraspinal muscles and masseter muscles; severe tension and asymmetry were observed in the upper trapezius muscles. When she was at rest in a sitting position, tension levels averaged 31.3 μV on the right and 17.7 μV on the left.

The shoulder shrug protocol. Muscle release and recovery can be assessed by having the patient hold a shoulder shrug for 20 seconds and then measuring tension upon relaxation. Normally, muscle tension after this exercise would almost immediately return to ≤4 μV and remain at that level until further activation. In Ms. M's case, muscle tension actually increased in intensity on her right side after the 20-second shoulder shrug: tension was 34.7 μV on the right side and 15.2 μV on the left. In addition, asymmetry was increasing. Ms. M reported little awareness of the significant fluctuations in tension.

Biofeedback cues. Over the next 10 weeks, Ms. M engaged in sEMG training to increase her awareness of muscle tension and muscle behavior in her upper trapezius muscles. During her sessions, she was given visual, auditory, and tactile feedback; she would then use the feedback to aid in achieving desired changes, such as decreased muscle tension, improved release of tension after activation, and general changes in muscle tension behavior.

For a primary visual aid, Ms. M preferred a picture of a flower that slowly bloomed as she released or lowered tension levels; when tension began to elevate the flower would start to close. Music was also used to provide feedback: It would start and stop in relation to changes in tension and/or asymmetry.

Measurable improvement

Ms. M continued working to improve autoregulation in the biofeedback sessions as well as in a home-based treatment program. For her home program, the therapist encouraged her to incorporate a combination of breathing, relaxation, and mindfulness techniques into her daily activities; these were to be practiced 1 to 3 times daily for about 5 to 15 minutes. Exercises included diaphragmatic breathing techniques, progressive muscle relaxation, and positive affirmations. Depending on a patient's learning preferences, the therapist may provide instructional handouts, audio CDs, videos, or Web site links to reinforce proper skill development.

After completing 10 sessions, Ms. M. underwent a follow-up sEMG assessment of the upper trapezius muscles. Improvement in muscle tension was excellent, with her resting tension levels averaging 3.7 μV on the right and 4.1 μV on the left (compared with pretreatment tensions levels of 31.3 μV on the right and 17.7 μV on the left).

Ms. M still struggles to fully release muscle tension after activation, but her improved body awareness helps her recognize the residual tension, and she uses diaphragm breathing to quickly reduce it to within normal range. She describes feeling empowered by having learned the biofeedback techniques that have helped her improve chronic pain management, enhance her quality of life, and strengthen her internal locus of control.

Because biofeedback focuses on the connection and communication between mind and body, it brings together both psychology and physical therapy. However, despite knowing that physical problems create mental stress and mental stress creates physical problems, many patients still struggle to address the negative effect that physical and mental stressors have on their health and quality of life.[14] Psychological factors, including mood, beliefs about pain, and coping style, play an important role in an individual's adjustment to chronic pain.[15]

Just as a scale doesn't change a person's weight, however, biofeedback doesn't change the body's stress response. Change remains the patient's responsibility, but biofeedback can greatly accelerate the learning process. Engaging in biofeedback may initially feel overwhelming, but with support and encouragement it becomes empowering. Instead of being a victim of pain, the patient learns to recognize and change physical responses, like tense muscles, shallow breathing, or cold hands, creating the shift needed to begin to disrupt the chronic pain cycle.[14,16]

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Sleep dysfunction, diabetes, and pain: A troublesome triad

Critical to helping patients break the stranglehold of these 3 comorbidities is an understanding of how they interact with one other.

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Sleep dysfunction, diabetes mellitus, and pain are overlapping conditions that clinicians see daily. Consider these statistics: As many as 70% of Americans have complaints about their sleep.[1] Diabetes is a national epidemic; 8% of the US population has it (a 10-fold increase from 1960) and another 25% has prediabetes.[2] Chronic pain is thought to occur in 15% of the population.[3] Research increasingly substantiates the overlap and interaction among these 3 comorbidities.[4-6]

The increasing incidence of sleep disorders, diabetes, and chronic pain underscores the need to approach these conditions with new insights regarding their interconnectedness. Such knowledge enables us to better understand how a patient's comorbidities influence each other. Understanding these interrelationships will also help physicians and other providers thoroughly assess a patient's clinical profile and develop a comprehensive treatment strategy that will improve outcomes—including quality of life.

Illustration: Dave Cutler

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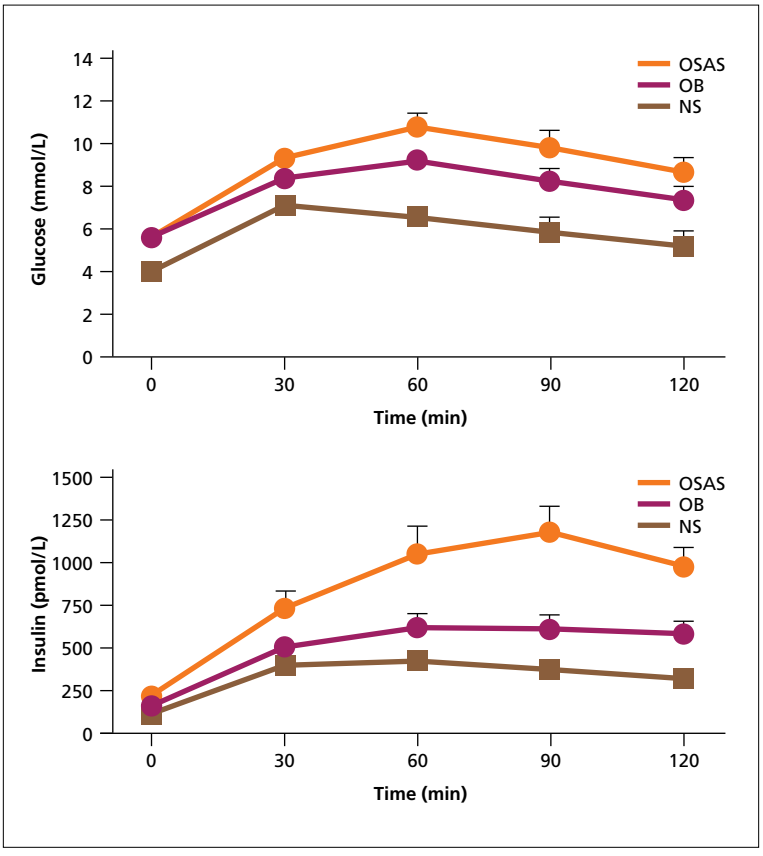
FIGURE 1: Obstructive sleep apnea independently increased risk of insulin resistance

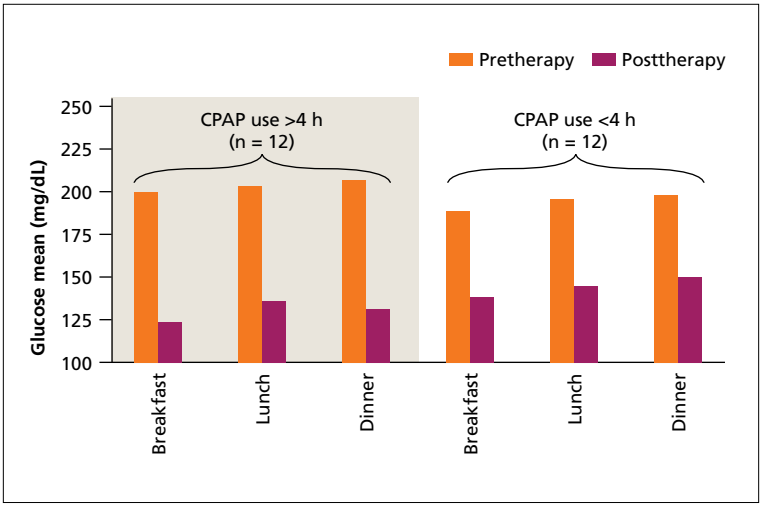
After an oral glucose tolerance test, obese patients with OSA (n = 30) exhibited higher serum levels of glucose and insulin than patients with obesity alone (n = 27) or normal subjects (n = 20) in a study conducted in Italy.



NS, normal subjects; OB, obesity; OSAS, obstructive sleep apnea (syndrome).
Source: Tassone F, et al.[13]

FIGURE 2: CPAP reduced postprandial glucose values

In patients with diabetes and a documented sleep disorder (n = 25), CPAP therapy consistently lowered glucose levels after meals, with the recommended duration of >4 hours yielding superior results.



CPAP, continuous positive airway pressure.
Source: Babu AR, et al.[14]

Sleep dysfunction and diabetes: An underrecognized association

Diabetes-related nocturia or pain from diabetic peripheral neuropathy (DPN) can worsen sleep or cause sleep loss. We also know that sleep dysfunction increases consumption of sugary foods,[7] which, in patients with diabetes and prediabetes will lead to worsening control of hemoglobin A1c (HbA1c). Sleep deprivation is also linked with prediabetes. In addition, lack of adequate sleep or fractured sleep is related to weight gain, and weight gain can worsen insulin resistance and glucose intolerance.

Obstructive sleep apnea (OSA)—all too often missed. Fifty percent of men and 20% of women with type 2 diabetes have OSA[4]; 97% of obese patients with diabetes are thought to have OSA.[8] Despite these staggering numbers, up to 85% of sleep apnea cases go undiagnosed.[9] Interestingly, OSA may have a causal role in the development of diabetes.[10] Worsening diabetes in patients with OSA has been attributed to such mechanisms as[11,12]:

- intermittent hypoxia (reduces insulin sensitivity)
- increased sympathetic activity with a rise in norepinephrine (NE) level
- increased hepatic glucose and muscle glycogenolysis
- lipolysis leading to a rise in free fatty acids (insulin resistance)
- a substantial increase in cortisol secretion
- increased glucagon and glucocorticoids
- an adipose leptin increase
- increased levels of interleukin (IL)-6 and tumor necrosis factor (TNF)-α.

Through these mechanisms, OSA is associated with insulin resistance independent of obesity,[11] depicted in FIGURE 1.[13]

Treatment of OSA with continuous positive airway pressure (CPAP) has been shown to improve diabetes control and reduce insulin needs (FIGURE 2).[14] Sleep practitioners should also be aware of the interrelationship of OSA and diabetes, because 30% of patients presenting to a sleep clinic have impaired glucose tolerance or diabetes, of which 40% are undiagnosed.[15] (See page S22 to read how one patient's comorbidities were managed in "Case: Providing pain relief to a patient with diabetes, neuropathic pain, and obstructive sleep apnea.")

The International Diabetes Foundation has recommended that everyone with type 2 diabetes be screened for sleep apnea.[16] This does not mean everyone with type 2 diabetes needs to undergo a formal polysomnography study.

But awareness of the comorbidity of diabetes and OSA should prompt an inquiry about sleepiness, snoring, and witnessed apnea and, if clinically indicated, referral for further testing or treatment.

Diabetes and pain: Focus on glycemic control

Sixty percent to 70% of patients with diabetes have some form of neuropathy, and it is particularly common in patients who have had diabetes for >25 years.[5] Neuropathy is painful for >30% of patients with diabetes,[5] but it can also produce tingling and numbness. And some patients with neuropathy are asymptomatic. Diabetic neuropathy can affect every organ system and can occur in various forms.

Causes of DPN are multifactorial and include such metabolic factors as high glucose, high fat, or low insulin; neurovascular factors that result in damage to vessels carrying oxygen and nutrients to the nerves; autoimmune factors that produce neurotoxic inflammation; mechanical injuries, most commonly carpal tunnel syndrome at the wrists and ulnar nerve entrapment at the elbows; and lifestyle factors, such as smoking and alcohol use. Exact mechanisms can vary and are thought to include polyol pathway activation, protein kinase C activation, oxidative stress, poly(ADP-ribose) polymerase activation, alteration in neurotrophic factors, advanced glycation end product formation, and essential fatty acid abnormalities.

Treatment of diabetic neuropathy begins with tight glucose control, which has been shown to slow the progression of DPN. Several medication options are also available (TABLE).[17-22] Tricyclic antidepressants, such as amitriptyline, desipramine, and nortriptyline, are inexpensive and effective in reducing the pain of DPN.[17] But they can cause dry mouth, constipation, and sedation.

Duloxetine, a serotonin-norepinephrine reuptake inhibitor (SNRI), is approved by the US Food and Drug Administration (FDA) for DPN and is usually helpful at 60 mg daily.[18] Nausea occurs in a third of patients. Duloxetine may act by improving neurotransmitter function in the periaqueductal gray matter and descending pain inhibitory pathways.

Anticonvulsants are commonly prescribed for patients with DPN. Carbamazepine was used for many years with success, but it can cause sedation and hyponatremia. Gabapentin, in the so-called gabanoid class, is usually taken in a dosage of 100 to 600 mg tid, but clinicians should watch for sedation, edema, and weight gain.[18] Another gabanoid, pregabalin, has a similar adverse effect profile and is FDA approved for DPN; the usual dosage is 50 to 200 mg tid.[19] Pregabalin is an α-2 γ calcium channel blocker and likely mediates its effects through reduction in substance P levels.[19]

Opioids such as oxycodone or opioid-like drugs such as tramadol can also be used sparingly. High-potency narcotics are not recommended.

Supplementation with α-lipoic acid 100 mg bid has been shown to reduce diabetic neuropathy deficits.[20] Metanx, a vitamin-B–derived supplement, is FDA approved for DPN.[21]

TABLE
Pharmaceutical and nutraceutical agents used to treat painful diabetic neuropathy[17-22]

Agent	Customary dose (maximum)
Tricyclic antidepressants	
Amitriptyline	10 (150) mg at bedtime
Desipramine	25 (150) mg at bedtime
Nortriptyline	25 (150) mg at bedtime
Serotonin-norepinephrine reuptake inhibitors	
Duloxetine	60 (120) mg/d
Venlafaxine	37.5 mg/d or bid (225 mg/d)
Anticonvulsants	
Gabapentin	100 (1200) mg tid
Pregabalin	50 (200) mg tid
Opioids/opioid-like substances	
Oxycodone	10 (40) mg bid
Tramadol	100 (400) mg/d
Nutraceuticals	
α-Lipoic acid	100 mg bid
Metanx (vitamin B supplement)	2 capsules daily

Pain and sleep dysfunction: Ask the right questions

While chronic pain affects 15% of the general population, its prevalence rises to >50% among older adults.[3] In chronic pain patients,

CASE Providing pain relief to a patient with diabetes, neuropathic pain, and obstructive sleep apnea

A 53-year-old man with diabetes was referred to our neurology department for painful diabetic neuropathy. He is obese and has had type 2 diabetes for 28 years. His feet have been numb for 5 years and painful for >1 year. He says that the pain is worse at night. The patient describes the pain as either burning or electrical, and it significantly interferes with his ability to sleep. Taking gabapentin 600 mg tid has helped reduce the pain substantially, but his weight has increased 50 lb in the last year. His wife says he now snores and stops breathing at night.

Patient history, physical exam findings, lab results

- Medications: Lantus (insulin glargine) 120 units at bedtime; NovoLog (insulin aspart) 20 units tid, plus sliding-scale insulin for meals. Four antihypertension agents—hydrochlorothiazide, atenolol, lisinopril, and nadolol. Gabapentin for diabetic peripheral neuropathy (DPN)
- Blood pressure: 150/92 mm Hg; body mass index: 36
- Nearly absent deep tendon reflexes; absence of vibration stimulation below the knees; diminished pinprick sensation in the feet. Romberg test is positive; tandem gait test is negative. Strength coordination, cranial nerves, and mental status are normal. Epworth Sleepiness Scale is 12 (>10 is pathologic and represents sleepiness)
- Hemoglobin A1c (HbA1c) level is 9.2%.

Initial management plan

The patient underwent a sleep study in which polysomnography revealed severe obstructive sleep apnea, with an apnea-hypopnea index of 69 events per hour. Oxygen desaturation reached a nadir of 78%, and apnea episodes lasted >60 seconds. Continuous positive airway pressure (CPAP) titration showed an optimal pressure of 13 cm, and nightly CPAP therapy was initiated.

We discontinued the patient's gabapentin because of his weight gain and daytime sedation, and prescribed duloxetine 30 mg daily for 2 weeks, then 60 mg daily. We also began α-lipoic acid for DPN.

Follow-up at 1 month

The patient adhered to his CPAP treatment and said he was feeling less sleepy. His Epworth Sleepiness Scale score dropped to 5. His wife said that he no longer snored. His blood pressure dropped to 122/82 mm Hg. The patient reported a number of hypoglycemic episodes, and his primary care physician reduced his Lantus dosage to 80 units at bedtime and his NovoLog boluses to 15 units tid. (Management of obstructive sleep apnea frequently improves diabetes control and increases insulin sensitivity.[14]) The duloxetine controlled the patient's DPN. And, with the elimination of gabapentin and treatment of his sleep apnea, his weight dropped by 10 lb.

Follow-up at 3 months

The patient's weight decreased an additional 15 lb without a change in diet. His blood pressure dropped further to 120/78 mm Hg, allowing discontinuation of atenolol and reduction of the nadolol dosage. His HbA1c was 7.8%, and insulin requirements were further reduced. He was sleeping well without snoring and was no longer sleepy during the day. The patient's DPN remained under control with duloxetine.

Patients enter a vicious cycle wherein pain interferes with sleep, and lack of proper sleep worsens pain.

>50% complain of poor or "unrefreshing" sleep, diminished or fragmented sleep, and increased pain.[6] Consequently, patients enter a vicious cycle wherein pain interferes with sleep, and lack of proper sleep worsens pain. Many chronic pain disorders commonly affect sleep: back pain, headache, facial pain and temporomandibular joint disorder, musculoskeletal pain, fibromyalgia syndrome, and premenstrual dysphoric disorder. Also, many pain medications used for these conditions can fragment sleep.

Investigating patients' sleep and pain connection starts with a thorough history of their sleep patterns. Do they have a sleep disorder, such as sleep apnea, restless legs syndrome, insomnia, or hypersomnia? Do they have circadian issues, such as advanced or delayed sleep phase, or do they do shift work? It is now known that, compared with those who work during customary daytime hours, shift workers have higher morbidity and mortality and increased risk of cancer, cardiovascular disease, mental illness, and gastrointestinal disturbances.[23,24]

How old are their pillows and mattresses? Mattresses should probably be replaced at least every 7 to 8 years.[25] Modern adjustable mattresses and various memory foams can improve

sleep for patients with chronic musculoskeletal complaints.

Is their sleep environment safe, quiet, clean, and comfortable? Sleep hygiene issues, such as having a computer in the bedroom or sleeping with a TV on, drinking too much caffeine, not having a wind-down ritual, minimizing the need for at least 7 hours of sleep nightly, or obsessing about sleep can all adversely affect sleep. Cognitive-behavioral therapy can usually correct refractive sleep hygiene issues.

Many medications can interfere with sleep, including antidepressants, stimulants, and β-blockers. Sedatives commonly prescribed for insomnia will worsen deep restorative sleep over time.

Lastly, do patients have a routine exercise program or adequate stress-coping mechanisms? Consider all of these issues when addressing chronic pain and sleep complaints. If patients are at risk for sleep-disordered breathing, such as sleep apnea, or complain of hypersomnia, refer them to a sleep specialist for formal sleep testing.

The importance of sleep architecture

Most people need to sleep 7 to 8 hours to feel rested. Some people need more or can do with less sleep, but inadequate (<4 hours) and excessive (>9 hours) sleep have both been associated with increased morbidity and mortality.[26]

Sleep is a highly regimented and organized series of altered states. Light sleep, stages 1 and 2, constitutes about 50% of sleep and is scattered throughout the night. Deep sleep (stages 3 and 4), which is thought to be restorative for the body and especially important for pain processing, constitutes around 25% of sleep by the fourth decade of life and is clustered only in the first 4 to 5 hours of sleep. People with chronic pain, such as patients with fibromyalgia or the elderly, typically have less than 5% deep sleep.[27] What is not clear is whether the lack of deep sleep is the cause or the effect of chronic pain. Most likely the relationship is reciprocal, a negative-feedback loop wherein pain affects sleep and lack of deep sleep affects pain.

Rapid eye movement (REM) sleep, the state associated with dreaming, constitutes approximately 25% of sleep and is clustered in the morning hours. Although the purpose of REM sleep is not entirely clear, it appears to be important for such mental processing as mood stabilization and memory consolidation. Depressed patients usually have more REM periods and start them earlier in the night, which interferes with deep sleep. Most antidepressants reduce REM sleep.[28]

Both deep sleep and REM sleep appear to be helpful in "resetting" pain thresholds. In particular, length and quality of deep sleep correlate inversely with pain. The mechanism of interaction between pain and sleep is not clear but may involve 5-HT serotonin receptors, NE release, and substance P neuropeptide regulation.

As mentioned, many pain and sleep medicines can interfere with normal sleep architecture. Because of the connection between deep sleep and pain, investigative approaches have used sodium oxybate, which significantly increases deep sleep. Sodium oxybate is FDA approved for narcolepsy-related hypersomnolence and cataplexy. However, in a study of more than 500 patients with fibromyalgia syndrome and chronic pain, sodium oxybate 4.5 or 6 g taken nightly significantly reduced pain by >30% in most patients and by >50% in nearly half of patients.[29] This degree of pain relief is equal to or greater than that provided by the 3 FDA-approved medications for fibromyalgia: pregabalin, duloxetine, and milnacipran.[29] Moreover, the added benefit of sodium oxybate for sleep and fatigue shown in the study is not seen with gabanoids or SNRIs.

Adverse effects of sodium oxybate include slower breathing, confusion, depression, edema, dizziness, vomiting, bedwetting, and sleepwalking. Avoid giving sodium oxybate to patients with a history of deep sleep parasomnias, such as sleepwalking or night terrors. Also, patients with heart failure and hypertension are not good candidates for sodium oxybate because it has a high salt content; the typical dosage contains several grams of sodium.

Both deep sleep and REM sleep appear helpful in "resetting" pain thresholds.

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