Pain messages travel from receptors at the site of an injury through the spinal cord to the brain stem. They are then relayed to the sensory, emotional, and cognitive regions of the brain. Anesthesia and pain medications work by blocking the pain pathways so that the pain messages do not reach the final brain areas. (Image credit: Kathryn Born)

**HOW ANESTHESIA WORKS**

General anesthetics work by shutting down the forebrain regions whose activity regulates cycles of arousal and quiescence. There are several kinds of general anesthetics, but those most commonly used enhance or mimic the action of the inhibitory neurotransmitter gamma-aminobutyric acid (GABA).

In contrast, a local anesthetic works by blocking the transmission of the pain message along a primary afferent nociceptor's axon. The message thus never reaches the central nervous system.
Pain Perception — The Dana Guide
By Howard L. Fields
November 2007

Sections include: the physiology of pain, the psychology of pain, pain treatments

Pain is an unpleasant sensory and emotional experience usually produced by something that injures, or threatens to injure, the body. Pain begins with a stimulus, but is influenced by physiological and psychological factors before it becomes part of our consciousness.

Although pain is something that we invariably want to escape or to stop, it serves several very important functions. Pain protects us by triggering a reflexive withdrawal from something damaging before we can suffer further injury, such as when we drop a hot pan before we sustain extensive burns. It is also a warning system that lets us know when an injury is about to occur: the burning ache in our muscles during extreme exertion warns us to stop using them. Pain forces us to immobilize or protect an injured part, such as a broken ankle, thus giving it a chance to heal. Pain also lets us know when we need to seek medical help, and teaches us what behaviors to avoid in the future.

This section concentrates on acute pain, which occurs almost immediately upon tissue damage or injury and lasts only a limited time. When pain persists and cannot be avoided, it can be quite destructive. In effect, it becomes a disease in itself. Pain that lasts for weeks, months, or years is called chronic pain and is a major source of suffering, disability, and economic loss.

The Physiology of Pain

The nature of pain has intrigued philosophers for millennia. The ancient Greeks conceived of pain as an emotion. In the late nineteenth and early twentieth centuries, the view of pain as sensation became preeminent: it was seen as a direct response to a stimulus. From the mid-twentieth century to the present, these two views have been combined, so medical scientists who study pain now think of it as a subjective experience with distinct discriminative and emotional components.

Pain is associated with a variety of behaviors. A painful stimulus will arouse us, as in “Pinch me to see if I’m awake.” It can focus our attention on the site of an injury: “I looked down at where it hurt and saw I was bleeding.” It can cue us to try to escape from the cause of an injury or immobilize us so that we do not suffer further damage. In addition, pain causes changes in heart rate and blood pressure, and an endocrine response with elevated stress hormones. For each response elicited by the pain-producing injury, there is a unique central nervous system pathway.

In healthy individuals, the sensory experience of pain is usually triggered by events in the body that activate specialized nerve endings, called primary afferent nociceptors. Nociceptors are activated by any process that either causes damage or has the capacity to cause damage if continued or intensified. Most primary afferent nociceptors respond to a variety of noxious stimuli—extreme hot or cold temperatures, intense mechanical manipulations (pinching, pinpricks, cutting), increased tissue acidity, and other causes of injury. Nociceptors can also be activated by a variety of chemical agents released from cells that are damaged or responding to a foreign body such as a splinter or infectious agent (for example, a bacterium).

There are two types of nociceptors, and the differences between them can easily be understood. Let’s say that you tripped and fell, landing hard on one knee. You would experience an acute, well-localized, painful sensation in your knee, followed by a dull and aching sensation. This reflects the two types of fiber systems that conduct pain from the periphery into the central nervous system. The first pain signals are carried by A-delta fibers, which are insulated with myelin and therefore conduct rapidly. The longer-lasting pain signals are carried by C-fibers, which are unmyelinated and conduct slowly.

Nociceptors from the body carry their message to the spinal cord, where they end in very specific areas. Those areas contain connections to the neuron pathways that conduct the message to the brain stem. Pain messages from the head arrive at similar groups of neurons in the hindbrain. The central nervous system neurons that receive the pain messages from all over the body target a variety of structures in the brain.

If significant tissue damage has occurred, or if there has been a prolonged or particularly intense activation of a primary afferent nociceptor, it will become sensitized. Sensitized nociceptors can be activated by moderate stimuli that normally do not produce pain. One common example of sensitized nociceptors is the agony produced by bath or shower water on sunburned skin. If you have arthritis, have “thrown out” your back, or have experienced a sports injury, you are also familiar with how you can be reasonably comfortable at rest but feel significant pain during normally innocuous movements. That is due to sensitized nociceptors in joints,
tendons, and muscles.

Chemical agents that do not activate nociceptors can also produce sensitization. The best known of these agents are prostaglandins, which appear when tissues are inflamed by infection, arthritis, or other factors. Their synthesis depends on the enzyme cyclooxygenase. This enzyme is inhibited by many of the medicines that are used to treat pain: aspirin, acetaminophen, ibuprofen, and the new cyclooxygenase 2 selective drugs, celecoxib (Celebrex) and rofecoxib (Vioxx). These drugs are particularly effective for pain associated with sensitization and are better for tenderness than for continuous severe pain.

The central nervous system’s pain transmission neurons can also become sensitized in a way similar to the primary afferent nociceptors. This process is called central sensitization, and it is set in motion by neurotransmitter chemicals released at the central terminals of nociceptors. Thus, when a person is injured, the subsequent activity of nociceptors produces a bigger and bigger response in pain transmission pathways; pain begets further pain, even if the stimulus that triggered the response remains the same.

**The Psychology of Pain**

Another part of the brain is at work when we experience pain, integrating the physical sensation with psychological factors. Perhaps the most familiar example of the power of psychological factors on pain involves headaches. It is almost a cliché that emotional stress can bring on a headache. Even our vocabulary of stress incorporates this concept: “This job is a real headache.”

Memories, emotions, thoughts, and especially expectations are now known to have an enormous influence on how people perceive pain. A rough outline of the central nervous system pathways that mediate these psychological effects is beginning to emerge. In fact, the regions of the forebrain that are involved in emotion (the frontal and temporal lobes and the amygdala) are known to feed into a neural circuit in the brain stem that directly controls the pain pathways. Furthermore, the control exerted by this pathway is bidirectional, meaning that it can either reduce or enhance pain.

This pain-modulating pathway was discovered in the mid–twentieth century during an exploration of the brain stem using electrical stimulation. An area was found, called the midbrain periaqueductal gray, which, when electrically stimulated, produced a profound reduction of pain in both rodents and people with chronic pain. We now know that this area is part of a circuit that receives connections from the frontal lobe, the amygdala, and the hypothalamus and, in turn, connects directly to the spinal cord neurons that relay pain messages from primary afferent nociceptors. This pathway mediates the pain-relieving effect of powerful painkillers like morphine. In fact, the circuit has neurons that secrete morphine-like compounds, called endorphins and enkephalins. These chemicals interfere with pain-impulse transmission and can significantly lessen the perception of pain.

In animals, the pain-modulating pathway is most easily activated under conditions of threat, such as in the presence of a predator. The animal’s system anticipates tissue damage, which would normally be painful, but being incapacitated by pain would lead to even greater injury; therefore, the animal has evolved the ability to dampen its perception of pain temporarily. It is not clear what situations activate this pathway in humans, but possible examples include athletes injured in the midst of competition, or soldiers wounded in combat; such people may not realize they have been hurt until after the stressful situation has ended.

In addition to its pain-suppressing actions, the same pathway can also enhance pain transmission. This raises the possibility that psychological factors that produce or exacerbate pain do so through this circuit. In fact, it has been shown that the anticipation of pain activates areas in the forebrain and midbrain that are part of this pain-modulating circuit, and that anticipation of pain can produce and enhance pain.

Studies have also shown that people can be trained to separate out the sensory intensity of pain from its unpleasantness, and to quantify each selectively. Imaging shows that two different parts of the brain are involved. Measuring the level of sensory intensity is associated with activity in the primary somatosensory cortex, whereas the unpleasantness is associated with activity in areas of the frontal lobe cortex usually associated with emotion (the anterior cingulate and insular cortices). In fact, certain surgical procedures, such as modified frontal lobotomies, can markedly reduce the suffering of severe pain without affecting its sensory intensity. This implies that the emotional aspects of an injury may be more significant than the extent of its physical damage in determining how intense we perceive the resulting pain to be.

**Pain Treatment**

In addition to the body’s own mechanism, there are a variety of approaches to treating pain. The best approach, of course, is to identify the cause and remove it. This should always be the primary goal. Once you or your doctors have identified the cause of a pain and, if possible, treated it in the best way, that pain no longer serves its purpose and should be eliminated as quickly and completely
Pain relievers (analgesics) are the most common over-the-counter medications, and they are quite effective against most everyday pains. Some people are reluctant to use these drugs, feeling they should “tough it out” or use natural methods of pain relief, such as muscle relaxation. It is true that pain depends on psychological factors, and the experience can thus be affected by our attitudes and mental states. Nevertheless, pain is, by definition, not enjoyable. There is no reason to prolong it if it is interfering with your comfort, performance, or sleep.

Physicians can also prescribe more powerful drugs to counter pain due to a bad injury, surgery, cancer, or other causes. The most common mistake health workers make in treating someone in pain is to give an inadequate dose of these medicines out of fear that the person will become dependent on them. The treatment goal should be relief of pain. There is no reason to delay treatment for acute pain, and there are strong arguments for immediate treatment. First of all, because of the tendency of pain to increase with time and the fact that lower-intensity pain responds better to drug treatment, earlier treatment may require less medication and therefore cause fewer side effects. This is particularly important for intermittent pain that has the potential to become severe, such as in the case of a migraine headache. For acute pain, there is no excuse for withholding powerful painkilling drugs such as morphine. If these drugs are used correctly, the risk of addiction is infinitesimal.

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