Neurobiology of Pain

By Neil Pearson

What is Pain?

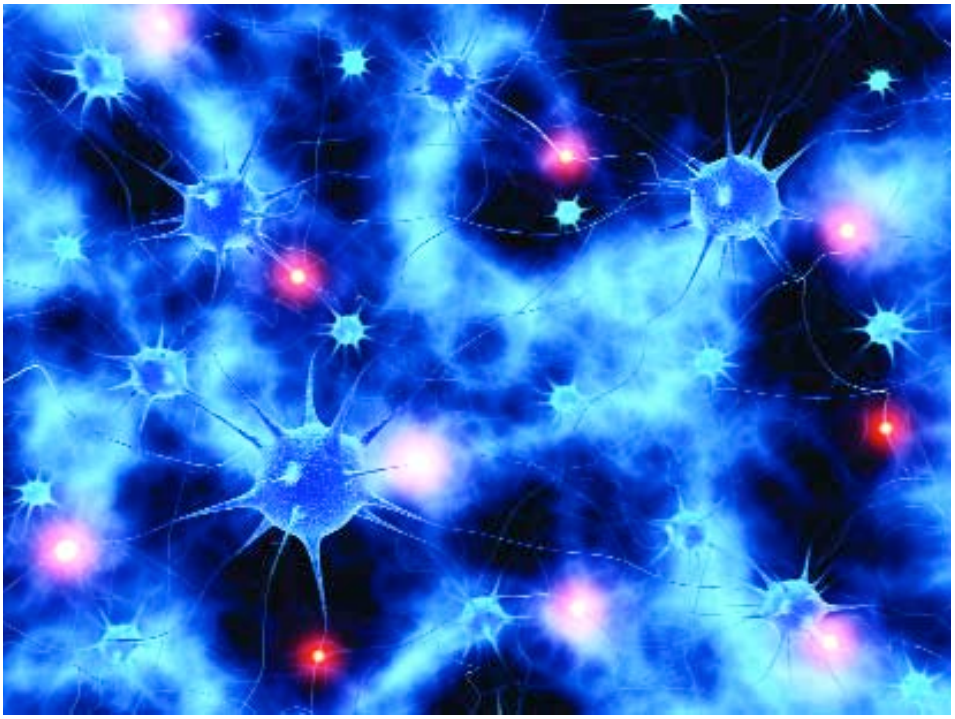
Pain is complex. It can arise for no apparent reason; it can be attributed to a specific event, an object or body part, or a physiological process or pathology. Ask a group of people how to complete the sentence "Pain is …*[blank]*" or to answer the question "What is the opposite of pain?" and its complexity becomes even more obvious. Pain is described as a symptom, a perception, the enemy, a teacher, a friend, and an experience; it is labeled as invisible, horrible, necessary, inevitable, and disabling. The opposite of pain can be stated as comfort, the absence of pain as bliss, calm, and sometimes, peace.

Pain is both a complex experience and a complex biological process. Yet its complexities are rarely explored, especially when we are in the midst of it. Only recently has science provided a new understanding of the physiological processes related to pain beyond the long-held views that pain and tissue damage are directly related. Understanding the intricacies of pain will help us respond to it in more helpful ways, both as yoga therapists and when we experience pain ourselves.

Neuroception Sometimes Starts with Nociception

Pain exists when neural circuits conclude that danger exists *and* that action is required.[1] As such, it is so much more than a symptom or a message telling us that there is something damaged or diseased in the body. Pain is an experience. It *motivates us to stop or change our behavior*.[2] Known as the *neuroception of danger*,[3] the experience begins subsequent to activity of special nerve cells (neurons) in the physical tissues of the body in response to potentially dangerous mechanical, chemical, or hot/cold stimuli. These neurons are called *nociceptors* because they are *receptors* (sensory neurons) that respond to potentially noxious stimuli, from the Latin word *noci*, meaning "to injure or hurt." Nociceptors are fascinating and multifunctional cells.

Nociceptors are classified as A-delta fibers or C fibers. Although both respond to similar stimuli, they are quite different in other ways. Because they are thicker and myelinated, A-delta fibers are able to send signals up to 20 meters per second. They primarily relay their information via the thalamus to the somatosensory cortex. C fibers are thinner and unmyelinated, so they send signals more slowly—up to 2 meters per second—and primarily relay their information via the thalamus to the insula. Recent research suggests that A-delta fiber inputs are the sensory apparatus of the central nervous system, whereas C fiber inputs are the sensory apparatus of the autonomic nervous systems.[4] The significance of these different types of fibers is that when something potentially dangerous occurs in the body, neurons can send signals to both the autonomic and central nervous systems and create a multitude of both automatic and volitional responses.



Nociceptors are found both internally—for example, in muscle, joints, and organs—and externally in the skin. Firing of nociceptive neurons is impacted by much more than what's occurring at the peripheral end of the neuron, where the sensors are. The signals they send are always influenced by activity in other peripheral nerves in the skin. For example, gentle stroking or applying soothing warmth over an area of pain can modify nociceptor signaling when it reaches the spinal cord.[5] Activity in the autonomic nervous systems, such as the increased sympathetic nervous system activity during a fight–flight response, can also enhance nociceptor reactivity. Even central nervous system activity such as expectations has been shown to either enhance or diminish how nociceptive signals are transmitted from the peripheral neurons to the spinal cord.[6] For example, believing that a posture will be painful or will aggravate an old injury can enhance nociceptive signaling, while a gentle comforting hand on our back or a calming breath can diminish the activity and signaling through nociceptive neurons.[3] In other words, each aspect of your nervous systems can influence nociceptors and nociceptive signaling. In fact, all systems of the body have an influence on these neurons, including respiratory, endocrine, cardiovascular systems, and especially the immune system. As such, it is important to view nociceptive neurons as dynamic. Their sensitivity, receptiveness, and sig-

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naling is always in flux, either adapting to (with less activity) or becoming hypervigilant (with more activity) to not only mechanical stresses or hot/cold and chemical stimuli, but to aspects of our internal and external environments.

Another fascinating aspect of nociceptors is that they are always ready and able to send danger signals toward the spinal cord and brain, even when there has not been any pain in a particular region or tissue of the body for weeks, months, or even years. Typically, cells that are not used will atrophy, so something different must be occurring with nociceptors. One possible explanation is that the cells are continuously active, always sending some signals to keep the nervous systems apprised of the physiological state of the body. This might lead one to wonder if we should actually be in pain all the time. However, these low-level signals can be inhibited by descending signals from the brain to the body, or they may be filtered out by brain mechanisms evaluating the importance or saliency of the signals. This is a similar situation to other physiological inputs that don't typically require your attention. For example, the brain is always getting information about skin temperature and bladder distention, but you don't know about this information until your attention is required and you need to act. This is important for two reasons: (1) it means that the experience of pain does not rely solely on nociceptive signaling from the body but also on neuronal cellular activity and processing in the central nervous system and (2) it means that when we experience increased pain, it may be the result of more nociceptive signals, the brain interpreting these signals as important for attention, or fewer descending inhibitory signals filtering the nociceptive inputs.

It is important to consider that nociception and pain are not only related to the activity of neurons. Neuronal activity is supported by cells referred to as glia, which were originally believed to be the cells "gluing" the nervous system together (the term *glia* means "glue"). Neurons make up only 10% of the brain's cells, while the majority of its cells are glia. These are considered to be neuroimmune cells.[7] The sophisticated interplay between both immune and neural cells and systems is beyond the scope of this article. However, given the potential links between yoga techniques and the immune system, this is an exciting area for us to observe as it develops.

Neuroception and the Brain

When we feel acute pain, many parts of the brain become more active. The amount of activity and the period of increased activity is as much dependent on the intensity of pain as it is on our thoughts, emotions, past experience, predictions of what this pain means for the future, our current internal physiological milieu, and all aspects of our external environment. In other words, just like tissue damage and pain intensity are not directly related, overall increases in brain activity are not directly related to pain intensity. The nervous systems—and even more so, the entire organism—are far too intricately interconnected for such a simplistic relationship.

The experience or perception of pain is believed to occur when neural circuits conclude that danger exists *and* action is required.

Beyond complexity, what we know about pain and the brain is that the brain does not have a pain center. When we experience pain, a network of brain areas is engaged. Interestingly, researchers have clearly demonstrated that this same network of brain areas is engaged during a number of experiences that can be theorized as important for defensive responses.[8] When we experience acute pain, the thalamus, insula, anterior cingulate cortex, dorsolateral prefrontal cortex, and primary and secondary somatosensory cortices typically become more active. Some researchers have unfortunately referred to this pattern of activity as the "pain neuromatrix," "pain network," or "pain signature." However, it is not specific to pain. This same network becomes more active when individuals experience potentially dangerous tactile vibration, noises, flashes of light, and experimentally induced social rejection.[8] In other words, this network is the *saliency* network—the network of brain activity that occurs when some form of defensive response is required. Ianetti goes so far as to state that this network allows us to bypass the details of an experience in favour of a defensive response, regardless of stimulus details.[9]

One key clarification is required here. Although we observe similar brain activity with acute nociception as with social rejection, this is not evidence that acute nociception is experienced in the person in exactly the same way as social rejection is or that social rejection should be treated with the same medications as acute tissue injury. There are similarities and differences in these experiences, and scientists have not yet found how to observe differences in how the brain encodes for the multitude of events we experience as potentially dangerous.

Brain scans of individuals with persisting pain* often differ from those with acute pain.[10-12] Differences are also observed related to differing pain conditions and how the experience of persisting pain has changed many aspects of the individual's life. However, since each part of the brain has many functions and each works in concert with many other areas, it is unwise to directly attribute specific changes seen on brain scans to the subjective experience of persisting pain. Possibly the most important thing to know about the changes that occur in the brain related to persisting pain is that they can be reversed—they are not permanent changes. Even those with disabling low-back pain who improve either via surgical intervention or with active rehabilitation show brain activity returning to normal when pain and function normalize.[13]

These changes in the nervous systems are referred to as *neuroplasticity*, which is defined as relatively enduring changes in the physiology (functioning) and structure (physical connections) of the nervous system. Learning something new, adapting to temperature variations, increasing tolerance to a noxious smell, and becoming more skilled in body awareness or a breathing technique are all associated with neuroplastic changes.

Research has shown neuroplastic changes in many brain areas in persisting pain, including important ones in the sensory and insular cortices, the amygdala and hippocampus, and the dorsolateral

*Persisting pain is often used as the preferred language for patients and clinicians. Although it is synonymous with chronic pain, it is a hopeful word, rather than suggestive of even worse pain to come.

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prefrontal cortex.[14] Changes in the sensory cortices have been related to the experience of pain spreading away from the original body area over time and to distortions of body awareness.[1] The insular changes, like sensory cortex changes, are often considered as both related to decreased sensory acuity and to body schema distortions experienced by many with persisting pain. Thankfully, there is evidence that the practice of body awareness leads to measureable neuroplastic changes in insula cell density and cellular interconnections[15] and may be associated with the benefits of decreased pain.

Learning something new, adapting to temperature variations, increasing tolerance to a noxious smell, and becoming more skilled in body awareness or a breathing technique are all associated with neuroplastic changes.

Increased activity reported in the amygdala is usually described as related to the increased hypervigilance and emotion turmoil (anxiety, grief, anger) of persisting pain. Unfortunately, when the amygdala is more reactive, it inhibits the hippocampus, one of the areas of the brain involved in spatial awareness (that we know is distorted in some individuals with persisting pain),[16] in turning short-term memory into long-term memory, and the ability to be present (temporal awareness).

The dorsolateral prefrontal cortex is associated with perceived control and with the brain's diffuse processes for inhibiting nociceptive inputs (diffuse noxious inhibitory control). The neuroplastic changes of decreased activity in this area on both the right and left hemispheres have been associated with learned helplessness and with increased pain from a diminished ability to inhibit nociceptive signaling via descending signals to the spinal cord.[17]

Nociception and the Autonomic Nervous Systems

According to Porges,[3] the neuroception of danger, and therefore our experience of pain, is impacted by activity of the vagus nerves. In his polyvagal theory, he describes three functions of the vagus nerves that serve to mediate our fight–flight response (sympathetic nervous system, SNS) and our freeze and social engagement responses (parasympathetic nervous system, PNS). Engaging the PNS inhibits the SNS and increases the neuroception of safety; this is related to greater inhibition of ascending nociceptive signaling.

When we breathe calmly and when we soften tension in the muscles of the face, vocal apparatus, and hearing, we increase the neuroception of safety. Complex alterations in the neural circuitry of the vagus nerve, the phrenic nerve,* the autonomic nervous system, insular cortex, anterior cingulate cortex, and the dorsolateral prefrontal cortices have all been implicated in the experiential changes, along with measurable changes in neurochemistry, cardiorespiratory, and cognitive and emotional factors.

Each of the factors listed below impact whether our neural circuits interpret movement as safe or dangerous. They are all highly interactive with the regions of the brain implicated in pain and the neural circuitry related to the neuroception of danger and safety. The experience and intensity of pain may well be intimately related to the current balance or imbalance between factors that increase and decreased the neuroception of danger:

- the mechanical pressure and/or stretch on the tissues
- how we are breathing
- the tension in face, jaw, and tongue muscles
- how we are listening and aware
- what we are thinking
- our emotional state

Many other factors are also implicated in the neuroception of safety. It is plausible that each of these may play a role in therapies and techniques used to create the neuroplastic changes related to less pain, greater ease of movement, and improved quality of life: social acceptance, compassionate listening, touch, music, smells, colors, fear, body awareness, body image, self-efficacy, and knowledge.

*The phrenic nerve provides motor and sympathetic supply to the diaphragm as well as sensory innervation to the fibrous aspects of the diaphragm, pericardium, and pleura, whereas the vagus nerve supplies parasympathetic innervation to the heart and organs.

The Role of Education in Changing the Experience of Pain

Moseley and others have studied the dramatic impact of knowledge on pain and recovery.[18-20] Findings from these randomized controlled trials (RCTs) showed that when individuals understood the role of the nervous systems in pain, their pain decreased, their ease of movement increased, and these immediate changes could persist for many months after just one session of education.

To date, few studies have measured brain changes related to the effects of explaining pain, although preliminary findings are promising. A case study report[21] showed that immediately following a single education session about pain neurobiology, brain scans of a woman with chronic low-back pain showed dramatic decreases in activity in the areas of the brain implicated in stress responses. Other findings reported in studies looking at the effects of education on pain neurobiology include diminished fear,[22] catastrophic thinking,[23] and peripheral sensitization.[24] In my opinion, when people understand how their pain is influenced by their thoughts and beliefs, their patterns of activity, and their social support systems, it increases their neuroception of safety and, by extension, it reduces their perception of pain. Adding support to the power of appropriate education are the research studies that demonstrate how education that focuses on pathology and fear-based language can lead to increased disability and pain.[25-26] These research findings on the power of education to change the experience of pain have direct implications for your clients. You might consider developing ways of incorporating pain education into your yoga therapy treatment plan. Many resources and workshops are available to assist with this.

Yoga is Education through Movement and Embodied Cognition

Multiple RCTs and four meta-analyses studying yoga[27-30] support the positive

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effects of practicing yoga on pain and function. To date, evidence suggests benefits for specific yoga practices provided to people with osteoarthritis, rheumatoid arthritis, low-back pain, whiplash-associated pain, irritable bowel syndrome, and fibromyalgia. Given the complexity of pain and the nervous systems, it is probable that there are many reasons that yoga can be effective for decreasing pain, improving ease of movement, and helping people live well again. It is possible that a large portion of yoga's benefits for people in pain arises from its powerful experiential and physical experiences. For many, the most impressive and believable changes arising subsequent to any therapeutic intervention are those that are experienced physically. The experience of functional improvements can feel more real to some than the experience of learning new ideas and concepts.

Adults learn in many different ways. Explaining pain through discussion and experiential lecture creates change primarily through cognitive experiences and cognitive shifts. Similarly, many of the techniques of yoga seek to create change through both physical and cognitive experiences, especially through the experience that change has occurred in physical functioning. Each time a yoga student experiences greater safety, whether this results from a cognitive and/or physical experience, the new experience is inconsistent with the brain's interpretation of danger. The practices of yoga can provide an opportunity to repeatedly experience more safety and less danger in the body, leading to positive neuroplastic changes. Each experience in which we move while breathing calmly, decreasing body tension, and quieting the mind, may be the perfect (re)education our nervous systems need to learn that movement and being in the body are not so dangerous.

The effectiveness of yoga for people with chronic pain likely relates to many factors beyond the nervous systems—including every other physiological system and their tissues, cells, and even their DNA. And the positive impacts of yoga on each of these likely relate to a wide array of factors found in each of the paths of yoga, including meditation, social connectedness, breath, movement, awareness, safety, and ritual.

Understanding pain through all of its complexities is important—indeed, it is the work of a lifetime. Taking the time to learn more about the neurobiology of pain is a great place to start—the anatomy and physiology of neurons, the spinal cord, the autonomic systems, and the brain. The added benefit of this knowledge for many is that it makes pain more tangible. When we understand more about the neurobiology of pain, we begin to truly know it as a body–mind–spirit experience rather than only a psychological phenomenon. This opens doors to more innovative applications of yoga for people in pain and to greater compassion for the people we serve in yoga. YTT

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