Nociception — More than just pain.

There seems to be a lot of confusion with regard to nociception and pain. These two are constantly used synonymously when, in reality, they are different than one another. To explain this, we need to start from the beginning and explain what nociception is and how it works. Nociceptors, commonly (although incorrectly) referred to as “pain cells”, are free nerve endings that transduce noxious, a fancy way of saying potentially harmful, stimuli and send a “danger” message to the spinal cord, where it gets relayed up to the brain. It is extremely important to realize that the danger message that your brain received is not pain. There are two main classifications of nociceptors, known as Aδ- and C-fibers. Think back to last time you stubbed your toe. Almost immediately, you get a sharp jolt of pain, followed by just enough time for you to say any of your favorite four letter words before you experience the flooding, burning sensations that follow. You can thank your Aδ-fibers for that initial jolt of pain, as they are myelinated and as a result, conduct signals extremely fast, approximately 40 miles per hour. Your C-fibers, which are unmyelinated, conduct signals at only about 3 miles per hour. Let’s take a small step backwards, to that danger message your brain received. That message your brain received said something like this, “something dangerous has just happened in your toe” (7). It is, at this point, your brain that has to decide what is or is not an appropriate response to this message, and many times, the answer is pain.
While this seems like an argument in semantics, it’s important to realize that chronic pain often times no longer accurately reflects the state of the tissues we experience pain in. I would like to quote a few sentences from a paper that was recently published, entitled, “TRPs and Pain” (1).

“Nociception is the process of transmission of painful signals by nociceptors in the primary afferent nerve fibers, which specifically respond to noxious stimuli”

“Painful signals generated by tissue damage are detected by nociceptors, which transfer the signals to the central nervous system to produce this unpleasant sensory and emotional response.”

Not only is this incorrect, but it is worded in a way that implies, “if we have pain, then we must have some kind of tissue damage that is producing it.” If pain were truly generated in the tissues, then pain intensity should always be the same in response to a given stimulus. However, a paper by Moseley et al. demonstrated that the context in which noxious stimuli was received influences how much pain is experienced (2). Subjects were prodded with an extremely cold rod and were shown either a red light or a blue light. Since red is typically associated with heat, when subjects saw the red light, they experienced more pain. In other words, subjects didn’t just “think” it hurt more — it actually hurt more. The brain received a danger message and coupled this information with vision, and the knowledge of what they were seeing to ultimately produce an appropriate response. To make things a little weirder, a 2009 study managed to elicit pain in a rubber hand (3). An illusion was created, whereby the subject’s real hand was moved out of sight and a rubber hand was put into their field of vision (see picture below). The researchers stroked the real hand at the same time that they stroked the fake hand until the subject got the eerie sensation that the fake hand ‘belonged’ to them. When poked with a pin, nearly 80% of participants felt pain in the
rubber hand. This is one of the coolest things I have read. It also shows that nociception is neither required, nor sufficient, on its own to experience pain. Pain will always be an output of the brain.

- “Where does it hurt?”

- “In the rubber hand.”

Up until now, we have only looked at nociception as it relates to pain. I would like to quote another sentence that, in my opinion, is possibly the most meaningful message in this article.

“We redefine nociception as the mechanism protecting the organism from injury...” (4)

This is extremely profound, as nociception has become demonized as our pain system, an imperfection in an otherwise miraculous human body. Nociception’s primary role is not to make us miserable, but to protect us from harm, and anything that is a threat to homeostasis can be considered harmful. For example, our body’s pH usually measures about 7.4. When we start exercising, think a fast paced run, our body is going to start breaking down carbohydrates for energy, producing more carbon dioxide and hydrogen
ions, both of which will act to lower pH. The “Exercise Pressor Reflex” is driven by these Aδ- and C-fibers in exercising muscles that detect chemical changes (Side note: they’re probably sending a danger message from the pressure on your butt as you’re sitting and reading this, you probably aren’t experiencing pain though). A danger message is sent to the brain saying, “pH is starting to get to low down here,” and the brain must take action. However, it doesn’t produce pain; it simply increases heart rate and ventilation to “blow off” the carbon dioxide and keep pH at appropriate levels (5,9). Also worth noting is the classical conditioning that happens with exercise and the pressor reflex, called the “anticipatory rise.” Prior to the start of exercise, both heart rate and ventilation rise above resting values. During the minutes before exercise our thoughts, our knowledge of where we are, maybe it’s inside a gym or your favorite cycling path, this information is all processed and your brain knows that, “we’ve been here before, pH is going to drop soon, and I’ll just get things going now.”

Let’s stick with the Exercise Pressor Reflex and imagine our bodies without a danger system. During our run energy demands are still going to increase, but with no way for the brain to detect these potentially harmful changes, how will the brain know how to respond? Researchers aimed to find out by using a nerve block in the spinal cord to block type III/IV afferent signals, and found that “During various types of intensities and durations of exercise a sustained hypoventilation, as well as reduced systemic pressure and cardioacceleration, were consistently observed with this blockade.” (8). A lack of nociceptive input actually hinders performance during exercise, because the brain does not realize anything is going on. Nociception is an amazing mechanism that is responsible for much more than just pain.
References


