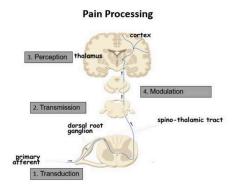


### Introduction

Pain is a complex experience, but it can be better understood when divided into three broad categories: nociceptive pain, caused by tissue damage, neuropathic pain, resulting from nerve damage, and the newly recognized psychogenic pain (also known as nociplastic pain). Nociplastic pain refers to physical pain caused or increased by psychological, emotional, or social factors rather than physical or neurological damage. Nociceptors (i.e. pain receptors) release neurotransmitters to the thalamus and other parts of the brain through the nervous system. Pain manifests as a physical and subjective experience. Despite the lack of a clear physical cause, and though some dismiss it as entirely psychological, psychogenic pain remains a genuine condition as it is both physical and psychological. While there is no clear underlying physical cause, and although some people may discount it being all in a person's head, psychogenic pain is still real.

### The Development of Pain

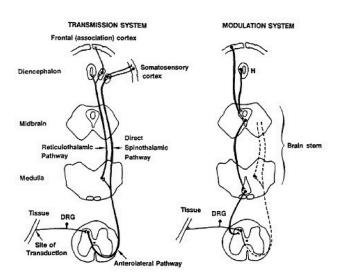


**Figure 1.** Pathway of pain signaling and processing (NIH, 2022).

There are four major processes in the development of pain. It starts with transduction, which refers to the activation of pain receptors in response to stimuli-either mechanical (i.e. pressure), heat, or chemical. Next, transmission involves the nociceptive message being sent from the peripheral nervous system (PNS) to the central nervous system (CNS). These nociceptive messages are encoded in the patterns and frequency of impulses from the nociceptor. Along this pathway, modulation occurs, altering the pain signals as they travel. Modulation is one of the reasons people experience pain in different severities, even with similar stimuli (Kirkpatrick et al., 2015). For example, the activation of nociceptors may not always lead to a sensation of stronger pain due to modulation. Finally, perception occurs and is the cumulative subjective experience resulting from an array of sensory signals. This step includes the attention, expectation, and interpretation of the pain messages and cannot be objectively measured unlike the other neural processes.

For instance, when you stub your toe, nociceptors are activated in response to a mechanical stimulus. The message would travel through the anterolateral system (a sensory pathway that carries information about stimuli such as temperature and touch) in the spinal cord and then to the brain (specifically, the thalamus then to various areas of the

cerebral cortex) as an electrical impulse, which is interpreted and experienced as pain (Institute of Medicine (US) Committee on Pain, Disability, and Chronic Illness Behavior et al., 1987)

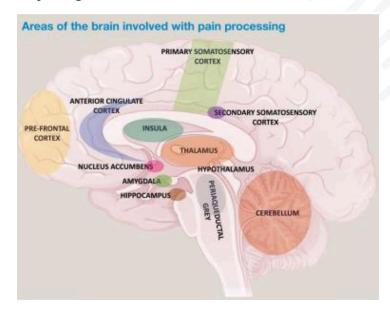


**Figure 2.** The major neural structures relevant to pain and pathway/development of pain from nociceptive transduction of stimulus from tissue. In psychogenic (nociplastic) pain, there is no physical stimulus (Institute of Medicine (US) Committee on Pain, Disability, and Chronic Illness Behavior et al., 1987).

### The Detection of Pain

Nociception-the process by which the nervous system painful stimuli-is crucial to understanding psychogenic pain and the mechanisms behind pain in general. Nociceptive pain refers to the activation of nociceptors in response to actual or threatened tissue damage. On the other hand, nociplastic (psychogenic) pain arises from the activation of nociceptors without the presence or clear threat of physical damage (Milner & Doherty, 2015). In this case, the excitation of nociceptors is mediated by retrograde activation by messages from the sympathetic nervous system (SNS). This means that the postsynaptic neuron, the cell receiving a signal, sends information back to the presynaptic neuron, the cell sending a signal. Nociceptors detect harmful stimuli and signal the CNS which causes the sensation of pain. So, retrograde activation in this context would involve the injured areas sending signals back to the nociceptors (Tao & Poo, 2001). Another way nociceptors could be activated is by reflex muscle tension. Prolonged muscle tension is often accompanied by increased sensitization of nociceptor terminals in muscles (Isagulyan & Kashcheev, 2022). Muscle tension is a reflexive response to stress and can significantly decrease the mechanical threshold for nociceptor activation in muscles (Chen et al., 2011). Essentially, elevated and extended periods of stress heighten muscle tension which generally lowers pain tolerance or increases sensitivity to stimuli.

# Factors Effecting the Development of Psychogenic Pain



**Figure 3.** Areas of the brain involved with pain processing (Gore, 2022).

There are a few proposed mechanisms for the development of psychogenic pain. Pathophysiologically, one mechanism pointed to is hyperresponsiveness to pain stimuli. Nociceptors may become more sensitive to stimuli and lower the threshold for activation, causing even seemingly nonpainful stimuli to produce pain (Bułdyś et al., 2023). The extent of nociceptor activation determines the input the CNS receives which determines the severity of pain experienced. Nociceptors sensitize, meaning their excitability can increase. As a result, there is a reduction of the threshold and an increase in magnitude of response to a stimulus (Gold & Gebhart, 2010).

Another potential influence could be hyperactivity and connectivity between regions of the brain responsible for perceiving pain, such as the medial prefrontal cortex (mPFC), anterior cingulate cortex (ACC), thalamus, and somatosensory cortex, which would also cause an amplified response to pain signals. Decreased activity and connectivity in the regions of the brain such as the rostral ventromedial medulla (RVM) and periaqueductal gray (PAG) can impact the development of psychogenic pain as well (Bułdyś et al., 2023). The PAG activates a pain inhibitory system and influences pain modulation by its connections with the RVM, which can both facilitate and inhibit nociceptive inputs (Ossipov et al., 2014).

Additionally, psychogenic pain may be caused by the nervous system's recognition of pain that has already healed, supporting the idea that confused signaling may be a part of the cause (Moini et al., 2023). Pain plasticity—the adaptive processes of the nervous system in response to pain stimulus—may lead to changes in nociceptors, causing them to activate atypically. Because of this plasticity

plasticity, signaling is amplified and a "pain memory" is formed (Price & Inyang, 2015). It is most likely a combination of these factors as many regions of the brain (ACC, mPFC, thalamus, somatosensory cortex, RVM, and PAG) work together to create the experience of pain.

Other important factors are cognitive and psychological. Psychogenic pain is commonly associated with psychosocial and emotional conflicts, as the brain can interpret mental distress as physical pain (Moini et al., 2023). Chronic stress can trigger or exacerbate pain because it can contribute to the sensitization of nociceptors, causing the brain to become hypersensitive to pain signaling (Hannibal & Bishop, 2014). In addition, problems with emotional regulation may lead to somatization—the expression of emotional/psychological conflicts as physical (somatic) symptoms (Lumley & Schubiner, 2019). Generally, positive emotions inhibit pain while negative emotions facilitate it. Issues with regulating negative emotions can heighten the amplification of pain signaling (Toledo et al., 2024).

The idea of "catastrophizing" can also be associated with the development of psychogenic pain. People who tend to catastrophize (i.e. exaggerating negative mentality) are more likely to experience more intense pain and have more difficulty managing it. This is linked to activation of PFC, ACC, and amygdala, which is involved in perception of pain and emotional regulation (Sullivan et al., 2000).

## Conclusion

Psychogenic pain most commonly manifests as headaches, stomach aches, and back pain, and is overall commonly associated with mental disorders like depression and anxiety (Galli, 2023). However, psychogenic pain is very complex and still not fully understood, so there is not a standard diagnosis or treatment of the condition yet. Due to its novelty, misunderstanding, and the general dismissive attitude towards it up until only recently, many patients suffering from psychogenic pain have not received the attention thev deserve. With many technological advancements and development of new research, new techniques for diagnosis, treatment and prevention of psychogenic pain are not far out of reach. In the meantime, a greater emphasis on recognizing and accepting this condition and approaching it with compassion and an open mind is crucial to ensuring patients receive the appropriate care.

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### **About the Author**

Lily Kushnick is a freshman at the University of Illinois majoring in neuroscience. Lily became involved in Brain Matters to learn more about the process of writing scientific articles and about current neuroscience research and innovations. In addition to writing for Brain Matters, she is a member of Healthcare Book Club and volunteers at Carle Hospital.