Mind Over Matter: A Systematic Review of the Role of Pain Neuroscience Education in the Treatment of Chronic Pain



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Mind Over Matter: A Systematic Review of the Role of Pain Neuroscience Education in the Treatment of Chronic Pain

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Mind Over Matter: A Systematic Review of the Role of Pain Neuroscience Education in the Treatment of Chronic Pain

Mind over matter is a common cliche, referring to the idea of having control over a physical condition by way of the mind. The power of the human brain and the complexities of stimuli perception are common themes across the field of neuroscience. With that, there exists a growing body of research pointing to the use of educational strategies, and ultimately the brain's impressive neural plasticity, as a tool to combat chronic pain. Pain Neuroscience Education (PNE) is an approach that aims to provide patients with a deeper understanding of the neurobiological and neurophysiological components of pain perception (Louw, 2016). Shifting the way an individual conceptualizes pain from strictly being interpreted as harmful to a biological process meant to protect the body has been shown to reduce pain intensity, pain behaviors, and disability (Wood & Hendrick, 2018).

The average person's conceptualization of pain does not expand beyond nociception, which is the process by which specialized peripheral nerve fibers detect tissue damage resulting from a harmful chemical, thermal, or mechanical stimulus and transmit this information to the brain to be perceived as pain (Kendroud et al., 2022). However, it is important to recognize the actual definition of pain, as stated by the International Association for the Study of Pain (IASP), is "an unpleasant sensory and emotional experience associated with, or resembling that associated with actual or potential tissue damage" (Bonezzi et al., 2020). This definition contradicts the traditional understanding as a sensation resulting from tissue damage and highlights the importance of recognizing the multiple mechanisms by which pain may be perceived and the role of top-down influences, such as pain-related cognitions, alterations to the sensitivity of central and peripheral neurons, and other factors that contribute to the pain experience.

Adapting a more broad perspective on pain is essential to understanding the effectiveness of PNE. For example, much of the success of PNE in reducing chronic pain is attributed to reductions in central sensitization (CS). CS is a state of hypervigilance within the nervous system, even after a noxious stimulus is no longer present (Wood & Hendrick, 2018). This sensitization of the central nervous system is characterized by increased responsiveness of nociceptive neurons to normal and subthreshold inputs (Louw, 2017). The perception of pain is further potentiated in cases of central sensitization because the increased activity of ascending pain pathways is coupled with decreased inhibition from descending neural pathways (Galán-Martín, 2020). Evidence for this physiological change was discovered through electrophysiological recordings from single biceps femoris α-motoneuron axons in rats (Latremoliere & Woolf, 2009). After being exposed to repeated peripheral noxious heat stimuli, sufficient to generate mild inflammation of the hind paw, these neurons exhibited increased excitability a reduction in action potential threshold, and enlargement of the cutaneous receptive fields even after inflammation had subsided (Latremoliere & Woolf, 2009).

Generalizing these results offers an explanation for pain perceptions under conditions in which there is no actual tissue damage due to alterations in the firing patterns and thresholds of neurons within the pain pathway. PNE thus aims to eliminate central sensitization by targeting brain areas that play a role in, not only, physiological pain modulation, by altering neuronal activity within both the central and peripheral nervous systems, but also an individual's cognitions, emotions, and behaviors, each of these contributes to the experience of pain (Shala et al., 2021). When pain is reconceptualized to be less feared, this shift in cognition can reduce facilitation and promote inhibition of nociception, as well as, alter pain response behaviors (Shala et al., 2021). Overall, PNE offers a solution to the critical issue of chronic pain, that when

implemented into a well-rounded treatment plan, has the potential to be both effective and widely accessible.

Chapter 1: In a World of (Chronic) Pain

Chronic musculoskeletal pain plagues more than 20% of the population, with prevalence only continuing to increase (Galán-Martín, 2020). Estimated reports indicate that 25.3 million adults in the United States experience daily chronic pain (Louw, 2016). These numbers and other significant statistics have led Harvard Health to refer to this critical issue as "The Chronic Pain Epidemic" (Lawrence & Cohn, 2016). The consequences of chronic pain are numerous, affecting not only individuals, but the healthcare industry, workforce, and society as a whole. The effects of chronic pain are best understood through a biopsychosocial lens, manifesting in individuals through changes in physical, mental, cognitive, and behavioral health and overall decreased quality of life (Fine, 2011). Chronic pain also exerts a significant economic burden due to lost working hours and increased expenditure of healthcare resources (Galán-Martín, 2020), costing the United States between $560-635 billion annually (Louw, 2016).

Chronic Pain and Mental Health

Aside from physical suffering, there are many comorbidities that prevail across the population of individuals who experience chronic pain. From a psychological perspective, the rate of psychopathological disorders among people with chronic pain disorders falls within the range of 33% to 46% (Fine, 2011). This is in comparison to the estimated incidence of 10% of people who do not experience pain, or experience pain for shorter durations (Fine, 2011). This includes higher rates of particularly major depressive disorder and suicidal ideation and/or attempts (Fine, 2011). This is not surprising due to the interference of chronic pain in social life, work, sleep, and daily activities (Fine, 2011).

The association between chronic pain and decreased psychological well-being has been an ongoing problem repeatedly confirmed by survey data worldwide. An early large-scale cross-national study of persistent pain collected survey data from representative samples of primary care patients from 15 centers in Asia, Africa, Europe, and the Americas, as part of the World Health Organization Collaborative Study of Psychological Problems in General Health Care (Gureje et al., 1998). Despite variation between centers regarding the prevalence of persistent pain and its relationship to disability, as measured by the "Occupational Role" section of the Social Disability Schedule (SDS), pain sufferers were significantly more likely to have an anxiety or depressive disorder, as indicated by scores on the WHO primary care version of the Composite International Diagnostic Interview (CIDI), across every participating center (Gureje et al., 1998). The results of this study identify psychological disorders as a common correlate of chronic pain, and that this association is observed in a wide range of cultural settings.

Not only does chronic pain affect the mental health and well-being of the person in pain, but the people with whom they have close relationships, such as family members or caregivers. There are several themes that appear to be consistent among families of those suffering from chronic pain. Losses are often reported to be experienced by the family in the form of financial losses or the loss of relationships with other family members or friends or the loss of social activities (West et al., 2012). Chronic pain is also often associated with life changes, such as changes in the emotional or sexual components of relationships between partners, the shifting of family members to take on a “nurse role” or changes in employment status (West et al., 2012) Families with a member suffering from chronic pain also experience emotional turbulence often characterized by feelings of self-blame, anger, resentment, and fear, particularly fear for the future (West et al., 2012). These common emotions of family members also have implications

on the pain sufferer, as guilt is often experienced because of the burden they perceive their pain has placed on their family (West et al., 2012).

Chronic Pain and Cognitive Processes

In addition to the associated costs and implications of chronic pain on mental health, cognitive processes, such as memory and attention, have been shown to be impaired in up to two-thirds of patients with chronic pain (Fine, 2011). The default mode network (DMN) is a group of cortical regions that normally activate to help maintain a restful neurological state and deactivate during task performance (Fine, 2011). However, a study comparing fMRI data of a sample of male and female chronic back pain patients to a sample of healthy individuals while performing a simple visual attention task showed decreased deactivation of the DMN regions in the chronic pain patients in comparison to the healthy group (Baliki et al., 2008). Specifically, it is believed that the anterior cingulate cortex (ACC), a region included in the DMN, plays an important role in the relationship between chronic pain and cognitive impairment. The ACC receives pain signals from the thalamus and, in turn, is believed to be involved in the affective-motivational dimension of the pain experience (Hart, Wade & Martelli, 2003). However, as a region that modulates emotional reactivity and contributes to an executive attentional system, it is hypothesized that the ACC mediates the impact of pain-related distress on cognitive functioning, including the allocation of attentional resources (Hart, Wade & Martelli, 2003). Ultimately, these results demonstrate the widespread cortical implications of chronic pain beyond just perceptual regions.

Chronic Pain and Pharmacology

Not only do the effects of chronic pain pose a societal problem worthy of addressing, but many of the current and popular pharmaceutical treatments have been shown to be ineffective or

are accompanied by costly side effects. In placebo-controlled trials, common medications used in the context of chronic pain management, such as gabapentin, an anticonvulsant often prescribed to treat nerve-related pain conditions, have been found to be ineffective when used long term, yet they are still prescribed due to a lack of alternatives (Borsook, 2012). Physicians are also beginning to shift away from opioids as a pharmacological treatment of chronic pain due to increasing research showing the limited long-term benefits and neurological changes produced by these drugs resulting in the risk of addiction (Borosook, 2012). However, as the stigma of abuse and the health risks of opioid use have gained attention from the general public, the use of over-the-counter (OTC) medications has increased as a popular strategy for the self-treatment of long-term pain (Eaves, 2015). Although portrayed as relatively harmless, serious risks such as hearing loss or liver injury are associated with their long-term use (Eaves, 2015). For example, the CDC estimated that acetaminophen was the leading cause of over 1600 cases of acute liver failure in the US in 2007 (Eaves, 2015). This information further supports why a neuroscience-based strategy may be effective in replacing risky pharmacological treatments of chronic pain and combating this pressing and widespread public health issue.

Chapter 2: The Pain is Temporary… Unless

Pain is an entirely normal, expected, and healthy human experience. Without pain, it would be impossible to recognize and protect the body from potentially harmful stimuli. The current definition of pain put forth by the International Association for the Study of Pain (IASP) is “an unpleasant sensory and emotional experience associated with, or resembling that associated with actual or potential tissue damage” (Bonezzi et al., 2020). More specifically, the IASP defines chronic pain as “pain that lasts or recurs for longer than 3 months” beyond the

initial injury (Bonezzi et al., 2020). It is critical to note chronic pain is defined in terms of duration as opposed to causation. This is because there are a number of pain mechanisms that, if persistent over time, can be the cause of chronic pain (Bonezzi et al., 2020). This definition put forth by the IASP contradicts most people's conceptualization of pain as a sensation resulting from tissue damage and highlights the importance of recognizing the complexities of, especially chronic, pain mechanisms and the role of top-down influences, such as pain-related cognitions. With a more broad definition of pain, it is now recognized that pain experiences can be classified under three identified mechanisms: nociceptive, neuropathic, and neuroplastic pain, all of which may contribute to or result in chronic pain.

Nociceptive Pain

The first pain mechanism that may underlie chronic pain is nociception. Nociception is a subcategory of somatosensation that refers to the neural processing and perception of noxious stimuli, such as tissue injury, extreme temperatures, or chemical exposure by the CNS and peripheral nervous system (PNS) (Kendroud et al., 2022). The resulting perception, and therefore the pain experienced with nociception is dependent on the action potential frequency of the neurons responding to the noxious stimuli, the time interval in between each action potential, and the integration of this information with signals from higher-order brain centers (Kendroud et al., 2022). Nociception is initiated by the detection of a noxious chemical, thermal, or mechanical stimulus by specialized peripheral nerve fibers. These peripheral nerve fibers include myelinated A-delta fibers, which are primarily activated by short-lived mechanical or thermal stimuli, and unmyelinated C-fibers, which typically respond to long-lasting mechanical, chemical, and thermal stimuli (Bonezzi et al., 2020). Once activated, the signal propagates along the length of the fiber which terminates within the dorsal horn of the spinal cord (Steeds, 2009). At this point

the A-delta and C-fibers synapse with second-order neurons which ascend to higher regions of the CNS, via the lateral spinothalamic tract, located in the peripheral white matter of the spinal cord (Steeds, 2009). These ascending tracts eventually reach the thalamus from where nociceptive information is transmitted to and processed as pain within the cerebral cortex most notably, the primary somatosensory cortex (Steeds, 2009). This region of the brain is somatotopically organized, meaning each location on the body corresponds to a specific point within the somatosensory cortex, allowing for the localization of sensory inputs (Steeds, 2009). There is also evidence of nociceptive signaling projections to other brain regions including the amygdala, medial prefrontal cortex (mPFC), anterior cingulate cortex, hippocampus, and nucleus accumbens (NAc) which are hypothesized to be involved in the emotional and behavioral responses to pain (Yang & Cheol Chang, 2019). Once signals are received by the cortex, neuromodulation allows the body to respond to the perceived stressful stimuli by transmitting signals via descending tracts to regulate the ascending input (Steeds, 2009). Specifically, the periaqueductal gray and the nucleus raphe magnus are two key brain regions that contribute to nociceptive modulation via inhibition of neurons within the dorsal horn (Steeds, 2009).

Chronic nociceptive pain, therefore, results from an imbalance between the excitatory and inhibitory signals of these ascending and descending pathways (Steeds, 2009). This imbalance is caused by prolonged or intense exposure of nociceptors to noxious stimuli, for example, chemical mediators released during inflammation, resulting in an enhanced responsiveness of the nociceptive nerve fibers (Scholz, 2014). This process, known as peripheral sensitization, involves a decrease in the activation threshold of nociceptors and upregulation of voltage-gated sodium channels responsible for the firing of action potentials and neurotransmitter release to the second-order neurons within the dorsal horn of the spinal cord

(Scholz, 2014). These neurons react to the rising input with heightened excitability, which has previously been defined as central sensitization (Scholz, 2014) This enhanced depolarization results in the recruitment of additional N-methyl-D-aspartate (NMDA)-type glutamate receptors and therefore a sharp increase in intracellular calcium, triggering signaling pathways and gene expression changes that promote a long-term shift in the activity of nociceptive circuits that resembles long-term potentiation of excitatory transmission in the hippocampus (Scholz, 2014). Altering the activity of neurons within the nociceptive pathways would thus result in the central sensitization characteristics described previously, such as a decreased threshold for firing or increased receptive field size.

Neuropathic Pain

The second type of pain that can result in chronic pain conditions is known as neuropathic pain. The IASP definition for neuropathic pain is “Pain caused by a lesion or disease of the somatosensory nervous system” (Bonezzi et al., 2020). Thus, unlike nociceptive pain, neuropathic pain does not stem from a specific stimulus causing activation of nociceptors, but rather it is the result of damage to the nerves within the PNS or CNS. Because of this, neuropathic pain is typically less localized than nociceptive pain and results in spontaneous pain characterized as shooting, burning, tingling, or numbness, allodynia, which is evoked pain brought on by a nonpainful stimulus such as cold or brushing against the skin, or hyperalgesia, defined as increased pain experienced from a normally pain invoking stimulus (Steeds, 2019). Common causes of neuropathic pain include nerve pressure or nerve damage following surgery or trauma, viral infections, cancer, vascular malformations, alcoholism, neurological conditions such as multiple sclerosis, and metabolic conditions such as diabetes. It may also be a side effect

of certain medications or, occasionally, there may be no identifiable cause, a case termed "idiopathic pain" (Steeds, 2019).

The damage to the nerve fibers within the CNS or PNS that causes neuropathic pain can lead to swelling that alters the gating properties of sodium channels, causing spontaneous ectopic impulses to be generated sans stimuli (Steeds, 2009). Not only are these signals perceived as pain by the CNS, but the damage triggers an innate immune response at the lesion site (Scholz, 2014). Activated microglia release chemical mediators, including brain-derived neurotrophic factor which effectively reduces the inhibitory effect of γ-aminobutyric acid (GABA) and glycine (Scholz, 2014). This disinhibition further enhances the abnormal input from the lesioned nerve and results in hyperactivity and decreased activation threshold associated with sensitization, similar to chronic nociceptive pain (Scholz, 2014). In sum, the outcome is a shift in neuronal activity and descending modulatory pathways that produces a profound imbalance between inhibition and excitation and the potential for neuropathic pain to manifest as a mechanism causing chronic pain (Scholz, 2014).

Nociplastic Pain

More recently, a third pain type, called nociplastic pain, has been identified and understood as a mechanism involved in chronic pain disorders. The IASP defines nociplastic pain as "pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain" (Bonezzi et al., 2020). This term was proposed in 2016 as a mechanistic descriptor for chronic pain states characterized by altered function of the pain-related sensory pathways in the periphery and CNS, but there is a lack of evidence indicating obvious activation of nociceptors or neuropathy (Fitzcharles et al., 2021).

Altered functioning may occur at various levels of the sensory pathway. At the peripheral level, some changes may include minor muscle pathologies, such as local pH changes or abnormal muscle fiber composition, or instances of peripheral sensitization involving alterations in the receptive field of peripheral nerves or elevated cytokine concentrations (Fitzcharles et al., 2021). Within the central nervous system, nociplastic pain may be caused by factors such as glial cell activation, elevated glutamate concentrations, decreased GABAergic transmission, or alterations in the shape and size of grey and white matter regions involved in processing (Fitzcharles et al., 2021).

Nociplastic pain is applicable to a wide variety of clinical conditions that share underlying neurophysiological mechanisms (Fitzcharles et al., 2021). These conditions are often referred to as chronic primary pain conditions, defined as "chronic pain in one or more anatomical regions associated with notable emotional distress or disability that cannot be better explained by another chronic pain condition" (Fitzcharles et al., 2021). Chronic primary pain can be further categorized as chronic widespread pain, including disorders such as fibromyalgia, complex regional pain syndrome, chronic primary headache and orofacial pain, chronic primary visceral pain, or chronic primary musculoskeletal pain (Fitzcharles et al., 2021). Due to malfunctions in the transmission, processing, and modulation of signals within the nervous system, pain symptoms are often accompanied by other CNS-derived symptoms, such as fatigue, sleep, memory, and mood problems (Fitzcharles et al., 2021). Nociplastic pain-based conditions are often more challenging to diagnose due to pain complaints being more difficult to describe, their association with subjective symptoms, and a lack of pathognomic clinical findings or biomarkers (Fitzcharles et al., 2021).

The onset of nociplastic pain spans a diverse range of causes. It is recommended that a biopsychosocial model be used when considering the root of nociplastic pain (Fitzcharles et al., 2021). Triggering factors may include interactions between the environment and gene expression, psychological or emotional stress, or biological factors such as organ-specific infections, such as irritable bowel syndrome, or underlying inflammatory rheumatic diseases (Fitzcharles et al., 2021). Current research is investigating candidate genes that may contribute to a predisposition to nociceptive chronic pain disorders (Fitzcharles et al., 2021).

Although scientists have identified three different mechanisms of pain, it is important to highlight that categorizing pain, especially chronic pain, to one mechanistic group is often an oversimplification. For example, cases of chronic low back pain often have components of nociceptive, neuropathic, and nociplastic pain and can be referred to as a mixed pain condition, which only further complicates the etiology and treatment of such situations. Ultimately, pain, in particular chronic pain, is a complex experience stemming from various underlying mechanisms and levels of transmission within both the PNS and CNS, therefore warranting a multidimensional treatment plan. The persistence of chronic pain is made possible through the plastic nature of the nervous system. PNE offers a strategy that targets this characteristic in order to alter the neuronal connections that promote sensitization and pain-related behaviors and cognitions.

Chapter 3: What is Pain Neuroscience Education

PNE Overview and Implementation

The average person does not have in-depth knowledge of the different types of pain and the role the nervous system plays in regard to pain perception. Most people associate pain with

tissue damage when in reality, pain is far more complicated. The correlation between pain and tissue health emphasized with a biomedical understanding of pain has been shown to lead to increased fear and anxiety (Evidence in Motion, 2020). These negative emotions promote fear-avoidance behaviors and pain catastrophizing (Evidence in Motion, 2020). Specific fears include fear of re-injury or fear of specific movements, referred to as kinesiophobia, or activities, which ultimately leads to disuse, disability, and lowers the threshold at which future pain will be experienced (Leeuw et al., 2007). These defensive escape behaviors reduce fear levels in the short term, however, this creates heightened muscle reactivity and cognitive hypervigilance that can cause the misinterpretation of nonthreatening stimuli, causing persistence and exacerbation of pain (Leeuw et al., 2007). Pain catastrophizing is understood as exaggerated and maladaptive cognitive and emotional ideas regarding actual or anticipated pain that can ultimately increase the likelihood of the feared outcome (Quartana et al., 2009). Both fear-avoidance and pain catastrophizing can result in a cycle that propagates the development of persistent pain. PNE aims to expand a person's knowledge of pain through a biopsychosocial lens and deemphasize the strict correlation between pain and tissue damage (Evidence in Motion, 2020). By reconstructing pain as something not to be feared but as a tool to provide informational feedback from the body, it is possible to alter pain-related behaviors and cognitions, reduce pain intensity and disability and improve overall functioning and quality of life (Louw, 2016).

PNE has been used in clinical practice in various countries including the United States, the United Kingdom, and Australia since 2002 (Pain Neuroscience Education (PNE), 2022). There are a considerable number of methods that can be used to implement PNE into treatment. PNE is primarily delivered verbally in one-on-one settings between patients and physical therapists using metaphors, pictures, flow charts, and books (see Appendix A) (Evidence in

Motion, 2020). Education sessions typically fall within a duration of 15-30 minutes and are held once or twice a week for four to six weeks (Evidence in Motion, 2020). Regardless of the delivery method, the information patients receive focuses on the difference between acute and chronic pain, pain transmission/spreading, factors that impact pain perception, and pain rehabilitation (Robins et al., 2016). Metaphors are a particularly effective way for providers to explain pain biology, outline treatment goals, and help patients reconceptualize the pain problem (Robins et al., 2016). An example of this is considering pain as a broken alarm clock that continues to sound even after a person is awake and attempts to turn it off. This situation parallels continuing to experience pain even when the body is no longer experiencing a threat (Robins et al., 2016). Additionally, The "*Why You Hurt: Therapeutic Neuroscience Education System*," designed by physical therapist and clinical neuroscientist, Adrianne Louw, has become a popular clinical tool in delivering PNE. Through the use of colorful educational flashcards, teaching cues, pain questionnaire cards, and homework cards, all aimed at facilitating, the system provides an innovative and engaging way to help providers execute PNE (Robins et al., 2016).

Group education models have also been considered to allow for a more time- and cost-efficient platform to educate patients with similar needs. This also gives individuals the opportunity to connect with other patients and learn from others' experiences (Robins et al., 2016). However, there are several variables that must be considered in the implementation of PNE in a group setting. This environment may prevent patients from asking questions or voicing concerns, which may be essential for clinicians to assist in a patient's individual reconceptualization of pain (Robins et al., 2016). Group composition, such as the size of the group, homogeneity/heterogeneity, and age must also be considered when evaluating this option (Robins et al., 2016). This suggests a combination of group and one-on-one sessions may be

ideal to increase efficiency under conditions that do not sacrifice the individually tailored care that may be critical for pain treatment (Robins et al., 2016).

PNE and Pediatrics

A major benefit of PNE is its adaptability and potential to serve a wide range of populations. One such group of interest is the application of PNE in children both with and without chronic pain conditions, from the perspective that if children are taught healthier beliefs and attitudes about pain and its treatment options, it may in fact have downstream effects later in life (Louw et al., 2020). Chronic pain in children is often overlooked, despite the fact that approximately 30% of the pediatric population suffers from chronic pain, with headache, abdominal pain, and musculoskeletal pain being the most prevalent types (Pere Bacardit et al., 2021). Children with chronic pain are more likely to experience social, academic, and recreational difficulties as well as impaired family functioning (Pere Bacardit et al., 2021). In addition, individuals experiencing chronic pain during childhood have a higher risk of suffering from chronic pain during adulthood (Pere Bacardit, et al., 2021).

In a study including 668 seventh-grade middle-school students, in which 220 received a PNE lecture designed to increase pain knowledge and promote healthier beliefs regarding pain, 198 received the usual school pain curriculum, and 250 received the PNE lecture followed by two booster sessions (Louw et al., 2020). Prior to, immediately after, and at the six-month follow-up, pain knowledge and fear of physical activity were measured. Additionally, six months after the initial intervention school physical education, recess, and sports attendance/participation, as well as healthcare choices for pain (doctor visits, rehabilitation visits, and pain medication use), were measured (Louw et al., 2020). Students receiving the PNE lecture and booster sessions used 30.6% less pain medication over the 6-month period compared to

those who received no PNE (Louw et al., 2020). The booster session group was also superior to the single PNE lecture for rehabilitation visits in students experiencing pain ($p = 0.01$) and the no PNE group for school attendance for students who suffer from chronic pain ($p = 0.004$) (Louw et al., 2020). These results indicate the ability of PNE to positively influence pain-related behaviors in middle school children.

In examining pediatric chronic pain it is also important to consider the role of caregivers. PNE can also be directed toward parents to alter parental pain-related attitudes, protective behavior in response to their child's pain, and perceptions of the child's functioning (Pere Bacardit et al., 2021). A better understanding of their child's pain may lead to adequate parental supportive behavior, based on the rationale that the child's pain behaviors can be driven by their parents or caregivers (Pere Bacardit et al., 2021). Thus, it is worthwhile to explore how parents or caregivers can be included in the PNE process and how to effectively change their own behaviors regarding their child's pain (Pere Bacardit, et al. 2021). Evidence of the ability to direct PNE toward parents was shown in a study including 27 healthy children, between the ages of eight and twelve, and their parents (Pere Bacardit, et al. 2021). Both the children and their parents attended a 45-minute PNE session designed for children (PNE4Kids), which included an interactive board game to teach pain science to children (Pere Bacardit et al., 2021). Demographic data were collected, and the Neurophysiology of Pain Questionnaire (NPQ), Fear of Pain Questionnaire—Parent Proxy Report (FOPQ-P), Pain Catastrophizing Scale (PCS) (see Appendix B), Pain Catastrophizing Scale for Parents (PCS-P), and the Pain Vigilance and Awareness Questionnaire (PVAQ) were completed by the parents before and after the PNE4Kids session (Pere Bacardit et al., 2021). In response to the PNE4Kids session, significant short-term (1 week) improvements were shown in the NPQ and the FOPQ-P (Pere Bacardit et al., 2021).

Parents' level of pain knowledge and children's fear of pain, reported by their parents, improved after a 45 min PNE4Kids session (Pere Bacardit et al., 2021). Based on these results, PNE4Kids should be further investigated in both healthy child–parent dyads and those with children with chronic pain, as it might be useful to target parents' and children's pain cognitions in both preventative and treatment circumstances.

PNE and Elderly Populations

In addition to the research that has been done in implementing PNE amongst children, PNE has also been investigated in elderly populations. This is especially relevant given that population aging is recognized as a global phenomenon, and that by 2050, one in six people in the world will be above the age of 65 years, up from one in eleven in 2019 (Vicente-Mampel et al., 2022). Additionally, chronic pain is one of the most common symptoms experienced in old age, suffered by at least 45% of elders worldwide (Vicente-Mampel et al., 2022). It is associated with a worse self-perception of health and it is the leading cause of disability among this population. In addition, chronic pain is also associated with lower mental health quality in terms of depression and anxiety, lower quality of life and physical function, and an increased chance of being institutionalized (Vicente-Mampel et al., 2022). Because of these factors, the effectiveness of PNE in older adults is worthy of research.

One recent study investigated the long-term effect (six months) of a PNE program in older adults with multimorbidity and chronic pain (Vicente-Mampel et al., 2022). Fifty participants were randomly assigned to the pain education therapy group and 26 were assigned to the control group (Vicente-Mampel et al., 2022) The experimental group received six, weekly 50-minute sessions focusing on the neurophysiology of pain, while the control group carried on with their usual life (Vicente-Mampel et al., 2022). The results of this study indicated statistically

significant decreases in pain perception in the PNE group, as shown by measures using the visual analog scale (VAS) (Vicente-Mampel et al., 2022). This indicates the use of PNE in isolation may be useful in older adults with chronic pain, however, additional research is needed on how to increase the effectiveness of PNE both alone and in conjunction with other treatments.

PNE and Athletes

Another population to which PNE may offer value is athletes, given high rates of pain conditions with research indicating that up to 65% of athletes experience recurring low back pain (Maguire, Chesterton & Ryan, 2019) and 27% of athletes with overuse injuries, especially those with pain related to tendons, show signs of central sensitization, which can effectively be targeted with PNE (Malfliet et al., 2017). Additionally, PNE offers a perspective that associates pain and psychosocial aspects. Considering psychosocial factors in sports sciences could also be valuable in optimizing strategies for a successful return to play (Malfliet et al., 2017). Recent literature provides evidence that psychosocial factors such as fear and catastrophizing have predictive value in therapy outcomes and the return to sports (Malfliet et al., 2017). This can be justified in that both fear and catastrophizing act as precursors of avoidant behavior, which in turn is associated with consequences such as disability, disuse, and depression (Malfliet et al., 2017). Thereby a vicious cycle arises that does not allow injured athletes to recover and adapt to their situation in an effective way, highlighting a need for a holistic approach to the treatment of sports injuries (Malfliet et al., 2017).

Research on the use of PNE in sports injuries is limited, however, one study investigated the effect of PNE on Sports Therapy and Rehabilitation (STR) students and their knowledge of persistent pain, measured by the Revised Pain Neuroscience Questionnaire, attitudes towards athletes with persistent pain, measured by the Health Care Pain Attitudes and Impairments

Relationship Scale (HC-PAIRS), and their clinical recommendations for athletes with persistent pain, via the use of athlete case vignettes (Maguire et al., 2019). This research was especially motivated by a preliminary survey that found that across a range of undergraduate healthcare degrees, less than 1% of the total curriculum was allocated to pain education (Maguire et al., 2019). The experimental group received a 70-minute PNE session providing information on the neuroscience of persistent pain, the modulating role of psychosocial factors on pain biology, and how this information can be used to inform clinical practice (Maguire et al., 2019). The control group received a red flags session on screening patients with persistent pain (Maguire et al., 2019). The results indicated that post-education, the experimental group showed a significant increase in pain neuroscience knowledge, improved attitude, and was more likely to make appropriate clinical recommendations regarding return to work, exercise, and bed rest, demonstrating the usefulness and value potential of PNE in the field of sports rehabilitation (Maguire et al., 2019).

Impact of Level of Education

As PNE has become increasingly popular in clinical practice an important consideration is how a patient's level of education (LoE) may be a factor. Because PNE is an educational treatment approach consisting of both re-learning, addressing and tackling misbeliefs regarding pain and tissue health, and re-education, teaching neurobiological and neurophysiological processes involved in pain experiences one may assume LoE of the receiver plays a role in the effectiveness of PNE (Bilterys et al., 2021). This was explored in a study including 120 chronic spinal pain (CSP) patients of various levels of education (Bilterys et al., 2021). Results of this study indicated no differences between higher and lower-educated participants for PNE effect on pain-related disability, measured using the Pain Disability Index, and kinesiophobia, measured

using the Tampa Scale for Kinesiophobia (see Appendix C) (Bilterys et al., 2021). These findings suggest that there are no clinically meaningful differences in the effectiveness of PNE between higher and lower-educated people.

Overall, PNE offers patients a renewed sense of confidence in movement and activity, which can utilize the remarkable plasticity of the brain to retrain their nervous systems away from pain to engage in physical therapies that can reduce symptoms, build fitness and combat chronic pain. This demonstrates the significance of treatment perception on its outcome. Knowing the science behind pain can allow patients to reframe their perception of their given care plan to foster an adaptive mindset and behaviors necessary to reduce chronic pain. The high number of various pain conditions and populations that can benefit from PNE supports the need for further research and implementation of PNE amongst both patients and healthcare providers alike.

Chapter 4: Knowledge is Power

Despite being a field of research that has only become more popular within the past decade, the efficacy of PNE has been studied across a wide variety of chronic pain contexts as a form of both treatment and prevention. The extreme diversity of chronic pain conditions and the various methods by which PNE may be incorporated into treatment offers many potential avenues for both research and application. It is equally important to consider the conditions for which PNE is best suited and how it can be delivered most effectively.

PNE and Chronic Musculoskeletal Pain

One of the most researched and promising areas of study in the effectiveness of PNE is in patients with chronic musculoskeletal pain (CMP). CMP affects more than one in five people with the prevalence increasing amongst the general population, becoming the leading cause of

disability (Galan-Martin et al., 2020). Specifically, CSP is the most prevalent type of CMP, often brought on by muscle atrophy and weakness due to inactivity or aging, improper posture or body mechanics during repetitive lifting, poor posture, traumatic injuries such as car accidents or falls, that lead to overcompensation or prolonged inflammation, or overuse injuries that cause stress to the spine and surrounding soft tissue (Galan-Martin et al., 2020). Patients with CMP often have been found to have high levels of kinesiophobia, catastrophism, fear-avoidance behaviors, and disability (Galan-Martin et al., 2020). These findings in combination with the presence of hyperalgesia, allodynia, and generalized pain in CMP patients are evidence for the role of central sensitization, and thus the potential for PNE as a possible treatment option, in cases of persistence of CMP (Galan-Martin et al., 2020).

In a double-blind and randomized clinical trial of patients between 18-70 with CSP, the experimental group (EG) participated in a program that combined group pain neuroscience education sessions carried out by physiotherapist (6 sessions, 10 h) and group physical exercise with playful, dual-tasking, and socialization-promoting components (18 sessions in 6 weeks, 18 h) (Galan-Martin et al., 2020). The control group performed the usual protocol of physiotherapy care performed in primary care. The experimental treatment improved Health-Related Quality of Life (HRQL) assessment scores, considering both physical and mental health components, catastrophism, scores, kinesiophobia, central sensitization, disability, pain intensity, and pressure pain thresholds based on PCS, Tampa Scale of Kinesiophobia (TSK-11), CSI (see Appendix D) and the Roland–Morris disability questionnaire scores (Galan-Martin et al., 2020). Differences between the groups were statistically significant ($p < 0.001$) improvements made by the EG were maintained post-intervention at an 11-week follow-up, demonstrating the promise of PNE as a treatment method for CSP (Galan-Martin et al., 2020). A potential limitation of this study

that should be noted is that the exercise program completed by the EG also differed from the CG, making it impossible to discern the PNE program as the primary factor responsible for between-group differences.

Spinal pain is not the only CMP region that has been studied under PNE treatments. Chronic neck pain is also a prominent subtype of CMP, especially among office workers (Javdaneh et al., 2021). For example, another randomized control trial was conducted including 72 patients between 20 and 50 years of age with chronic nonspecific neck pain allocated randomly between three groups characterized as therapeutic exercises alone, combined therapeutic exercises, and PNE, and a control group that did not receive any intervention during the study but was instructed to maintain the proper position at work and home via informative brochures (Javdaneh et al., 2021). Each program took place three times a week for a total of six weeks (Javdaneh et al., 2021). The disability index, pain catastrophizing, fear–avoidance beliefs, and pain self-efficacy, measured by the Neck Pain and Disability Scale (NPAD), PCS, Fear–Avoidance Beliefs Questionnaire (FABQ), and Pain Self-Efficacy Questionnaire (PSEQ), respectively, were utilized to assess participants before and after the intervention (Javdaneh et al., 2021). Participants who received the combined intervention of both therapeutic exercises and PNE demonstrated a greater reduction in more measurements of disability, pain catastrophizing, and fear–avoidance beliefs than participants who participated in a therapeutic exercise program alone ($p \leq 0.05$) (Javdaneh et al., 2021). No statistically significant differences were demonstrated upon analysis of PSEQ scores between groups, however, the group that received PNE did still show greater improvements following treatment for pain self-efficacy reports (Javdaneh et al., 2021). The design of this study combats some of the limitations of the previous study on patients with CSP, given that the two experimental groups both completed the same

therapeutic exercise program indicating an increased likelihood of PNEs' direct role in improving disability, pain catastrophizing, and fear–avoidance beliefs.

PNE has also been studied under less-specific musculoskeletal conditions such as osteoarthritis (OA). OA is a chronic degenerative disease of the mobile joints characterized by the deterioration of cartilage, formation of osteophytes (bony lumps that cause stiffness), and joint inflammation (Ordoñez-Mora et al., 2022). This disease affects more than 300 million people worldwide, causing pain in joints such as the knees, hips, and hands, with the greatest symptomatology typically reported within the knee joint (Ordoñez-Mora et al., 2022). Due to associations shown between OA and a reduced pain perception threshold and maladaptive pain coping behaviors, the effectiveness of the institution of PNE to OA treatment plans has become a research topic of interest (Ordoñez-Mora et al., 2022). A systematic review study of randomized controlled clinical trials synthesized the results of four articles that implemented PNE ranging between one to six sessions, suggests that there is an improvement for variables such as pain catastrophizing and kinesiophobia of patients who received PNE, however, additional research is needed to address changes in disability and pain intensity (Ordoñez-Mora et al., 2022). The authors of this study note the limitations of a meta-analysis approach, specifically with difficulties in accurately assessing the sum effect size of variables due to the use of various scales and measurement methods across the studies included, and advise further research and implementation of standardized practices for better evaluation of the efficacy of PNE as part of the treatment protocol for both OA and other chronic pain conditions (Ordoñez-Mora et al., 2022).

PNE and Fibromyalgia

Fibromyalgia (FM), a chronic pain disorder reported to affect 4 million people in the United States, is another chronic pain condition that, in the limited research that has been conducted, shows potential to benefit from the incorporation of PNE into treatment (van Ittersum et al., 2014). FM patients experience chronic widespread pain, fatigue, sleeping difficulties, headache, and gastrointestinal problems (van Ittersum et al., 2014). With a lack of specific diagnostic tests or pathognomonic findings, the exact pathophysiological mechanism of FM is largely unknown and patients often struggle for acceptance, recognition, and understanding by others and themselves (van Ittersum et al., 2014). This lack of understanding has made the treatment of FM difficult and inconsistent, often consisting of mitigating its symptoms with drugs or even using invasive procedures since no specific treatment currently exists (Areso-Bóveda et al., 2022). The latest recommendations of the EULAR (European League Against Rheumatism) for treating patients with FM indicate that exercise is the only recommended therapeutic option that is strongly supported by evidence (Areso-Bóveda et al., 2022). If this fails, other individualized alternatives should be explored such as psychological and pharmacological treatments (for severe pain or sleep alterations) and/or multi-modal rehabilitation programs (in the case of severe disability). Additionally, patients who do not clearly understand the processes underlying their symptoms appraise pain as more threatening and develop inappropriate cognitions, catastrophizing, and maladaptive coping strategies (Areso-Bóveda et al., 2022). These cognitive factors imply more pain and disability, less psychological well-being and treatment compliance, and poorer treatment outcome (Areso-Bóveda et al., 2022). On the other hand, being well-informed about the nature of the

disease is thought to reduce anxiety and the threatening appraisal of pain and hence improve patient outcomes (Areso-Bóveda et al., 2022).

In recent years, abundant evidence has been obtained that has defined FM as a Central Sensitization Syndrome (Areso-Bóveda et al., 2022). With this understanding, the interactions between inflammation, genetic, psychological, and behavioral factors contribute to a permanently "hyperalert" nervous system that amplifies sensory stimuli, and results in the symptomatology of FM (Areso-Bóveda et al., 2022). This perspective has indicated the potential benefits of PNE, with the assumption that understanding the neurobiological mechanisms involved in the experience of pain reduces the cerebral perception of threat and that these cognitive changes thus effectively moderate the activation of motor, sympathetic, and neuro-endocrine protection mechanisms responsible for chronic pain symptoms (Areso-Bóveda et al., 2022).

PNE has been studied and shown promise as a treatment for FM patients across a variety of samples and methods. One randomized controlled study included 40 patients in which The experimental group underwent PNE sessions over 6 weeks in addition to pharmacological treatment, and the control group was given only pharmacological treatment (Saracoglu et al., 2021). Functional status, measured by the Fibromyalgia Impact Questionnaire, pain pressure thresholds, and kinesiophobia, measured by the Tampa Scale of Kinesiophobia, were all assessed before the intervention and at the end of the 6th and 12th weeks by the same blinded researcher (Saracoglu et al., 2021). The PNE group had significantly greater improvement than the control group in terms of the mean total scores in the Fibromyalgia Impact Questionnaire and Tampa Scale of Kinesiophobia, as well as significantly greater improvement in the pain pressure

threshold values of the cervical, thoracic, lumbar, elbow and calf regions, thus demonstrating the value of incorporating PNE as an element of FM treatment (Saracoglu et al., 2021).

Similar results were also reported from a multicenter randomized, open-label, controlled trial that was conducted to assess the effectiveness of a structured group intervention based on PNE in patients with FM (Barrenengoa-Cuadra et al., 2021). A total of 139 patients were split between the PNE group, which received seven group sessions of education in the neurobiology of pain, and/or the control group, which received treatment as usual (Barrenengoa-Cuadra et al., 2021). At one year, the patients receiving the structured group intervention were found to have significant amelioration of the impact of the disease based on scores of the Fibromyalgia Impact Questionnaire, the Health Assessment Questionnaire, the Hospital Anxiety and Depression Scale, the Pain Catastrophizing Scale and the Polysymptomatic Distress Scale as compared with only treatment as usual (Barrenengoa-Cuadra et al., 2021). These findings are particularly significant due to the implementation of PNE as a group intervention, demonstrating this method to be a more cost and time-efficient method, while maintaining beneficial treatment outcomes (Barrenengoa-Cuadra et al., 2021).

PNE and Chronic Pain Prevention

The effectiveness of PNE as a preventative measure to reduce chances of developing chronic pain. A situation in which the use of preventative PNE is particularly practical is prior to cancer treatments. Chronic pain is one of the most common long-term side effects of cancer treatments with about one-third of cancer survivors (34.6%) reporting having chronic pain (Simon, 2019). That is almost double the rate in the general US population (Simon, 2019). One study on the relationship between providing PNE and chronic pain of cancer survivors, of seven

different cancer varieties, provided a 30-45 minute one-on-one education session with a physiotherapist, and an information leaflet to 30 cancer survivors (Pas et al., 2019). The sample consisted of 24 women and 6 men, with a mean age of 62.97 years and breast cancer being the most prevalent cancer type (Pas et al., 2019). Participants were educated on the overall physiology of the nervous system and pain, characteristics of acute versus chronic pain, the purpose of acute pain, how acute pain originates in the nervous system, how pain becomes chronic, and potential sustaining factors of persistent pain, such as emotions, stress, pain cognitions, and pain behaviors (Pas et al., 2019). At baseline and two weeks after the PNE, variables including pain intensity, pain catastrophizing, and health-related quality of life were measured using the Visual Analogue Scale (VAS), the PCS, and the Short Form-36 Health Status Survey (SF-36) (Pas et al., 2019). Researchers found a significant decrease in pain intensity and two of the three subscales, rumination, and helplessness, of pain catastrophizing significantly decreased following PNE as well (Pas et al., 2019). Health-related quality of life did not show significant change following PNE and the study noted the need for verification of results with a larger randomized, controlled trial (Pas et al., 2019).

PNE has also been studied in cancer patients undergoing surgical procedures. An example of this is the use of PNE, as opposed to traditional biomedical education (BME), which focuses primarily on anatomical structures and tissue histology, to reduce the CS-related symptoms of persistent post-mastectomy pain in breast cancer patients. In a retrospective case-controlled study of 118 patients, 58 who received BME combined with physiotherapy and 60 patients who received PNE combined with physiotherapy. One year after surgery, pain intensity, and interference were measured via the Brief Pain Inventory (BPI), CS-related symptoms were measured via the Central Sensitization Inventory (CSI), and pain catastrophizing

was measured with the Pain Catastrophizing Scale (PCS), which were all significantly lower in the PNE group than in the BME group (Manfuku et al., 2021). These results support that PNE offered patients a better outcome of pain management and reduced functional disability and CS-related symptoms following surgery (Manfuku et al., 2021).

Limitations and Effective Delivery

It is important to note that not all research has supported the efficacy of PNE. For example, a study exploring the effectiveness of a newly developed Pain Neuroscience Education program for children (PNE4Kids) with functional abdominal pain disorder (FAPD) showed no significant between-group differences were found between children who participated in both hypnotherapy (usual treatment) and the PNE4Kids program versus hypnotherapy alone (Pas et al., 2020). However, the author notes several limitations of this study and despite the lack of indication of the benefit of PNE4Kids, encourages further research, especially considering there were no worsening effects (Pas et al., 2020). Future research should also be pursued considering the efficacy of PNE4Kids in significantly changing pain-related knowledge and fears of parents and children in the previously mentioned study (Pere Bacardit et al., 2021). Differences in these results may suggest the effectiveness of PNE4Kids in altering cognitions, but not causing significant changes in already present pain symptoms.

Likewise, the methods by which PNE can be delivered may be somewhat limited in order to produce meaningful changes in patients' pain experience and well-being. Most research has focused on PNE delivery with at least some direct contact between the healthcare provider and patient, even if education is supplemented by additional resources. Research examining the effectiveness of written education about pain neuroscience has not been well studied, the findings of a double-blind, multicenter randomized controlled trial comparing written pain

neuroscience education with written education about relaxation techniques in 114 patients with FM revealed that written pain neuroscience education only slightly improved illness perceptions of patients with FM, but it did not impart clinically meaningful effects on pain, catastrophizing, or the impact of FM on daily life, as evidenced by scores on the revised Illness Perception Questionnaire, Pain Catastrophizing Scale, and Fibromyalgia Impact Questionnaire (van Ittersum et al., 2013). The written pain neuroscience education was comprised of a booklet with pain neuroscience education plus a telephone call to clarify any difficulties, while the relaxation group received a booklet with relaxation education and a telephone call (van Ittersum et al., 2013). The results of this study indicate the importance of face-to-face sessions of PNE as a requirement to produce meaningful change (van Ittersum et al., 2013).

The need for face-to-face PNE sessions can likely be attributed to the fact that face-to-face sessions allow for patients' appreciation and understanding of the information can be checked, and consequently, education can be adjusted to the individual patient's needs (van Ittersum et al., 2013). Additionally, nonspecific factors, such as the patient's emotional processing of the encounter with the healthcare professional, the quality of the therapeutic alliance, empathic understanding from the clinician, and patients' treatment preferences, have been found to enhance the treatment effect (van Ittersum et al., 2013). Thus in order to optimize the outcomes of PNE, education sessions should be patient-tailored, taking into account the specific psychosocial factors and cognitions of the individual patient that can therefore be altered to have top-down effects, reducing the patient’s pain experience and symptoms of central sensitization (van Ittersum et al., 2013). Despite being more cost-effective and less time-consuming, information booklets with written education about pain neuroscience are best

used to reinforce treatment sessions or to inform patients' significant others (van Ittersum et al., 2013).

The former research suggests it is not only the information provided, but how the content is delivered and the importance of the therapeutic alliance in establishing the efficacy of PNE. Motivational Interviewing (MI) is a strategy with goals that align with those of PNE and by integrating the two techniques, the informational content of PNE may be more effectively delivered to optimize the patient care experience, treatment outcome, and the comprehensiveness of the pain management program (Nijs et al., 2020). MI is a communication process in which the health care professional is supportive, empathetic, positive, and hopeful and aims to strengthen the patient's personal commitment and treatment adherence by respecting the individual's autonomy and assisting them to reach a specific goal by exploring personal intentions or reasons for change (Nijs et al., 2020). MI is a strategy that originates from the field of alcohol and other substance abuse and has since been tested and applied to a variety of patient populations, including obesity, arthritis, and cancer to promote behavioral changes and increase treatment adherence (Nijs et al., 2020). It is important to emphasize that MI is not a separate treatment component or treatment module; on the contrary, MI is a communication style that should be integrated throughout a given treatment (Nijs et al., 2020).

Integrating MI and PNE would begin by obtaining specific consent from the patient to receive PNE (Nijs et al., 2020). This would result in the patient being more engaged and receptive to the message and would prevent a rupture in the therapeutic alliance in the case that the patient may accuse the provider of thinking that the patient's pain is "all in their head" when proper MI based communication does not occur prior to PNE (Nijs et al., 2020). The MI approach may also be taken while delivering informational content of PNE, using the MI

strategy of elicit-provide-elicit (Nijs et al., 2020). In this format the provider would inquire about the patient's already existing knowledge, provide the new information and then ask the patient to make connections between what they knew and what they learned (Nijs et al., 2020) An example of this would be to first ask patients about their thoughts on the role of stress in their daily pain experience (elicit); ask permission to explain why stress influences pain and how coping skills may be used to address those stressors (provide); then ask patients about their thoughts on this new information (elicit) (Nijs et al., 2020). Using this strategy of information exchange builds on patients' personal knowledge and experience, assesses their understanding of the new information, and allows for feedback in a nonconfrontational manner (Nijs et al., 2020). Overall, the learning objectives of PNE, therefore, focus on decreasing the threat value of the pain experience, and increasing the patients' knowledge of pain, whereas MI is more focused on inviting a person to engage in a behavioral change (Nijs et al., 2020). Such a behavioral change in patients with chronic pain can potentially be facilitated and accelerated through PNE supplemented with MI.

Overall the scope of PNE research is rapidly expanding. In addition to the studies already mentioned, PNE has been demonstrated to be promising in showing improved patient outcomes in many other conditions such as frozen shoulder (Sawyer et al., 2018), migraines (Minen, et al., 2021), and chronic plantar fasciitis (Mills et al., 2020). Although not included in this review, PNE is also being studied in instances of acute pain as well. The studies discussed in this section support the effectiveness of PNE, particularly in regard to reducing pain intensity, central sensitization-related symptoms, and maladaptive pain behaviors, as well as improving functioning and quality of life. More research is needed to determine the most effective timeline, strategies, and situations in which PNE should be offered.

Chapter 5: The Best of Both Worlds

Given the complex nature and etiology of chronic pain, it makes sense that numerous strategies for treatment have been implemented, some of which include pain management by medication, patient education, ergonomic training, and physical therapy (Scascighini et al., 2008). It has been shown that multidisciplinary interventions are more successful, in contrast to no treatment or standard medical treatment, especially among patients suffering from fibromyalgia and chronic back pain (Scascighini et al., 2008). Most studies investigating the effectiveness of PNE do not implement PNE as the only form of treatment but rather as an adjunct to another form of care, mainly physical therapy. As a stand-alone treatment, PNE has been found useful in improving kinesiophobia and pain catastrophizing, however, this is not the case for pain intensity and disability (Louw et al., 2020). With this consideration, PNE is most effective when supplemented by additional treatment, such as movement-based interventions (Louw et al., 2020)

According to the American Physical Therapy Association (APTA), "physical therapists are movement experts who improve quality of life through prescribed exercise, hands-on care, and patient education." The goals of physical therapy (PT) closely align with those of PNE including improved quality of life, mobility and functioning, pain management, and reduced disability (APTA). In relation to chronic pain, the mechanistic evidence of PT also correlates to PNE. It has been demonstrated that exercise-based therapies activate endogenous inhibitory systems in the central nervous system, reduce central excitability, and alter ion channel expression of nociceptors to effectively combat persistent pain (Louw et al., 2021).

PNE and Manual Therapy

Despite the apparent compatibility of PNE and PT, there is some opposition to the incorporation of PNE into PT, particularly in conjunction with an area of physical therapy in which a biomedical model is exceptionally prevalent: manual therapy (Louw et al., 2021). Manual therapy is a "hands-on" approach that involves direct manipulation and mobilization of muscles and joints (Louw et al., 2021). The contrast between manual therapy and PNE, as considered a "hands-off" approach, has resulted in clinicians categorizing patients as either needing to receive PNE (with no hands-on) or hands-on with no PNE. The primary argument for the need for categorization is that manual therapy, or PT in general, may shift the patient's focus back to tissue damage as the source of pain, conflicting with the ideas of PNE (Puentedura & Flynn, 2016). However, under a model of central sensitization in situations in which a patient's nervous system has become hypervigilant, PNE has been found to be beneficial when paired with manual therapy (Louw et al., 2021).

Manual therapy consists of a variety of techniques including manipulations, mobilizations, and massages that target desired outcomes such as increased range of motion, re-alignment of soft tissues, improved circulation, and decreased muscle spasms and pain (Bialosky et al., 2009). When considering the effects of manual therapy, it is also important to note the complex interplay between the musculoskeletal and nervous systems, suggesting that manual therapy exhibits neurophysiological effects of its own. A more comprehensive view of manual therapy recognizes the implications of a mechanical stimulus on the peripheral nervous system and therefore ascending and descending pathways to and from the brain mediated by the spinal cord (Bialosky et al., 2009). This interaction between an applied external force and the central nervous system greatly expands the potential of manual therapy to have effects on pain

modulatory effects within the spinal cord that target central sensitization by a similar mechanism to PNE (Bialosky et al., 2009). These pain modulatory effects are evidenced by studies that report patients that experience hypoalgesia, and therefore a decreased perception of pain, following manual therapy, due to descending inhibitory effects (Bialosky et al., 2009). Overall, the effects of manual therapy on the central nervous system further support the argument for the use of PNE and PT in concert with one another.

In cases of chronic lower back pain (CLBP), the application of manual therapy alone rarely results in a long-lasting reduction of pain or regain of function (Puentedura & Flynn, 2016). In recent years, manual therapists have become more aware of the "top-down" effects of pain production, which include a patient's beliefs and cognitions regarding their pain, and how manual therapy can be used to induce changes in these effects (Puentedura & Flynn, 2016). The ability of manual therapy to alter top-down pain production relies on mechanisms involved in gate control theory. The rationale behind this stems from the idea that a non-noxious sensory stimulus, in this case, a joint mobilization or massage technique performed by the physical therapist can inhibit a noxious stimulus at the level of the spinal cord, thus "closing the gate" and preventing the painful stimulus from being perceived (Puentedura & Flynn, 2016). By combining this concept with PNE, a patient's interpretation of stimuli and pain expectations can be altered in a way to best support the top-down changes generated by manual therapy (Puentedura & Flynn, 2016).

The combination of manual therapy and PNE is also supported by the effects of pain and neuroplasticity on the brain's "body schema" or the somatosensory system which includes a cortical representation of the "self" (Puentedura & Flynn, 2016). Studies have found chronic pain patients show impairments in body laterality judgments and tactile acuity, indicating a disrupted

body schema (Puentedura & Flynn, 2016). Based on these considerations, PNE combined with an emphasis on the top-down components of manual therapy has been able to improve tactile discrimination and conception of the body schema to reduce pain and increase mobility (Puentedura & Flynn, 2016).

PNE and Exercise Therapy

Manual therapy is not the only form of PT that is shown to improve patient outcomes with the inclusion of PNE. PNE has also been proven to be beneficial when combined with physical exercise (Galan-Martin et al., 2020), aquatic therapy (Pires et al., 2014), and dry needling (Valiente-Castrillo et al., 2021). In a review of 13 articles, with five investigating education-only approaches and eight combining PNE with movement-based therapies, the latter was found to have a more favorable response in patients (Louw et al., 2016). Thus, current research supports the argument that PNE and physical therapy are not only compatible but that a multimodal treatment approach to chronic pain is more effective.

Advised movement and activity in the management of pain conditions are nearly ubiquitous across all treatment guidelines (Blickenstaff & Pearson, 2016). As support and interest in PNE have continued to grow, healthcare providers, particularly physical therapists, have sought for ways to reconcile these two components of treatment. One perspective that seeks to emphasize the consistency between education and movement-based therapies suggests that movement be conceptualized as kinesthetic education (Blickenstaff & Pearson, 2016). Under this model pain neuroscience education would first be implemented to eliminate maladaptive pain-related cognitions, such as catastrophizing and kinesiophobia, and promote endogenous pain inhibitory responses (Blickenstaff & Pearson, 2016) By doing so, the threat associated with movement would be decreased and by engaging in subsequent prescribed movement-based

exercises would further solidify the patients newly established pain beliefs (Blickenstaff & Pearson, 2016). In order for movement to best enhance the effects of PNE and vice versa, it is important that movement is integrated via a graded exposure strategy, beginning with more tolerable exercises and progressing over time (Blickenstaff & Pearson, 2016). Beginning with more tolerable movements decreases the risk of negative experiences with movement that would threaten new pain beliefs and diminish the patient's attitude toward recovery. This framework proposes PNE as a way to enhance traditional exercise-based therapies by offering a treatment that engages both the mental and physical realms of a patient to enforce desired behavioral changes that favor recovery and improved functioning.

PNE is Not Just for Patients

Research has also shown that PNE can be beneficial toward treating chronic pain conditions indirectly via the education of physical therapists, as opposed to direct patient education. Studies investigating the quantity and quality of instruction related to pain and the pain experience suggest a lack of consistency and little time that is dedicated to the understanding of the pain experience, particularly outside of a traditional biomedical approach (Talmage et al., 2020). Considering it is well established that chronic pain is multi-factorial, a more expansive view based on the principles of PNE, including the psychological, social, and behavioral components of the pain experience should be viewed as a necessary component of the curricula used to prepare health care professionals, such as physical therapists (Talmage et al., 2020). Incorporating PNE into the physical therapy education curriculum has been shown to enhance healthcare providers' ability to effectively classify patients with chronic pain states, and thus deliver more appropriate treatment. Furthermore, studies have shown that healthcare providers who have been taught PNE demonstrate increased knowledge of pain, are positively

impacted in their attitudes and beliefs regarding chronic pain, and they become more empathetic and compassionate towards people with chronic pain (Louw et al., 2022).

A recent study involving 49 Doctor of Physical Therapy (DPT) and Physical Therapy Assistant (PTA) students at Arkansas State University found that following participation in one 45-minute PNE lecture, there was a significant improvement post-lecture in student's scores on both the Neuroscience Pain Questionnaire (NPQ) and Health Care Providers Pain and Impairment Relationship Scale (HC-Pairs), that were administered pre and post-lecture (Talmage et al., 2020). The NPQ was re-administered at a 6-month follow-up, at which there was no significant difference between immediate post-NPQ and NPQ at 6 months, indicating that the students successfully retained the knowledge gained from the lecture (Talmage et al., 2020). These improvements in NPQ and HC-PAIRS scores indicate a single, isolated PNE lecture to be effective in increasing knowledge about chronic pain and the nociceptive pathway, as well as improving care providers' attitudes and beliefs towards populations with chronic pain and how it relates to disability and impairment (Talmage et al., 2020). Additionally, the graduate students (DPT) were given case vignettes to challenge their clinical decision-making skills in response to exposure to PNE (Talmage et al., 2020). The results of this found the DPT group was able to apply their understanding of chronic pain to effectively respond to clinical scenarios with a mean score of 81% correct, demonstrating the potential of PNE to improve clinical assessment and decision-making (Talmage et al., 2020).

Another way PNE is able to be provided to physical therapists is through the use of continuing education programs. A study was conducted to explore the impact of 25 licensed physical therapists attending a self-paced 3-hour online PNE program on low back pain (LBP) patient outcomes and clinical practice patterns (Louw et al., 2022). The program used images

metaphors and examples to provide information on peripheral sensitization, central sensitization, biopsychosocial factors associated with pain, threat appraisal of the brain, nociception, stress and endocrine responses to pain, and various therapeutic endogenous strategies to ease pain (Louw et al., 2022). Despite finding no significant difference for change in pain scores, measured using the numeric pain rating scale (NPRS), at discharge for patients treated after therapist continued education training, patients did demonstrate significant improvement in their disability scores, measured using the Oswestry Disability Index (ODI) (Louw et al., 2022). Additionally, after completing the continuing education training, for each episode of care, therapists tended to use fewer total visits and billed fewer units per visit (Louw et al., 2022). These findings suggest that not only may PNE improve patient condition upon completion of physical therapy, but may offer a strategy for increasing the time and cost efficiency of physical therapy sessions. The delivery of PNE via an online platform also highlights the accessibility of this information and the multitude of ways PNE can be taught to both clinicians and patients.

Chapter 6: Oh the Places PNE Will Go

PNE Is Economical

The integration of PNE as a component of regular clinical practice has the potential to not only improve the quality of life of millions of individuals, but to reduce the societal burden created by widespread chronic pain. PNE shows promise in relieving some of the economic stress and consumption of healthcare resources rooted in the issue of chronic pain. A study that integrated PNE into the rehabilitation for lumbar radiculopathy patients showed that one year after surgery, the group that received PNE spent 45% less on health care in the year following surgery and spent an average of over $2000 less seeking help for their persistent pain and

disability (Louw et al., 2016). The Health Policy Institute of Georgetown University, reports chronic back pain as a leading cause of missed work days, attributing to an estimated 83 million work days per year (Shirey & Rogers, 2019). The population of US citizens suffering from back pain has also been reported to have lower annual income and higher rates of unemployment (Shirey & Rogers, 2019). With more research on the most cost-efficient and effective methods of the clinical use of PNE, it is possible to combat the economic load presented by chronic pain.

PNE as an Alternative to Pharmaceuticals

The use of PNE also offers a possible chronic pain treatment alternative to pharmaceutical strategies, such as the prescription of opioids that not only have been shown to be ineffective in the long-term treatment of pain, but pose dangerous side effects or risk of addiction. Despite the passing of more intense regulation of opioid prescription within the past decade, opioid use disorder (OUD) and opioid addiction remain at epidemic levels in the U.S. and worldwide (Azadfard et al., 2022). In addition, three million US citizens and 16 million individuals worldwide have had or currently suffer from OUD (Azadfard et al., 2022). The shift away from opioids and toward nonpharmacological therapies for the treatment of chronic pain has posed challenges for healthcare practitioners and patients. Reduction of medication-based chronic pain practices requires shifting the focus of treatment from completely eliminating pain to minimizing the impact of pain on quality of life (Wenger et al., 2018). These ideas of altering pain expectations and understanding pain as a normal experience align with the central themes of PNE. In order to be effectively put into practice, providers, such as physical therapists, must adopt an understanding of the neuroscientific mechanisms of chronic pain, the biopsychosocial components of chronic pain management, and issues related to opioid use (Wenger et al., 2018). This knowledge, partnered with good communication skills, allows for an interdisciplinary and

individualized approach to chronic pain management that is especially critical for patients undergoing the opioid tapering process (Wenger et al., 2018).

Recent PNE research has specifically included individuals who are dependent on or prescribed high doses of opioids. One case study was conducted investigating a 75-year-old female with chronic lower back pain (CLBP), who had been taking a high dosage of opioids for 15 years that, in combination with her chronic pain, were determined to be contributing to her symptomatology of acute episodes of nausea, vomiting, abdominal pain, and shortness of breath (Agarwal et al., 2020). Researchers paired physician-delivered PNE with opioid tapering and found at the end of the 12-week period, the patient's self-reported back pain rating decreased from 7/10 to 0/10, and opioids were completely abolished (Agarwal et al., 2020). Both of these positive results were still intact at the final six-month follow-up. PNE sessions were between 25 and 45 minutes and utilized resources including metaphors, the Why You Hurt card system, and YouTube videos (Agarwal et al., 2020). The medication was tapered according to physician dictation based on symptom reports over the course of seven appointments (Agarwal et al., 2020). Given the nature of this study examining the results of only a single patient, the results should not be generalized to a population; however, this case study indicates that research exploring PNE as a non-pharmacological alternative or as a tool to reduce opioid use in patients who have relied on pharmaceuticals as a long-term solution for pain management, is worthwhile to explore further with studies of larger sample sizes.

PNE directed to healthcare providers may be an alternate mechanism by which to reduce the use of and dependency on pharmaceuticals in chronic pain treatment. There are various opinions on what it will take to curb the pain and opioid epidemic, however, it is generally agreed upon that interventions must begin earlier, taking an "upstream" approach to the issue,

meaning providers at the initial point of patient contact must shift away from the mindset that pain should be treated exclusively by means of pharmacological interventions, especially narcotics. One such group that may be effectively targeted by such intervention is Physicians Assistants (PA). One study focused on how PNE may alter the beliefs and treatment choices of a convenience sample of PA students after attending a 2-hour PNE lecture (Louw et al., 2020). Following the PNE lecture, there was a significant shift in decreasing the choice of medical interventions and pharmaceutical use and increasing alternative pain strategy interventions (Louw et al., 2020). Further, non-pharmaceutical treatments shifted towards cognitive and active movement approaches, such as mindfulness, relaxation, physical therapy, psychology, and cognitive behavioral medicine, and away from passive treatments, such as massage therapy and chiropractic care (Louw et al., 2020). In addition, PA students were less likely to recommend an orthopedic surgeon to treat chronic pain following the PNE lecture (Louw et al., 2020). If this shift in treatment plans was recognized by an increased number of providers, the result would be a widespread reduction in healthcare expenses associated with chronic pain, as well as reduced rates of drug addiction and dependence.

PNE is Accessible

PNE is still a relatively new practice in the world of chronic pain management. Research has a long way to go in determining the most effective and efficient methods. Especially in the age of the internet, the lack of physical contact involved with PNE, makes this form of treatment incredibly accessible, even virtually. For example, a study was done demonstrating reduced kinesiophobia in patients with chronic neck pain who participated in virtual PNE sessions during the COVID-19 pandemic (Khosrokiani et al., 2022).

Despite being most effectively applied by trained clinicians with experience in treating chronic pain, PNE is becoming increasingly more accessible to the general public (Pain Neuroscience Education (PNE), 2022). In 2018, a systematic review was conducted to examine the availability, characteristics, and content of YouTube videos addressing the neuroscience of pain (Heathcote, 2019). 106 unique videos were found to meet the inclusion criteria of being less than ten minutes, in English, and including information regarding the neuroscience of pain (Heathcote, 2019). Almost three times as many videos that met the inclusion criteria were posted within five years prior to the search compared to those posted 5–10 years prior to the search, highlighting the increasing use of YouTube as a tool for disseminating information about pain (Heathcote, 2019). With this search taking place now five years ago and PNE still being a relatively new strategy, it can only be assumed this number would be significantly larger if the review were done today (Heathcote, 2019). Accessibility to these videos can be taken advantage of in both a clinical and at-home setting and can be an effective and cost-efficient resource for an interdisciplinary approach to chronic pain. This study was limited in that it did not address the extent to which patients find the videos engaging and whether they are effective in promoting effective learning and behavior change, thus these are areas that should be addressed in future research.

The accessibility of PNE is also increasing to a greater number of populations via various cultural adaptations. Being a relatively new institution within clinical practice, PNE is still mainly restricted to Caucasian patient populations, and, specifically mainly to populations in North America, Australia, Europe, and Canada (Orhan et al., 2018). However, due to the fact that chronic pain is a global issue, considerations in the variations of pain perceptions, beliefs, and related outcomes among different population groups, the development, and research of

culture-sensitive PNE materials is warranted (Bashir Mukhtar et al., 2021). Furthermore, cultural sensitivity is defined by two dimensions: surface and deep structures. Surface structure involves matching intervention materials and messages to observable superficial characteristics of the target population which may involve using people, places, language, clothing, etc. that are familiar to and preferred by the target audience, whereas the deep structure encompasses the integration of cultural, social, historical, environmental, and psychological factors that influence the target health behavior in the proposed target population (Bashir Mukhtar et al., 2021).

The first cultural adaptations to PNE to be researched and developed were intended for use by first-generation Turkish patients with chronic pain. As one of the largest migrant groups in Europe, it has been reported that first-generation Turkish migrants, especially, struggle to integrate fully into new societies because of significant language restrictions, different cultural backgrounds, and lower socioeconomic status, all of which consequently impede access to healthcare facilities and programs (Orhan et al., 2018). In prior literature, evidence has indicated differences in pain beliefs, cognitions, perceptions, and behaviors between patients of Turkish origin and native patients (Orhan et al., 2018). For example, when compared to native patients, Turkish migrants take less responsibility for the treatment of their diseases, believe they have a lower capacity for healing, and display greater external locus of control, meaning they tend to believe outcomes are the result of factors such as fate or luck as opposed to being within the realm of ones' own control (Orhan et al., 2018). Furthermore, it has been reported that Turkish patients more likely prefer to use passive coping strategies such as thermal agents, massage, and herbal remedies (Orhan et al., 2018). Thus, the application of PNE by using more simple methods, patients' native language, and examples related to Turkish culture may be necessary in order to be implemented effectively (Orhan et al., 2018).

Under these considerations, Dutch researchers recruited ten participants (eight international health professionals and two first-generation Turkish patients with chronic pain) were recruited to complete a three-round modified Delphi study to reach a consensus on the content and compatibility of culturally-sensitive in-clinic PNE teaching materials and a home education leaflet for Turkish patients (Orhan et al., 2018). After editing the teaching materials and the home education leaflet based on the experts' suggestions and opinions from Round 1 and Round 2, an acceptable agreement level was achieved in Round 3 on the culturally sensitive PNE for Turkish patients (Orhan et al., 2018). This modified Delphi survey may provide a direction for future research to determine the effectiveness of culturally sensitive PNE in Turkish patients when compared to standard translated materials and a framework for additional variations to be produced (Orhan et al., 2018) The same methods of the modified Delphi survey have been used several times since this original study to adapt PNE to various cultures and languages. Notably, an adaptation was put forth for Hausa-speaking patients with CSP (Naziru et al., 2021). This study was unique in that it was the first time PNE was translated into an indigenous African language as well as the use of an internet-based Delphi survey, demonstrating the increasing flexibility and accessibility of PNE (Naziru et al., 2021).

Future Research and Conclusions

Future studies should focus on standardizing the strategies used to deliver PNE and examining individual differences in the effectiveness of PNE interventions based on factors such as sex, medical history, age, culture, and pain location, description, and etiology. With PNE only gaining popularity within the past decade or so, additional investigations should be done to determine the long-term outcomes of PNE in managing chronic pain both as an isolated treatment and in combination with manual and exercise-based therapies.

The current literature suggests a promising future for PNE. PNE has proven applicable across countless populations and conditions, including, but not limited to, children, athletes, and chronic musculoskeletal, fibromyalgia, and cancer patients, showing the versatility and broad scope of this treatment strategy. Given its accessibility and low associated costs, PNE also has the ability to reduce chronic pain-related healthcare expenditures and pharmaceutical usage. It would be extremely unrealistic to consider PNE as the solution to the worldwide issue of chronic pain, however when used appropriately and in supplement to additional pain management strategies, increased use of PNE may significantly improve patient outcomes and reduce the stress chronic pain puts on healthcare resources and providers.

A utopian vision of the future of chronic pain treatment would be to make up-to-date, evidence-informed information knowledge about our body's function, including pain science, a part of the normal school curriculum. This may be wishful thinking, but an effective first step towards this would be to target the education of healthcare providers. Even without offering formal PNE sessions to patients, practitioners with a deeper knowledge of the neuroscience of pain can communicate information about pain more effectively, deliver more well-rounded care and hopefully make a positive impact on the lives of those suffering from chronic pain.

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Yang, S., & Chang, M. C. (2019). Chronic Pain: Structural and Functional Changes in Brain Structures and Associated Negative Affective States. *International journal of molecular sciences*, 20(13), 3130. https://doi.org/10.3390/ijms20133130

Appendix A

Graphics Used for Pain Neuroscience Education

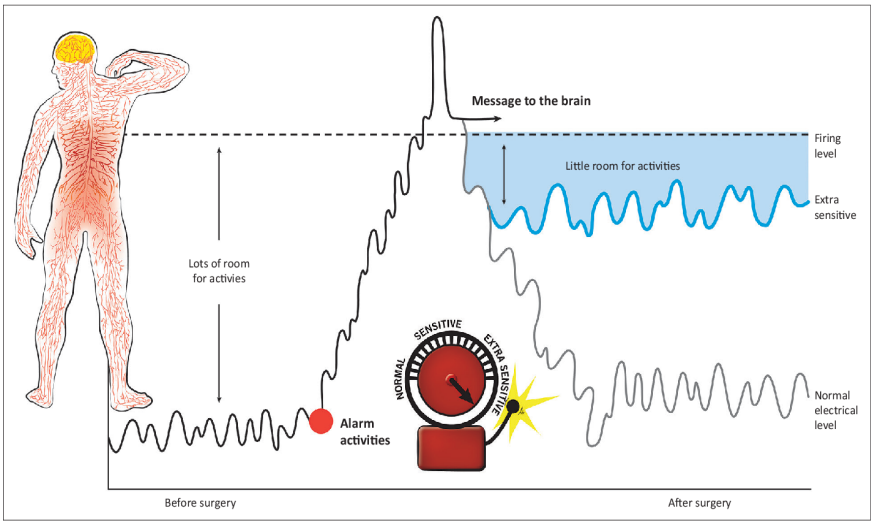

Figure 1. Picture used to explain central sensitization using the metaphor of an extra-sensitive alarm and the way this inhibits a person's level of functioning.

Louw, A., Puentedura, E.J., Diener, I., Zimney, K.J., & Cox, T. (2019). Pain neuroscience education: Which pain neuroscience education metaphor worked best? *The South African Journal of Physiotherapy, 75*.

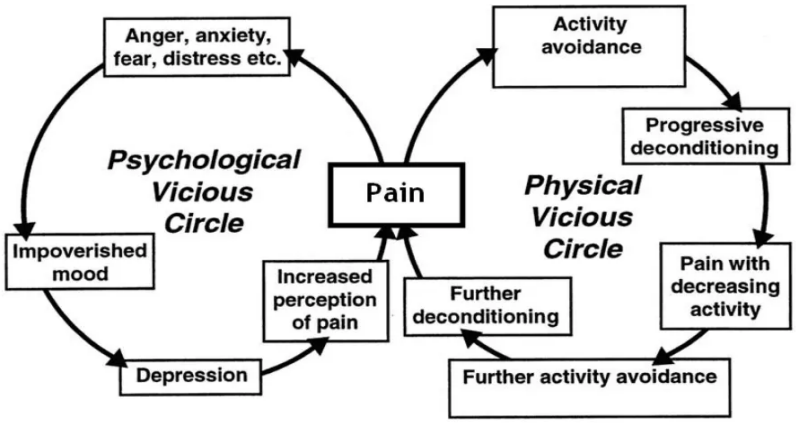

Figure 2. Diagram used to depict the various psychological and physical factors that influence a person's pain experience.

Amar, A. (2022, September 27). *Breaking the pain cycle*. AMS Clinic. Retrieved March 21, 2023, from https://amsclinic.ca/blog/breaking-the-pain-cycle/

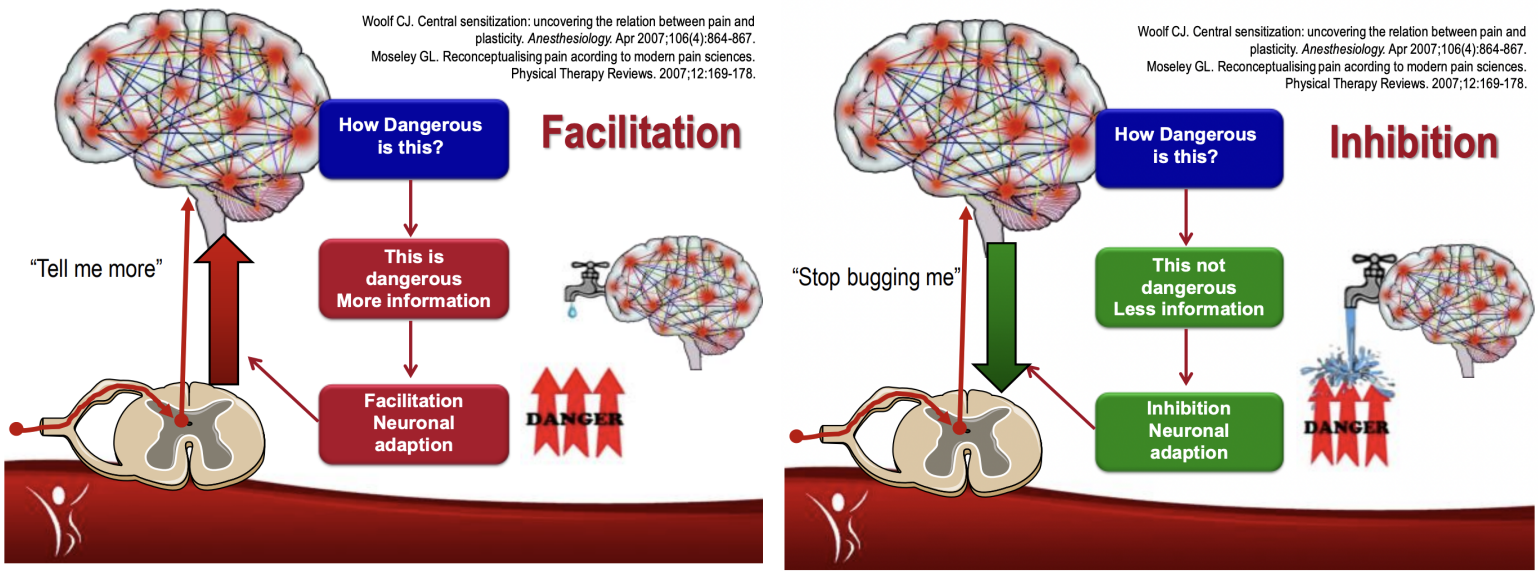

Figure 3. Diagram representing how cognitions may facilitate or inhibit persistent pain signals via descending signals to the spinal cord.

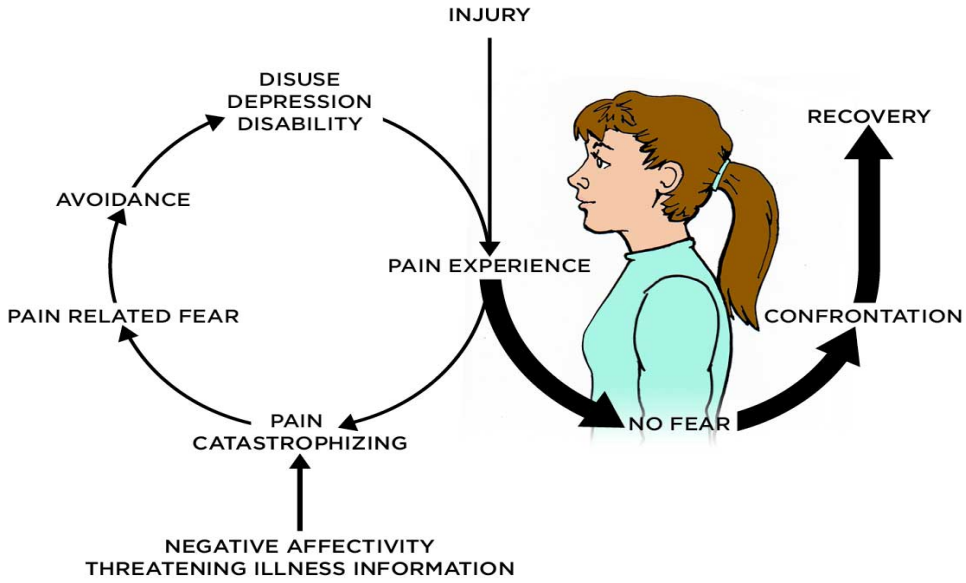

Figure 4. Diagram that shows how psychological factors influence a person's ability to recover from injury

Pain Education Middle School Program. Therapeutic Neuroscience Research Group. (2016). Retrieved March 21, 2023, from https://neuroscienceresearch.org/middle-school-program/

Appendix B

Pain Catastrophizing Scale (PCS)

Pain Catastrophizing Scale (Copyright 1995, 2001, 2004, 2006, 2009 Michael JL Sullivan, PhD)
Everyone experiences painful situations at some point in their lives. Such experiences may include headaches, tooth pain, joint or muscle pain. People are often exposed to situations that may cause pain such as illness, injury, dental procedures or surgery.

We are interested in the types of thoughts and feeling that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time
I worry all the time about whether the pain will end	0	1	2	3	4
I feel I can't go on	0	1	2	3	4
It's terrible and I think it's never going to get any better	0	1	2	3	4
It's awful and I feel that it overwhelms me	0	1	2	3	4
I feel I can't stand it anymore	0	1	2	3	4
I become afraid that the pain will get worse	0	1	2	3	4
I keep thinking of other painful events	0	1	2	3	4
I anxiously want the pain to go away	0	1	2	3	4
I can't seem to keep it out of my mind	0	1	2	3	4
I keep thinking about how much it hurts	0	1	2	3	4
I keep thinking about how badly I want the pain to stop	0	1	2	3	4
There's nothing I can do to reduce the intensity of the pain	0	1	2	3	4
I wonder whether something serious may happen	0	1	2	3	4

Appendix C

Tampa Scale for Kinesiophobia

(Miller , Kori and Todd 1991)

1 = strongly disagree
2 = disagree
3 = agree
4 = strongly agree

1. I'm afraid that I might injury myself if I exercise	1	2	3	4
2. If I were to try to overcome it, my pain would increase	1	2	3	4
3. My body is telling me I have something dangerously wrong	1	2	3	4
4. My pain would probably be relieved if I were to exercise	1	2	3	4
5. People aren't taking my medical condition seriously enough	1	2	3	4
6. My accident has put my body at risk for the rest of my life	1	2	3	4
7. Pain always means I have injured my body	1	2	3	4
8. Just because something aggravates my pain does not mean it is dangerous	1	2	3	4
9. I am afraid that I might injure myself accidentally	1	2	3	4
10. Simply being careful that I do not make any unnecessary movements is the safest thing I can do to prevent my pain from worsening	1	2	3	4
11. I wouldn't have this much pain if there weren't something potentially dangerous going on in my body	1	2	3	4
12. Although my condition is painful, I would be better off if I were physically active	1	2	3	4
13. Pain lets me know when to stop exercising so that I don't injure myself	1	2	3	4
14. It's really not safe for a person with a condition like mine to be physically active	1	2	3	4
15. I can't do all the things normal people do because it's too easy for me to get injured	1	2	3	4
16. Even though something is causing me a lot of pain, I don't think it's actually dangerous	1	2	3	4
17. No one should have to exercise when he/she is in pain	1	2	3	4

Appendix D

Central Sensitization Inventory (CSI)

Please circle the best response to the right of each statement.

1	I feel tired and unrefreshed when I wake from sleeping.	Never	Rarely	Sometimes	Often	Always
2	My muscles feel stiff and achy.	Never	Rarely	Sometimes	Often	Always
3	I have anxiety attacks.	Never	Rarely	Sometimes	Often	Always
4	I grind or clench my teeth.	Never	Rarely	Sometimes	Often	Always
5	I have problems with diarrhea and/or constipation.	Never	Rarely	Sometimes	Often	Always
6	I need help in performing my daily activities.	Never	Rarely	Sometimes	Often	Always
7	I am sensitive to bright lights.	Never	Rarely	Sometimes	Often	Always
8	I get tired very easily when I am physically active.	Never	Rarely	Sometimes	Often	Always
9	I feel pain all over my body.	Never	Rarely	Sometimes	Often	Always
10	I have headaches.	Never	Rarely	Sometimes	Often	Always
11	I feel discomfort in my bladder and/or burning when I urinate.	Never	Rarely	Sometimes	Often	Always
12	I do not sleep well.	Never	Rarely	Sometimes	Often	Always
13	I have difficulty concentrating.	Never	Rarely	Sometimes	Often	Always
14	I have skin problems such as dryness, itchiness, or rashes.	Never	Rarely	Sometimes	Often	Always
15	Stress makes my physical symptoms get worse.	Never	Rarely	Sometimes	Often	Always
16	I feel sad or depressed.	Never	Rarely	Sometimes	Often	Always
17	I have low energy.	Never	Rarely	Sometimes	Often	Always
18	I have muscle tension in my neck and shoulders.	Never	Rarely	Sometimes	Often	Always
19	I have pain in my jaw.	Never	Rarely	Sometimes	Often	Always
20	Certain smells, such as perfumes, make me feel dizzy and nauseated.	Never	Rarely	Sometimes	Often	Always
21	I have to urinate frequently.	Never	Rarely	Sometimes	Often	Always
22	My legs feel uncomfortable and restless when I am trying to go to sleep at night.	Never	Rarely	Sometimes	Often	Always
23	I have difficulty remembering things.	Never	Rarely	Sometimes	Often	Always
24	I suffered trauma as a child.	Never	Rarely	Sometimes	Often	Always
25	I have pain in my pelvic area.	Never	Rarely	Sometimes	Often	Always
					Total=	