SECTION 3

Chronic pain: when it goes on and on

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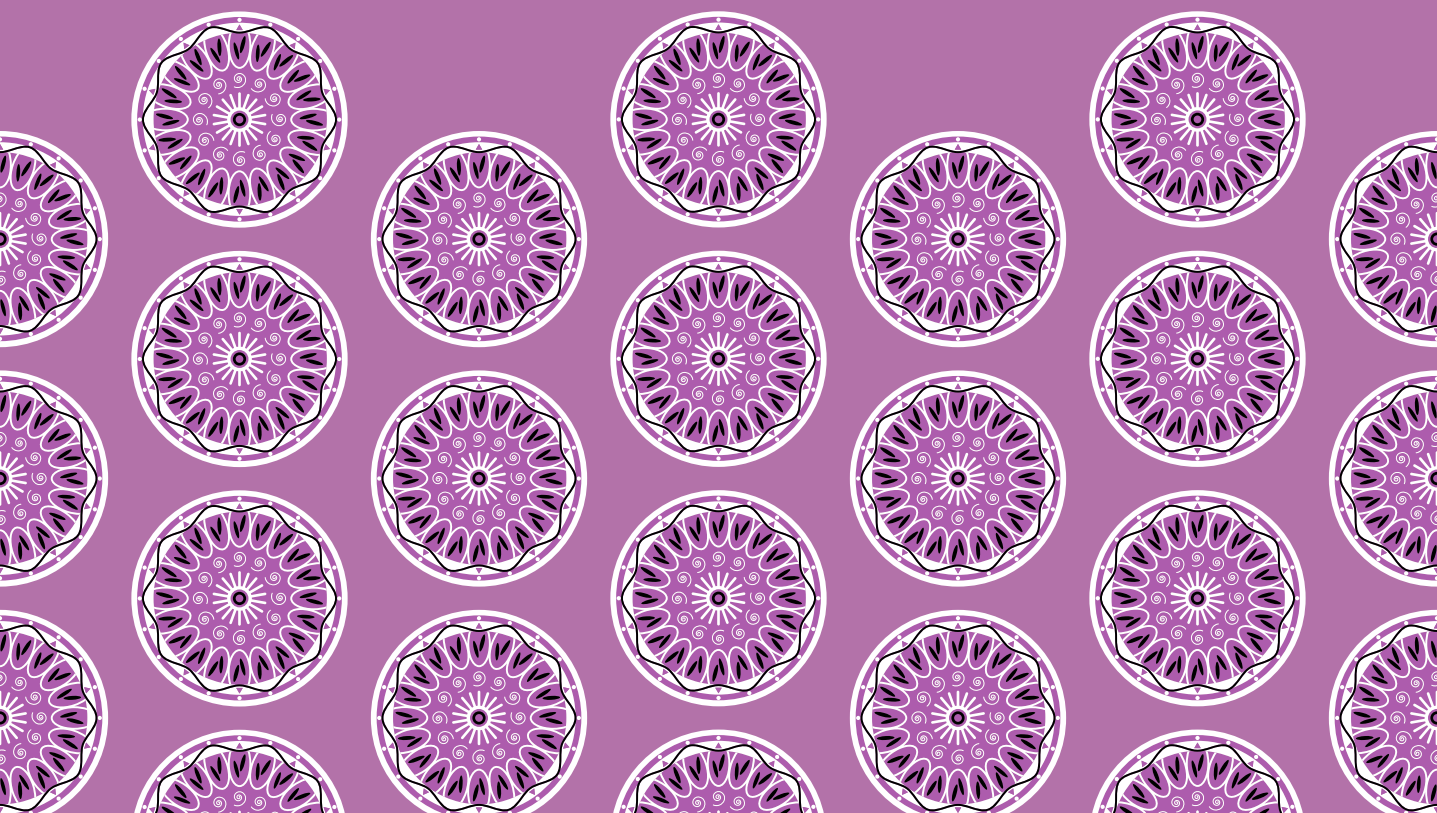

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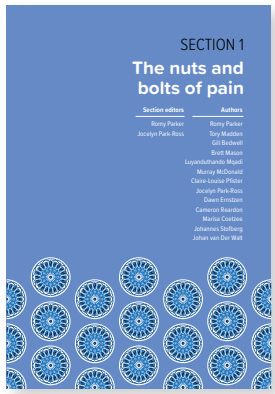
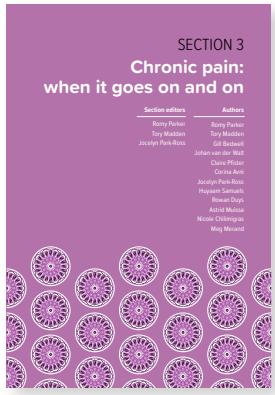
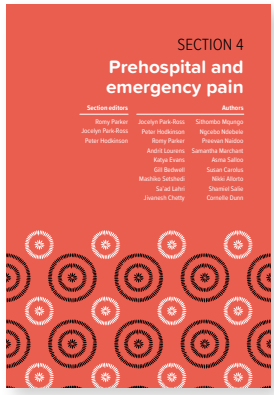
About the book

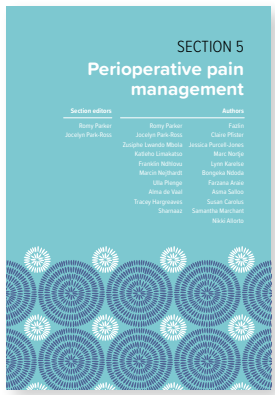
This open access textbook is aimed at all healthcare disciplines, including nurses, doctors, rehabilitation and allied healthcare and prehospital care providers.

Throughout the book, essential evidence-based pain knowledge is interwoven with contextual case studies and patient stories, centering the patient experience to enhance understanding of the physiology, assessment, and treatment of pain.









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1 Introducing Chronic pain

Romy Parker
Jo Park-Ross
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Chronic pain is a problem

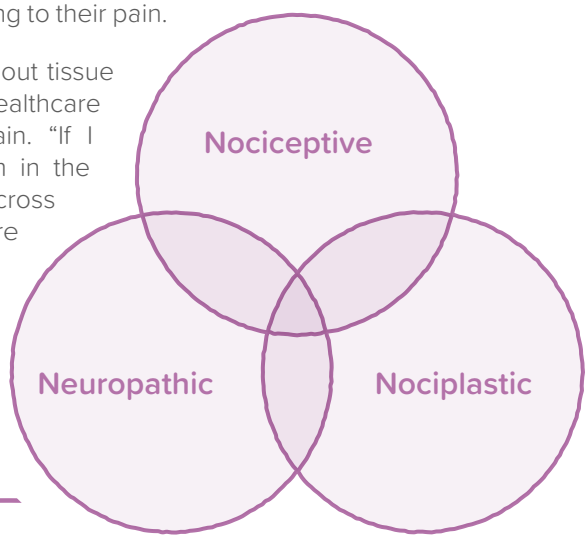
Globally, 20% of the population suffers from chronic pain (1). In South Africa, 1 in 5 people reports having pain on most days for more than three months i.e., chronic pain (2) – that is a lot of people. Chronic pain is defined as pain on most days for more than three months – in other words, pain that has persisted beyond normal tissue healing times. This means that, wherever you work as a healthcare professional, you are likely to encounter someone living with chronic pain.

Regardless of the initial cause of the pain, if the pain continues (becomes chronic), it is likely that the nervous system will be sensitised. In other words, although a nociceptive event (warning of tissue injury), or neuropathic event (lesion or disease of the nervous system), may originally have been the strongest contributor to the pain, over time, nociplastic processes will contribute to pain. In essence, the nervous system becomes oversensitised: it starts to magnify the transmission of only slightly threatening signals and may even misinterpret normal sensations as threatening.

We can see evidence of nociplastic pain in the large number of people with chronic pain who experience symptoms that are more severe than would be expected by the amount of tissue or nervous system pathology. But, as previously described in Section 1, nociplastic pain seldom occurs in isolation, and a combination of pain mechanisms is more likely. The skill for the healthcare professional working with the person with pain is to work out where on the diagram this person is situated. That allows you to facilitate a treatment plan that will target all the mechanisms contributing to their pain.

Figure 3.1: People with chronic pain may present with overlapping pain mechanisms.

The idea that pain is not always about tissue damage can sound crazy to healthcare professionals and people with pain. “If I have pain, I must have a problem in the tissues of my body.” However, across all the medical disciplines, there are descriptions of conditions that cause severe debilitating pain and dysfunction, in the absence of demonstrable tissue pathology (Table X.1). People present with pain and suffering, in patterns that healthcare professionals



recognise, but we are unable to explain why the pain and suffering is occurring if we use only a nociceptive or neuropathic lens. It's not only healthcare professionals who encounter pain we can't describe. Ask almost anyone, and they could tell you about a chronic pain in their foot or knee or neck or back, that troubled them intermittently over many years. They may even have sought help for the problem, but the symptoms have eventually disappeared, on their own. No explanation, and, importantly, no long-term negative consequences for their health.

Table 3.1: Conditions recognised to have a central sensitisation or nociplastic pain component.

Speciality Area	Condition	Features
Urology	Bladder Pain Syndrome	Pain on bladder filling. Investigations may show evidence of inflammation of the bladder, but the association between the symptoms and microscopic features remains unclear. The pain syndrome seems to cause the bladder inflammation, rather than the other way around (3).
Gynaecology	Endometriosis with chronic pelvic pain	The pathology explains some of the pain, but up to a third of women with proven endometriosis are asymptomatic. i.e. the pathology can't always explain the pain (4).
Gynaecology	Vulvodynia	Allodynia at the opening of the vagina, often with no identifiable cause (4).
Thoracic Surgery	Thoracic outlet syndrome	The relationship between 'thoracic outlet obstruction' and pain is unclear. Surgery may remove the cause of the tissue problem, but pain frequently persists or no obstruction can be identified to explain the pain (5).
Maxillo-facial surgery	TMJ pain	Pain of the temporomandibular joint with no identifiable cause (3, 4).
Hepatobiliary medicine	Chronic pancreatitis	In some patients, the pathology is quiescent. I.e. clinicians are unable to demonstrate biological evidence of new flares of pancreatitis, but the pain flares persist (6).
Rheumatology	Fibromyalgia	Everywhere is tender, and everywhere hurts, even in response to non-dangerous stimuli such as gentle touch. How can a gentle touch cause tissue damage? So why does your body perceive this as a threat? (3)
Dermatology	Chronic itch	Chronic itch with no clear cause or itch that persists after tissue healing (7).
Orthopaedics	Osteoarthritis	OA is interesting because, in some people, the association between degeneration of their joints and chronic pain seems clear. However, some people have minor joint damage with severe pain, and others have severe joint damage but no pain. Up to 43% of people over the age of 40 have features of OA on imaging, but have NO pain. The relationship between the extent of the tissue damage, and the severity of the pain, is not consistent (8).
Orthopaedics	Whiplash-associated disorder	Injuries to the neck with pain more severe than would be expected for the tissue damage present, and in which the pain continues beyond tissue healing times (4).

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Neurology	Functional Neurological Disorder	"Functional disorders" can be found in many other specialties, too. The term describes syndromes of severe pain or dysfunction, where extensive tests are unable to demonstrate pathology in the tissues where the pain is felt. The pain and dysfunction are located in peripheral tissues, but the pathology is in the functioning of the central nervous system (9).
Gastroenter-ology	Irritable bowel syndrome	People suffer from abdominal pain, cramping, gas, diarrhoea and/or constipation with no evidence of disease (4).
Neurology	Chronic Fatigue Syndrome/Myalgic Encephalomyelitis	Characterised by post exertional neuroimmune exhaustion, with fatigue, cognitive impairment, autonomic symptoms, pain, IBS, sensitivities, immune dysfunction (10).
Neurology	Restless leg syndrome	A sleep disorder featuring an urge to move the legs, typically at night (11).
Physiotherapy	Non-specific low back pain and painful tendinopathies	Pain with no evidence of inflammatory or mechanical musculoskeletal changes (12).

A paradigm shift is needed when working with chronic pain

↑ Please note that this list is by no means exhaustive and is likely to change, and probably expand over time as our knowledge and understanding of central sensitisation and the nociplastic pain conditions improves.

Nociceptive mechanisms alone cannot explain chronic pain: the pain can be severe and it goes on and on, but it is not associated with significant tissue pathology or nervous system injury. However, we have noticed that practitioners, patients, and society often cling to the idea that there must be a tissue pathology cause. In the pursuit of finding a tissue cause for their pain ("there is something wrong in my abdomen causing the pain in my abdomen"), people are often subjected to batteries of tests, unsuccessful treatments, and surgeries. All these efforts to find tissue pathology come with high financial and personal cost, and often have limited or no benefit.

When pain is primarily nociplastic, an interdisciplinary team which develops person-centred care plans that are informed by a mechanism-based understanding of pain, achieves the most success (13). The interdisciplinary team facilitates work on all the areas of the life of the person with pain that may be influencing their pain. Offering someone with chronic nociplastic pain an exercise plan as part of their therapy, without also addressing their depressed mood, is unlikely to succeed. But helping them understand how their mood is affecting their pain, and their ability to exercise, alongside offering the exercise plan, can empower them to actually benefit from the exercise plan.

A central feature of a person-centred interdisciplinary team is the coordination of the different components of the treatment. It is critical that all members of the team provide consistent messaging about pain to avoid confusion. This means that the team must invest in the time to sit together and discuss each person in depth. Further, the team should focus on the therapeutic goal of a return to meaningful life roles, with the person with pain taking the lead (14). In our experience, people with pain often talk about wanting to "regain control" over their lives.

DON'T MISS THIS

All pain is about more than tissue damage

We can all picture two people lying side by side in a ward having undergone the same operation. They have similar levels of tissue damage and are receiving similar treatments. Yet, it is entirely possible that they will have very different pain. The first person may be lying there half asleep, heavily sedated on their analgesics, waking only occasionally to shout "I'm in paaaaaaaaaain, so much paaaaaaain" before they drift off and continue snoring gently. While in the bed next door, the person who had the same operation on the same day, sits on the edge of their bed, walking stick in one hand, ready to get out of bed to walk with the physiotherapist saying to anyone that will listen "I'm ready for discharge. Send me home." Tissue damage alone is not sufficient for us to understand the difference between these two people who have had the same injury, the same surgery and are being managed with the same multimodal analgesia. We have to ask the question "What else is going on?"

To successfully manage chronic nociplastic pain, the healthcare professional must first understand that all pain is about more than tissue damage. Then, an understanding that nociplastic pain, or central sensitisation, is an over-protective pain system, can be transformative. This understanding enables a therapeutic paradigm shift, from focusing on fixing the tissues, to fixing or facilitating a change in the over-protective pain system.

In this section of our book Understanding Pain, Huyaam, Jo, and Em are going to share with you their experiences of chronic pain. The main difference between this section and Section 2 (which discussed managing pain at the primary level of care), is that Huyaam, Jo, and Em were managed by interdisciplinary chronic pain teams working at the tertiary, specialised level of care. As you read this section, you may be surprised that it isn't all about complex drugs, sophisticated new surgical procedures, or complicated expensive treatments. To date, the most effective treatment for chronic nociplastic pain is integrative. These treatments combine education with exercise or activity, mindfulness-based practices, engagement in meaningful life roles, and sleep, with pharmacotherapy, surgery, or other interventions that are used to facilitate engagement with these active treatments.

DEEP DIVE

Who should be in the interdisciplinary chronic pain team?

Complex chronic pain is best managed by an interdisciplinary team which, at a minimum, should include the person with pain, their family or support person, a prescriber (this is commonly an anaesthetist), a nurse, a physiotherapist or occupational therapist, a psychologist, and a psychiatrist. For different conditions, other medical specialists such as a gynaecologist (for chronic pelvic pain); a rheumatologist (for autoimmune or inflammatory arthritis pain), or an orthopaedic surgeon (for musculoskeletal pain), can be included in the team. And then, depending on the needs of the person with pain, we may wish to include a social worker, a pharmacist, a teacher, a speech therapist or audiologist, or any other person who can play a role in helping the person with pain re-engage with their lives.

DON'T MISS THIS

African metaphors to explain chronic pain

In society we often use metaphors to explain ideas or concepts. Metaphors are useful when we are learning a new concept or trying to help someone shift a paradigm because the person hearing the metaphor has to make sense of it. This "sense making" facilitates deeper and more personal learning. Here are some examples of metaphors we use to help people understand pain.

Pain which has continued despite tissue healing

When I was a child, we used to play in the veld where there were lots of ant hills. Ant hills were great fun: you could climb up them and look over the long grass, or you could hide behind them and ambush your brother. Sometimes the ants were still living in the ant hill and when we climbed up on to their homes and damaged the walls, the ants would all come out and start to repair the damage we had done. We didn't really notice the ants' hard work though. The next day we would come back and climb up again and damage it again, and once again the ants would have to come out and make repairs. After a while, we noticed the ants' hard work and how clever they were about fixing their home, but we didn't stop playing and climbing up the ant hills! Then we noticed that the ants started to come out even when we didn't climb up and damage the walls. The ants felt the vibrations as we ran nearby, they could hear us, they knew what was coming next and they set off the alarm and sent out the worker ants to get to work.

Pain which occurs when nothing dangerous has happened

In the summer in my grandmother's village, the bush gets very dry, and everyone worries about fires. Fires destroy homes and burn the crops and the grazing. If there is a fire, everyone needs to come and help to fight it. There is an old man who lives at the top of the hill; he can see long distances from his house. It's his job to look out for smoke so that he can warn everyone in the village of any fire by ringing a big bell next to his house. When the bell rings, everyone drops whatever they are doing, they grab their buckets and sacks, and they come together to fight the fire and save their homes. This system has always worked well and kept the village safe. But this summer the old man rang the bell almost every day, so everyone kept stopping their work and getting ready to fight a fire, only to find that there was no fire! After a few times of this happening, everyone started to get annoyed, because they weren't getting any work done! Finally, my grandmother went up the hill to talk to the old man and find out what might be happening. As she got to the top of the hill, he shouted "smoke!" and started to run off to ring the bell. My grandmother turned to look where he was pointing and saw...fog! Wait, don't ring the bell: it's not smoke, it's fog coming in from the sea!

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Pain becoming more and more severe despite minor or no tissue damage

I remember how, during the drought, everyone kept telling us to make sure that taps were properly turned off. Don't waste water! A dripping tap wastes lots of precious water. Where I grew up, the droughts were always in winter. It was bitterly cold at night. We would get into bed and wriggle around until we were warm and comfortable before going to sleep. Sometimes, though, just as I was warm and comfortable and nearly falling asleep, I would hear it, the tap was dripping! Oh no! It's too cold to get out of bed! So, I would pull the blanket over my ear so I couldn't hear the dripping and get to sleep. But I could still hear it! I would put the pillow over my ear, but the dripping got louder! I pushed my hand against the pillow, against my ear and tried to ignore it, but it got louder! Eventually I had to get out of my warm bed and walk to the cold bathroom to turn off the tap. I'm sure that little drip couldn't be that loud!?

Pain depends on context

My family loves to sit around a fire at night and tell stories. Sometimes we tell funny stories, sometimes we tell scary stories. If someone is telling a scary story I can feel my heart beating in my chest, my throat squeezes tight, and I get really scared! One night my uncle was telling us a really scary story. In the middle of the story, my brother crept around behind me, and put his hand on my neck. I nearly died of fright! I screamed, I jumped up, my heart nearly jumped out of my chest and my legs were like jelly! It's funny, because my brother often does that to me during the day, he creeps up behind me and puts his hand on my neck, but during the day it never gives me a fright, I just turn and smile and say hello!

Pain when there is nothing wrong with the tissues

My husband travels away from home a lot and he worries about me being home alone. He decided it would be a good idea to install a very fancy new burglar alarm system all the way around the outside of the house. This system worked with sensors and beams, so if anything went through the beam, the alarm would go off. He thought this was a good idea because then I would know if someone was coming too close to the house, and I could be warned and respond before anything dangerous had happened. But the second night of setting the alarm - it went off! The dogs started to bark, I jumped out of bed and grabbed a torch, the telephone rang from the armed response company – everyone was ready for attack! But there was nothing and no one there. It was all OK, false alarm. Eventually I got back to sleep! But the next night the very same thing happened! Oh no, obviously my home is being targeted. The thieves must know my husband is away. Check the doors and locks, be careful! A few nights later it happened again! Oh no! Now what do I do? I asked the armed response guards to drive past

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my house many times, I didn't sleep well, I kept waking up to check that all was safe. Every little noise made me jump! The next night I couldn't get to sleep, I was so scared. I sat and stared at the dark garden, and then I saw it - the Cape Eagle Owl swooping across the garden, and as he swooped the alarm went off! Of course! Owls hunt at night, and alarm beams aren't going to stop them flying into my garden to catch a mouse or a lizard! Having a super sensitive alarm to warn us before anything dangerous came close to the house sounded like a good idea, but now it was causing more stress and trouble, not less.

Some people are just more sensitive than others

My aunt had a small herd of cows which got milked every morning. When we were visiting her it was exciting to get up early in the morning and go into the barn with all the cows. My aunt made milking look so easy, but it was hard for me to learn how to do it. My aunt knew each of the cows and their preferences. Many of the cows were very relaxed and as soon as my aunt sat down and leant against them with her forehead, their milk would come in and she would start squirting milk into the bucket. These were the cows she let me practice on. But there was one cow who was different. My aunt said she was just a bit sensitive, a bit special maybe. That one cow, my aunt first had to talk to her a little bit and rub her face, then my aunt had to run her hand along her spine and down to her back legs. Finally, before starting to milk her, my aunt would ask the cow if she was ready, and that cow would turn and look at my aunt as she put her hand on her udder. If my aunt did all of these things, the cow's milk would come in and my aunt said she was the most reliable milk producer she had. But, if my aunt didn't follow this routine, or if anyone else tried to milk this cow – then no milk! There would be kicking and stamping and even if there was some milk the bucket would probably get kicked over!

2 Mixed nociplastic and nociceptive pain

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Astrid Muissa

From victim to warrior: Huyaam's ongoing battle

Introduction

> *Hello Readers*
> *I am Huyaam Samuels, a 24-year-old female living in Cape Town, South Africa. I am currently pursuing my Masters degree in Organisational Psychology at the University of Cape Town (UCT). I suffer from a rare medical condition called Pseudoachondroplasia and Hypermobility Syndrome, which is characterised by chronic pain, chronic fatigue, and joint instability resulting in dislocations of major joints. My joint instability contributed greatly to my limited mobility.*

Pseudoachondroplasia and Hypermobility

Pseudoachondroplasia (PSACH) is estimated to affect one in 30 000 to 100 000 people (15, 16). It is a rare genetic condition resulting in short-limbed dwarfing (16). The condition is caused by a mutation in the cartilage oligomeric matrix protein gene which affects not only bone growth but also results in joint hypermobility. While babies born with the condition are normal size at birth, as they begin to walk and grow it becomes apparent that their development is not following a normal curve. Their gait is characterised as "waddling" and in addition to short limbs, brachydactyly (short digits – fingers and toes), and marked hypermobility in all joints is typical.

The joint hypermobility means that people with PSACH are at risk of joint dislocations and spinal deformities such as scoliosis. One of the most common symptoms people with PSACH suffer from is joint pain. Joint pain arising from chronic mechanical instability abnormally loading the joints, joint pain from resultant osteoarthritic changes or damage to the joints, and joint pain from acute subluxation and dislocation. In addition to the joint pain, compensatory muscle spasm (to stabilise the hypermobile joints) causes further pain and contributes to fatigue.

Diagnosis of PSACH is seldom made at birth as the abnormalities in development are not apparent at that time. Diagnosis is usually made as the child begins to walk and become more active with the gait pattern, short stature, hypermobility and joint pain (especially in the large joints of the lower limbs), all key diagnostic features (15).

Huyaam's pain spirals out of control

A significant milestone for my medical condition was six years ago when I was in matric (Grade 12). At the time, I was managed by a paediatric pain management team whilst on high dosages of pregabalin, diazepam, ibuprofen, paracetamol and morphine. I was studying for my final exams and sitting for extended periods studying worsened my chronic pain. Consequently, the muscles in my lower back began to spasm which exacerbated pain levels quite badly and limited my mobility. At this time, I did not realise the importance of standing up regularly, particularly with my medical condition. This resulted in one of my worst hospital admissions, to curb my pain using a ketamine IV as I became resistant to morphine after using it for more than seven years. I was unable to use the bathroom on my own, had to wear a neck brace, do dry needling, and complete daily physiotherapy during these episodes. I was constantly resting in bed, and it seemed as if my body just gave up. Although I was resting, my pain levels were still high. My medical team at the time struggled to reduce my pain, and although we were increasing my medication dosages, it did not appear to be working sufficiently.

Huyaam's medications at the time of her admission

Medication	Mechanism of action
Pregabalin (150mg TDS)	Reduces spontaneous activity of the Calcium channels in the spinal cord by binding to the $\alpha_2\delta$ subunit of the calcium channels (17).
Amitriptyline (50mg nocte)	Tricyclic antidepressant targeting spinal cord and brain activity.
Diazepam (10mg TDS)	A benzodiazepine targeting central nervous system by increasing levels of GABA. It is used to reduce anxiety and muscle spasms.
Ibuprofen	Non-steroidal anti-inflammatory drug targeting peripheral nervous system by reducing inflammation in the tissues
Paracetamol	Central and peripheral nervous system action inhibiting COX/POX, activating serotonergic pathway and enhancing endocannabinoid.
Morphine (slow release 40mg BD; and oxycodone 15mg PRN for breakthrough pain)	Peripheral, spinal cord and brain action binding with mu opioid receptors (μ-opioid).
Ketamine infusions for exacerbations	Targets spinal cord activity

Pain mechanisms – nociplastic and nociceptive pain

The pain Huyaam experiences is complex, and it is chronic. She has had pain for most of her life. However, the term 'chronic pain', as a time-based definition of pain, does not give us insight into the underlying physiological mechanisms which contribute to her pain. It is therefore more helpful to understand her pain as nociplastic and nociceptive pain. Huyaam's pain has two phases: there is a phase when she has pain, but it is a constant pain, a pain she is familiar with. This pain

occurs all over her body, often moving around, but it is a pain that is manageable. This pain is nociplastic – pain arising from non-dangerous stimuli activating her sensitised nervous system. Sometimes Huyaam's nociplastic pain flares up, perhaps during exams or other stressful times when the synergistic systems sensitise the nervous system further. This is still nociplastic pain, pain arising not because there is potential or actual tissue damage, but pain arising because her sensitised system is generating pain in response to non-dangerous stimuli.

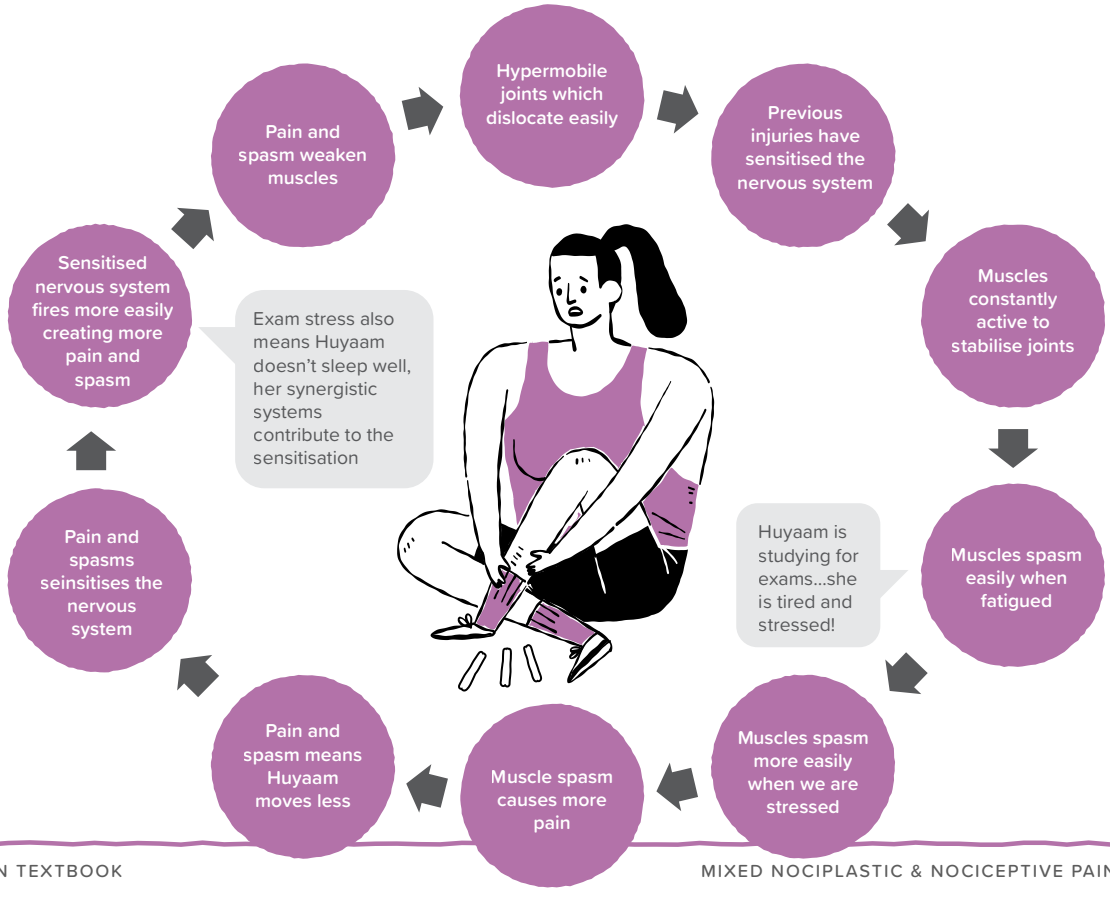
There are times when Huyaam suffers from nociceptive pain too. Her hypermobile joints frequently subluxate or dislocate with associated joint and other soft tissue damage, muscle spasm and inflammation. Let's break it down and see what was contributing to Huyaam's pain when she had this severe episode in her matric year.

Peripheral Nervous System

Huyaam was sitting for extended periods of time studying for her exams. The human body is designed to move. Sitting for long periods of time is not healthy for anyone (no matter how 'perfect' the posture) and evidence suggests that we should all stand up and move around for 10 to 15 minutes every hour (motion is lotion!) (18). Maintaining a single position for extended periods of time affects multiple musculoskeletal structures and nociceptors may fire – not typically leading to pain, but rather motivating us to move! However, if we fail to move enough and continue to maintain the single position, nociceptors will continue to fire. In addition, muscles will fatigue and if the position is held beyond fatigue, then muscle spasm often ensues as a compensatory mechanism.

Figure 3.2: Huyaam's spiral of sensitisation

Now, let's consider the effects of sitting for extended periods of time in Huyaam's case. Her joints are hypermobile, her muscles are already working at extra capacity to stabilise those joints and allow her to move and function. She has had numerous injuries as a consequence of hypermobility. This cycle means that she has a sensitised peripheral nervous system which fires more easily (Figure x.1).



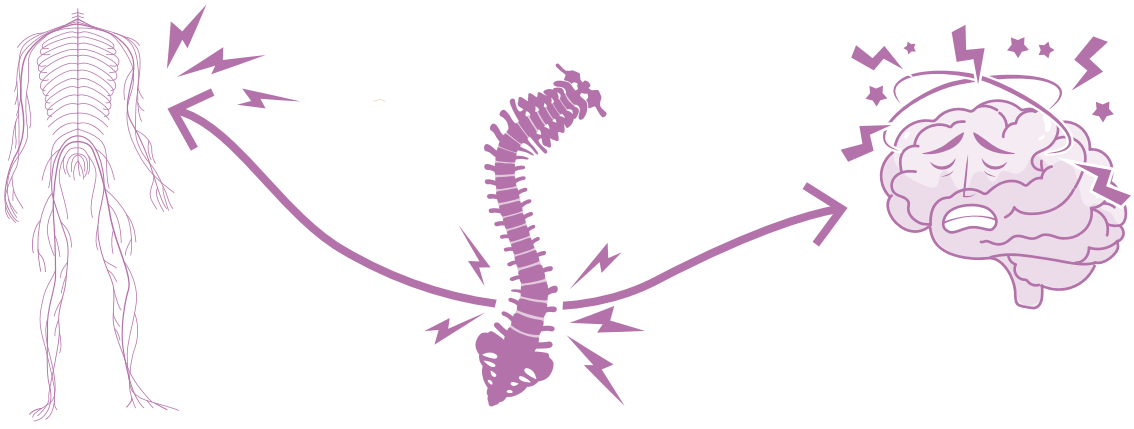
Therefore, in the peripheral nervous system there will be underlying peripheral sensitisation from nociplastic changes, with acute nociceptive signalling arising secondary to the muscle spasm... all leading to a cycle of peripheral sensitisation.

Spinal Cord

So, Huyaam's peripheral nociceptors are firing. No wonder she has pain! But the pain was so severe that not even morphine was helping, and she needed to be admitted for an intravenous ketamine infusion. Ketamine is an anaesthetic drug which targets NMDA receptors in the spinal cord. It is a unique anaesthetic drug that can cause sedation as well as analgesia. Ketamine seems to depress the transmission of impulses in the medullary reticular formation, which is also important for the transmission of the affective-emotional component of nociception from the spinal cord to higher centres. The S(+) isomer of ketamine also has some opioid mu-receptor blocking activity, similar to drugs like morphine (19).

Remember, Huyaam lives with nociplastic pain all the time; she lives with a sensitised nervous system. The peripheral nociceptors were delivering messages to sensitised neurons in the spinal cord. She experienced pain from stimuli that are usually non-painful (allodynia) even before this episode of severe pain when she was studying. This tells us that she has sensitisation in the spinal cord. Huyaam's description that "my body just body gave up. Although I was resting, my pain levels were still high" suggests she was sensitised.

In this severe pain episode, Huyaam's peripheral nociceptors fired easily because they were sensitised from sitting for a long period of time. They delivered their messages to sensitised second-order neurons in the spinal cord. The sensitised spinal cord neurons have lowered firing thresholds, increased receptor field sizes, and increased responsiveness to stimulation. This all means that there was now a barrage of nociception going up to the brain.



The brain

Huyaam lives with nociplastic pain. This means that her brain is extra responsive to nociception: it has lowered firing thresholds and generates pain quickly in response to a perception of threat – all sorts of threat, not only (potential) threat to tissue damage, but also threats such as exam stress. Now her sensitive brain was receiving a barrage of nociception – of course it's going to generate a pain response! Huyaam's feelings that her "body gave up", that she couldn't walk, she couldn't hold her head up without a brace, all suggest that her brain was sensitised. This made her feel pain all over her body, impacting on all her muscles working, affecting her ability to move, her ability to walk, her ability to be.

All of this information gives us insight into some of the areas of her brain which may be contributing to her pain experience. Pain all over her body, spreading in ways that don't make sense if we consider the neuroanatomy of the peripheral nervous system, but do make sense if we consider the mapping on the somatosensory homunculus, points to the role of the brain in this situation. Huyaam's struggling with motor control, movement, walking, holding up her head also suggests that the functioning in her pre-motor and motor cortices is impaired. Huyaam's report that her pain got worse as she got more stressed about exams suggests that the limbic system was also contributing to her pain. And finally, Huyaam's fear that she wouldn't be able to write exams, that all of this meant that her dream of independence and a career was not possible, tells us that her amygdala (a key centre for fear and involved in the generation of pain) is also involved.

The synergistic systems

Let's acknowledge here the role of the synergistic systems in Huyaam's situation. Any exams are stressful. Matric exams are especially stressful. Prolonged stress would activate the HPA axis. As pressure mounted, Huyaam's autonomic nervous system would have become imbalanced, with overactivity of her sympathetic nervous system and underactivity of the parasympathetic nervous system. As her pain worsened, so did the stress, she would have struggled to sleep, further reducing parasympathetic activity. The more pain and muscle spasm she experienced, the more superficial her breathing would have become, further reducing parasympathetic activity. As the exams drew nearer and nearer, her sympathetic upregulation would have continued, leading to a spiral of sensitisation until Huyaam was in severe pain, all over her body, all day and all night, unable to function.

DON'T MISS THIS

Diaphragmatic breathing for Huyaam's pain

As we discussed in Section 1, diaphragmatic breathing stimulates the vagus nerve – the cranial nerve which has bidirectional connectivity to the viscera, and which is fundamental to the healthy functioning of the autonomic nervous system – in particular, the parasympathetic nervous system. Huyaam's sympathetic nervous system was very active. By focusing on diaphragmatic breathing which emphasises the exhalation phase, Huyaam could restore activity of her parasympathetic nervous system by stimulating the vagus nerve (20).

Huyaam is challenged to try a different approach

Because of this episode, Professor Parker was consulted and was horrified by my state and all the medication I was on. From here, we began the transition to an adult Pain Management Team at Groote Schuur Hospital as I was of age. I have to admit, I did not mind the change, but I was rather against the new treatment methods of the adult pain team, and I was not too particularly fond of their new approach. From the beginning, we changed a few medications and largely focused on adopting a "no-medication approach" and "exercise" approach to help alleviate chronic pain. At the time, it was rather difficult for me to change the way I have been managing and treating my pain through loads of medication because I have suffered from pain for such a long time, even though it was trial and error with using medication. It took eight years for a doctor to believe in me and finally provide a diagnosis. Hence, I couldn't help but think "Why are you taking away the only thing that brought me comfort and alleviated my pain?". I often struggled with daily tasks and caring for myself, such as brushing my hair or cutting my nails, and doing chores was difficult as an adolescent. My knees often dislocated, and I wasn't able

to walk without having anxiety about suffering a dislocation. It was humiliating to be walking with a friend and randomly fall or dislocate my knee. Consequently, I was using a wheelchair due to my severe and frequent knee dislocations all the time. However, using the motorised wheelchair was a bad idea too. This worsened the pain I experienced in my back and resulted in another pain episode where I was admitted for Ketamine infusion. This, coupled with having the intention to start university, resulted in a long period when I was uncertain whether I could pursue my studies due to my chronic pain and condition.

Assessing Huyaam's pain

The chronic pain management team at Groote Schuur Hospital includes anaesthetists, physiotherapists, nurses, a consultant liaison psychiatrist, and a psychologist. Assessing Huyaam started with a thorough review of her condition, ruling out red flags and acute illness, her treatment to date, and a full physical examination. The interdisciplinary team then discussed the mechanisms we hypothesised were contributing to her pain. From her history we were able to gather a lot of information as outlined in Table 3.2 below.

Table 3.2: Pain history from Huyaam using the O, P, Q, R, S, T, U, V, W framework.

Gather information on the...	What questions to ask	Huyaam's responses	What did this information tell us?
Onset	• When and how did this start? • How long does the pain last? • How often do you get the pain?	The background pain has been there for years. The pain in the back with the spasms, spreading up my spine and throughout my body has been gradually getting worse over 3 weeks.	Reminded us that Huyaam has a history of a chronic nociplastic pain condition, and she is now experiencing an acute flare up.
Provoking and palliating activities	• What causes the pain? • What makes it better? • What makes it worse?	Huyaam felt that sitting for long periods of time seemed to make it worse. But it was hard for her to identify any specific movements or other positions that made it better or worse. Huyaam said that exercise used to make her feel better, she used to do 30mins of Pilates every day, but since this episode started, it was just too painful to try to exercise.	Sitting itself is not a dangerous position, the severity of Huyaam's pain did not match this aggravating factor. Coupled with Huyaam struggling to identify easing and aggravating factors, this unusual pain behaviour suggests nociplastic sensitisation contributing to her pain. Huyaam might also have developed sensitivity to physical activity – suggesting her descending inhibitory mechanisms are impaired. Huyaam was able to tell us that the stress of exams seemed to make her pain worse. This suggested that her synergistic systems were contributing to her pain, likely her HPA axis and sympathetic nervous system (SNS) further sensitising her nervous system.

continued...

Gather information on the...	What questions to ask	Huyaam's responses	What did this information tell us?
Quality of the pain	• Can you describe your pain?	Agony! Severe! Huyaam was not using specific words suggestive of mechanical nociceptive (sharp, shooting, throbbing) or neuropathic (electrical, burning, pins and needles) mechanisms	This pain description was also suggestive of nociplastic pain from a sensitised system.
Region or radiation	• Where is the pain? • Does the pain spread? • Where does it spread to?	It started in the back but now radiates up into the neck and head, across the shoulders, down the legs...Huyaam's whole body was in pain.	The general spread of pain beyond discrete areas, and not referring into clear dermatomes or peripheral nerve distribution, again suggests nociplastic mechanisms.
Severity	• How severe is your pain? • How severe is it right now/at its best/at its worst and on average? • How severe is your pain when you try to be active?	Agony! Severe! Ten out of ten! I am brave, I am strong, I live with pain all the time, but this is too much, I can't!	Huyaam's pain was severe, she was unable to function, it was affecting her mood, her cognition, and every aspect of her life. On the Brief Pain Inventory she scored 10/10 for both Pain Severity and Pain Interference with Function.
Treatment	• What treatment have you tried for your pain? • How well has it worked? • Have you had any side-effects from these treatments?	**Pregabalin** - was helping but now makes no difference. **Diazepam** – helps to make me sleep but doesn't seem to help the spasm or the pain and Huyaam had to take so much she was feeling "zonked out". **Amitriptyline** – seemed to help before, and makes her sleepy but now don't know if it's having any effect. **Ibuprofen** – at first this helped a bit but now it's making no difference.	**Pregabalin** – targets the calcium (Ca^{2+}) channels in the spinal cord and is indicated for neuropathic pain and some nociplastic pain if spinal cord sensitisation is hypothesised to be contributing. Controls spontaneous firing of the second order neurons in the spinal cord. Lack of effect suggests sensitisation of Ca^{2+} channels not a key factor. **Diazepam** – is a benzodiazepine which helps to relax her muscle spasms and has a calming effect on her mind. Clearly it is not being effective now. **Amitriptyline** – a tricyclic antidepressant which at low doses is effective for nociplastic pain but which didn't seem to be offering her any relief. **Ibuprofen** – a non-steroidal anti-inflammatory. Its lack of effect suggests that there is not an inflammatory process contributing to her pain.

continued...

Gather information on the...	What questions to ask	Huyaam's responses	What did this information tell us?
Treatment (continued)		**Paracetamol** – taking it by the clock as she was taught but really doesn't think it's doing anything. **Morphine** – dosages have been increased and increased but it's not helping at all.	**Paracetamol** – targets CNS pain mechanisms. It does not appear to be having an effect. **Morphine** – a mu receptor antagonist, takes the edge off but doesn't really help. She feels totally zonked, "out of it", just wants to sleep and can't study. Now pain is worse and increasing doses don't help. Widespread allodynia and hyperalgesia with morphine suggests this may be morphine-induced.
Understanding beliefs and impact	• What do you think is causing your pain? • What do you think is wrong? • What can you not do because of your pain? • How is this pain affecting you and your family?	Huyaam was sure that her pain was because her joints were so unstable that they were going to dislocate. She has suffered multiple dislocations of various joints over the years which are extremely painful and frightening. She was frightened to move when she had such severe pain and spasm as she was sure she was going to dislocate, and it would be bad if she dislocated in her spine! She could not function at all, and it was having a big impact on herself and her mother who had to assist with all her care.	Huyaam had high fear avoidance beliefs. She completed the Tampa Scale of Kinesiophobia and scored 36 indicating high levels of fear of movement. Over the years of living with her condition her joints have become more and more unstable as her muscles have weakened. She had become frightened of movement and pain as, to her, both indicated that she was going to dislocate. In many ways, this was a logical fear for Huyaam to develop as a consequence of her hypermobility. However, high levels of fear mean that there is a lot of activity in the limbic system (emotions), hippocampus (memory) and amygdala (fear). High levels of limbic activity promote sensitisation in the brain. The more fearful we become, the easier it is to generate pain. In addition, the amygdala is closely associated with the vagus nerve, critical to autonomic nervous system functioning. High levels of fear are also associated with sympathetic nervous system activation – the synergistic system contributing to pain.
Values	What is your goal in getting your pain treated? What do you want me as a healthcare professional to do for your pain? What are you not doing because of your pain that you want to be able to do?	Huyaam was desperate for her pain to be controlled so that she could study, write her exams, and do well to get accepted into university. She told us she just needed the pain to go away so she could get on with studies!	We were very aware that Huyaam needed treatment that would allow her to re-engage with life. Her treatment to date had slowly been increasing her disability. She had been advised to protect her joints, to wear joint braces, to be careful of dislocating, to take more and more medication which left her sleepy, "zonked", and struggling to motivate herself to do anything. While these treatments had been reducing her pain in the short term, they seemed to have made her more vulnerable for more frequent episodes of severe pain. She was slowly getting weaker, more vulnerable, and less able.

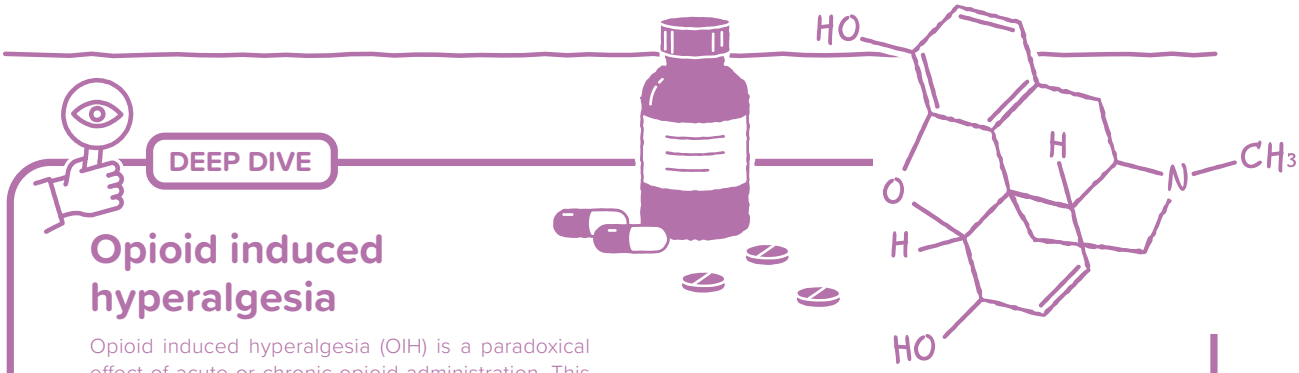
continued...

Gather information on the...	What questions to ask	Huyaam's responses	What did this information tell us?
What else?	• What else is going on in your life? • How are you generally?	The key factor here was that Huyaam was writing matric. She was a high-achieving student who studied hard and had set herself goals to perform and get into university. During Grade 11 and Grade 12, the stress built and built. Huyaam was not happy with her Grade 11 marks. Now she was putting more pressure on herself for matric. She was struggling to sleep, her appetite was poor, and she wasn't doing any exercise, seeing friends, or going out.	Huyaam's synergistic systems were contributing to this episode significantly through stress and autonomic nervous system dysfunction.

Table 3.2: Pain history from Huyaam using the O, P, Q, R, S, T, U, V, W framework.

On physical examination there was widespread muscle spasm throughout Huyaam's body, not just adjacent to her spine. When muscle testing could be performed, her strength was only Grade 4 out of 5. Multiple joints were hypermobile, including her knees, elbows, wrists, and fingers, with Huyaam feeling very anxious when these joints were assessed. She did not have any localised signs of inflammation and no orthopaedic special tests were positive, suggesting that there was no acute tissue damage. Huyaam had widespread allodynia. Light palpation everywhere was painful, as we would expect in someone with nociplastic central sensitisation. She had no areas of loss of sensation.

The team hypothesised that Huyaam was suffering from opioid-induced hyperalgesia. While her primary pain condition was nociplastic central sensitisation pain, with some secondary nociceptive pain, these were being upregulated by the long-term use of high doses of morphine. We also acknowledged that while her current treatment regimen was targeting the nociplastic sensitisation mechanisms of her pain, it was not optimal and was possibly contributing to her becoming further sensitised. We therefore developed a two-part plan. In the short-term, we needed to wean Huyaam off the morphine and manage this severe episode of pain. We then had a long-term plan to reduce Huyaam's reliance on drugs and increase her use of effective non-pharmacological strategies, with the goal of reducing her disability and enhancing her quality of life.



DEEP DIVE

Opioid induced hyperalgesia

Opioid induced hyperalgesia (OIH) is a paradoxical effect of acute or chronic opioid administration. This means that the drug has the opposite effect to what it should usually be, instead of reducing pain, exposure to opioids in this situation results in hyperalgesia and allodynia – worse pain! This sensitisation is distinct from the original pathology that resulted in pain. The condition is typically seen after rapid escalation of opioid dose and is characterised by widespread, ill-defined pain and sensitivity (21).

The administration of exogenous opioids results in a response from the central and peripheral nervous system in an attempt to restore equilibrium. As part of this response, pro-nociceptive neuropeptides are expressed throughout the nervous system, resulting in widespread sensitisation.

The clinical presentation of OIH may be difficult to distinguish from opioid tolerance because both conditions are associated with a decreased analgesic benefit despite increased opioid administration. However, the administration of an increased dose of opioid will induce analgesia in the tolerant patient but worsen pain in OIH. Conversely, reducing or discontinuing the opioid will improve analgesia in OIH but worsen analgesia in tolerance. Once a diagnosis of OIH has been established, the management options include opioid dose reduction, opioid rotation, and the use of opioid antagonists/partial agonists, NMDA antagonists, gabapentin, alpha2 adrenergic agonists, and non-pharmacological opioid-sparing interventions.

"Tell me more!!"

Professor Parker began hydrotherapy with me. From the beginning Professor Parker was always so energetic and enthusiastic. Every physiotherapy session also became a valuable learning lesson that opened my train of thought. I did not realise that exercise could alleviate chronic pain to such a large extent and improve my quality of life drastically. There are many things that I can do today, that I never thought would be possible due to my condition. Only years later, I reflected upon this method of being treated as a patient and realised that this was the true definition of patient-centred care as I was involved in every aspect of treating my condition. I've realised that learning about pain and little snippets about the human body and the mind, particularly how my one reacts, has helped my pain levels and how I manage my condition.

From the transition, the adult pain team largely focused on educating me about pain and also trying to stabilise my joints as most of my pain came from dislocations. However, what I didn't know at the time was my body tended to overreact and was so dramatic that when one thing went wrong, everything else did too, like a domino effect. For example, if I had lower back pain, my knees would be painful as well and my body just couldn't calm down. I always thought why are they teaching me, why do I have to attend these pain education workshops? I was quite naïve at this point and did not realise the true value of educating myself to better my medical condition because now, a few years later, I'm like "Tell me more!!" After completing the PEEP (Pain Education Empowerment Programme) at Groote Schuur, my toolbox to manage my condition became well-rounded. I was able to walk without dislocating my knees, complete my chores, and manage my health steadily. Being a university student also means extremely high levels of stress, and stress is known to exacerbate pain levels. It is imperative that I have been equipped with proper coping skills to manage my condition daily.

A long-term treatment plan for Huyaam

Pain science education was our first strategy to treat Huyaam's pain (22). Her fear of the severe pain she was experiencing and what she thought it meant was leading to a spiral of disuse, more pain, and more fear. Over a lifetime of living with her condition, Huyaam had been given well-meant but unhelpful messages reinforcing her beliefs about how fragile her body was. This meant that Huyaam was relying on splints to support her joints, rather than building up her muscles – her body's natural splints. She was avoiding doing anything that was painful or might be painful. She was resting more and more, doing less and less, avoiding pain based on a belief that pain was telling her that she was damaging her body.

Our beliefs drive our behaviours

In every single consultation with the pain team, we discussed pain with Huyaam and her mother.

I am weak and fragile

The human body is fragile and breaks down easily. Once its broken its always weaker and there is nothing I can do about it.

I am strong and capable

The human body is resilient. It has multiple ways to adapt and compensates naturally and automatically. It learns and can also get stronger - even in the elderly.

DON'T MISS THIS

Key pain science education messages we worked on with Huyaam were:

1: Pain is not an accurate measure of tissue damage.

2: Nociceptive pain and nociplastic pain are different types of pain.

3: Nociplastic pain occurs when the pain "alarm" system becomes too sensitive.

4: It is safe to exercise when you have nociplastic pain, and exercise treats pain.

5: It is possible to have pain when there is no tissue damage at all.

6: Stress can cause pain.

We then discussed with Huyaam why and how we suggested changing her medication, with a long-term goal to wean her off the opioids. We emphasised that this would be done slowly and carefully and when she was ready. We proposed to Huyaam that changing her use of medication would go hand in hand with her participating in active rehabilitation with the physiotherapy team.

Following her admission and treatment with a ketamine infusion, Huyaam's prescription was changed. She went home with Buprenorphine patches (10mg), morphine PRN for breakthrough pain (10mg), clonidine (25mcg 8hrly) (clonidine is an alpha-2 adrenoceptor agonist which targets activity in the spinal cord), pregabalin, amitriptyline and paracetamol by the clock. A few weeks later, Huyaam was struggling with dizziness which seemed to be a side effect of the clonidine, so that was stopped.

Now it was time to start increasing Huyaam's skills in using non-pharmacological pain management strategies, such as exercise. We hypothesised, that the less activity Huyaam did, the weaker she became, the more sensitised her nervous system became, and the more likely it was that she would have severe episodes of pain like this one. Our goals with exercise were to (i) increase strength and joint stability; (ii) increase function and her ability to participate in life; (iii) stimulate endogenous descending inhibitory mechanisms; (iv) expose Huyaam to feared movements and activities to gradually reduce her disability; (v) introduce some fun into Huyaam's life (23). Once Huyaam understood that it was safe to exercise, we discussed what exercise she would like to do. We started with land-based exercise supervised by physiotherapists who understood pain and progressed to physiotherapy-led hydrotherapy sessions. At all exercise sessions we integrated the pain science education, reinforcing the key messages all the time.

Our goals with exercise for someone with nociplastic pain:

Increase strength and joint stability;

Increase function and her ability to participate in life;

Stimulate endogenous descending inhibitory mechanisms;

Expose Huyaam to feared movements and activities to gradually reduce her disability;

Introduce some fun into Huyaam's life

The team also planned an active strategy to upskill Huyaam and empower her to become an active participant in her interdisciplinary health team, with the ultimate goal of Huyaam becoming the team leader. We aimed to do this by increasing her self-efficacy using goal setting and problem-solving approaches (24). Throughout her treatment, we didn't tell Huyaam what she should do or what treatment was to be followed, rather we facilitated her own problem-solving to seek solutions and find alternative ways of managing. We also taught Huyaam about SMART goals and she gradually became more confident and adept in her own management. As she learnt to set goals, goals which she achieved, Huyaam's self-efficacy rose, and she gradually became more and more active in her own management.

The final step in Huyaam's transition to becoming an active self-manager and becoming her own team leader was participating in the Pain Education Empowerment Program (PEEP) (25-27). PEEP is a group-based 6-week outpatient, physiotherapy led programme which integrates pain science education, exercise, mindfulness, and relaxation training. A workbook (link to it here) is used to facilitate weekly discussions (also known as psychoeducation), goal setting, exercise and mindfulness or relaxation training for groups of between 4-10 people living with chronic nociplastic pain. Huyaam and her mother participated in the group intervention, ensuring that they were on the same page about Huyaam's management. In addition to embedding the skills Huyaam had learnt so far in her treatment, she also learnt and implemented mindfulness strategies to manage stress – a key component to succeeding in her future studies and career.

DON'T MISS THIS

Resources

There are many freely available resources to facilitate pain science education – we have compiled a list of them here. The workbooks which we have developed and shown to be effective in South Africans with chronic nociplastic pain, OA pain and chronic pain in HIV are also freely available for use. You can access them here.

By the time of the Covid-19 pandemic and lockdown, Huyaam had developed the knowledge and skills to manage her pain well, with the members of the pain team providing guidance. Her management included daily exercise, hiking, running, and hydrotherapy weekly in a warm pool. During the 2019-2020 lockdown period, Huyaam weaned herself off her opioids and pregabalin and is now on a maintenance regimen of amitriptyline and paracetamol for her pain, and baclofen to control her muscle spasm. Huyaam primarily manages her pain using pacing strategies, mindfulness and exercise (she is now an exercise addict!).

The person with pain – the leader of the inter-disciplinary team

> *Eight years of training with Professor Parker and managing my chronic pain in a rather empowering manner has been the biggest blessing. Education and knowledge is power. Providing me with psychoeducation as a form of treatment has been life changing. This is not to say, I don't have little hiccups down the road with my health and require guidance from the medical team, but I am much more independent and through this have developed myself. This condition and dealing with chronic pain, have given me an upper hand in every aspect of my life, whilst climbing this never-ending mountain, I have been fortunate enough, to establish myself as a strong, resilient, a bit too ambitious but independent young woman. In 2020, at the start of the pandemic, after being on quite strong medication for more than nine years, I made the decision to reduce most of my medication and wean off them, as a result of regular training and proper management skills whenever a flare-up occurs, and the best part of it was that the pain management team encouraged me and supported my decision. Finally, I realised what they were trying to tell me all along. Chronic pain is debilitating but I think being mindful and taking everything in my stride has made everything much more manageable. Reflecting, practising mindfulness, and using my toolbox along with exercise have been pivotal in managing my condition. I am no longer defined by my chronic pain, but rather, I am in control of defining it.*

DON'T MISS THIS

Taking the long view

This treatment has taken 8 years. Huyaam is now the leader of her interdisciplinary team. She is knowledgeable and empowered to partner with her health care team to optimise her quality of life. The fact that she took the initiative during lockdown to wean herself off her medications is a clear indication of how she has taken the lead. She continues to engage in active methods to manage her pain, using exercise and mindfulness daily. She participates in hydrotherapy exercise in a warm pool whenever possible and she manages her work/life balance carefully using pacing strategies. In the university environment Huyaam works with her lecturers and the disability support unit to enable her to pace her work and she continues to achieve academically. Huyaam rarely has exacerbations. She is living a full and rewarding life, despite her pain.

2 Complex Regional Pain Syndrome (CRPS)

Jo Park-Ross
Johan van der Walt
Romy Parker

Nociplastic and neuropathic pain - how an acute traumatic injury led to a downward spiral, and how drawing a map allowed a reimagining and reclaiming of life.

Introduction

I am a paramedic. Before my accident, I worked on ambulances, helicopters, and airplanes all over South Africa, and was so proud of my job. Every day was different and unpredictable – in a single day I could be hoisted down onto a mountain to rescue someone, treat patients at a car accident, and care for a critically ill baby. My job was so much of my identity.

I had an accident while riding my horse. He tripped doing a simple exercise and flipped over forward onto his back! He twisted to not fall on me, but in the fall, I took both of our weights onto my right hand and dislocated my thumb. He was bleeding and I was panicking, and I just relocated my thumb to help him get his saddle off. I don't remember any pain, only remember being worried that he was hurt and not being able to get his saddle off because my fingers wouldn't move. Thinking I had just dislocated my thumb, I immobilised it as is normal and took some time off work. I am right-handed, and I couldn't move most of my fingers. It took me a long time to seek any care because I was so convinced that I was just waiting for my dislocated thumb to heal.

Thumb dislocations

Falling onto an outstretched thumb would have resulted in forced hyperabduction of the metacarpophalangeal joint with resultant rupture of the ulnar collateral ligament and dislocation of the joint – an injury known as skier's thumb (28). However, the name is misleading, as while this injury accounts for 86% of all injuries to the base of the thumb, only 10% of them are reported to have been sustained during skiing. The most common cause of injury is a high-speed fall onto the hand in a range of sports, including falling from a horse, as happened here (29).

The obvious symptom in this case was the dislocation of the joint. Bravely, Jo reduced the dislocation within minutes, but she continued to have the other classic symptoms of the injury: swelling, weak grip or inability to grasp, bruising, and pain on any movement of the thumb and of the wrist. Conservative management would include immobilisation in a thumb spica for 4-6 weeks, up to 12 weeks if a severe lesion (30). If the ligament rupture is complete or conservative management has failed to restore joint stability, then surgical repair is indicated followed by 6 weeks of immobilisation. Whether managed conservatively or with surgery, rehabilitation with physiotherapy or occupational therapy is usually required for up to 3 months. Jo managed her own injury, correctly immobilising it and taking time off work. However, it did not seem to be healing and she then underwent surgical repair.

Jo can't get back to work

"We don't know how long it will take" the surgeon replies when I ask when I can go back to work. "Maybe six months, maybe a year, maybe five". I can barely remember what he told me during that first meeting. He explained to me that I had very few ligaments left in my thumb, "a skier's thumb", and they would reconstruct and anchor the ligaments to regain movement. Within a few weeks of my surgery, I was on unpaid leave, and it was clear I had to resign from my job, with no idea of how to support myself and massive medical bills exceeding the support of my medical insurance. My rehabilitation was slow, and for months my fingers didn't move.

"I dont think anyone will believe how much pain I am in"

The next year is a blur. I missed the final exams for my masters degree, and I couldn't think straight on strong pain killers. After months, I got an office job at the same service. After work every day, I got into bed in my work clothes with no interest in food and fell asleep immediately, and slept through my alarm every morning.

I work as hard as I can with my physiotherapist, I do my exercises furiously. I want to go back to work. Most of the time I can't remember what he says through the heavy haze of analgesia, so we film my exercises on my phone for me to copy at home. I work and work and work. And one day it all starts moving. I can lift fingers, I can hold and drink from a mug using both hands, and it all feels miraculous but I am still in constant agony. But I am still scared of hurting myself, still feel frail, scared to take my cast off at all and in an endless fog of pain with no answers. I struggled to talk about my pain or my injury because I don't think anyone will believe how much pain I am in or understand me.

Jo's pain treatment so far

Jo's story underlines the importance of assigning the correct place and time for initiating certain medications in treating acute and chronic pain. W e are privileged to live in an era where we have multiple different classes of analgesic agents available to treat pain. But it would also be correct to say that in many instances we use them incorrectly and become overly dependent on them. At the time of Jo's initial injury, it would have been correct to use multimodal analgesia starting with Paracetamol, NSAIDS and weak opioids like Tramadol (31). The use of stronger opioids for a short period of time (7-10 days) would also be justified. It is critical that we treat acute pain properly, as the risk of chronification of pain significantly increases if we do not (32). However, all medication comes with side-effects. While short-term use of NSAIDs is appropriate during the inflammatory phase of healing, their long-term use may cause gastric ulcers due to their effects on the COX1

pathway, as well as kidney problems and bleeding tendencies (33). Therefore, we must partner with the person with pain to ensure that they understand the treatment, how to use it properly, and what to expect. Finally, they need to be given clear guidelines on when to expect to start feeling better, and what action to take if they are not feeling better – including coming back to the healthcare team.

Opioid use is associated with gastro-intestinal upset and constipation (34). Most importantly, long-term opioid use is associated with drug dependence (35). The long-term use of opioids results in tolerance to the analgesic effects of the drug, requiring higher doses (36). In addition, the continued use of high dose opioids for chronic pain may cause a paradoxical increase in pain called opioid-induced hyperalgesia, as we discussed in the previous chapter with Huyaam (37). Finally, long-term opioid use may have negative cognitive and emotional effects.

Mechanisms of pain

The mechanisms contributing to pain after this injury have transitioned over time from acute nociceptive pain to a chronic, nociplastic, and neuropathic pain. Initially, the pain would have been driven by a strong nociceptive barrage in the peripheral nervous system but, over time, the dominant mechanisms have changed.

Peripheral nervous system

As would be expected following an injury such as this one, the peripheral nervous system would have been sensitised with the inflammatory process associated with the injury. Peripheral sensitisation (lowered firing thresholds, increased responsiveness to stimulation, and activation of silent nociceptors) would present, with primary hyperalgesia – increased pain to a stimulus that is normally painful, in the area of tissue damage. There was also bruising and swelling. As the inflammatory process settled, this sensitisation should have settled down and normalised.

DEEP DIVE

Inflammation is normal with acute tissue damage

In response to the damaged tissue, vasodilation brings a rush of pro-inflammatory cytokines like TNFα, IL-1β, IL-6, and IL-8 into the area. These pro-inflammatory cytokines kickstart tissue healing. The inflammation is evident in increased temperature, redness, and swelling at the site of injury. The high concentration of pro-inflammatory cytokines together with the raised local tissue temperature sensitises A-delta and C-fibres (nociceptors). *This is normal, and useful* for acute injuries. But it becomes problematic when the sensitisation of nociceptors is maintained after the tissue has healed.

However, it is possible that the ongoing instability of the joint (due to the ligament rupture) led to ongoing stimulation of the nociceptors before the surgery, contributing to more and more peripheral sensitisation. Before the stabilising surgery, Jo was not using her hand, and it is likely that when she did use it, the joint moved to the point where the sensitised nociceptors fired, not because it was dangerous but because the nociceptors were sensitised. Then there was surgery, a new inflammatory insult to a sensitised peripheral nervous system. This may have supported ongoing sensitisation despite adequate tissue healing after the surgery. Tissue healing did take place; she gradually got movement and function back – but the pain was unremitting. The pain was no longer coupled to the tissue healing processes.

Spinal cord

The barrage of nociception from the periphery to the spinal cord will have caused spinal cord sensitisation with allodynia, referred pain, and secondary hyperalgesia. Pain from normal touch, pain referred to her whole hand, wrist and forearm, and hyperalgesia to stimulation would be expected during the inflammatory phase and into the second, regeneration phase of healing (remember your stages of healing? – hyperlink to Section 1). However, as she entered the third, remodelling phase of healing, this sensitisation should have been normalising – but it did not. For months

after the surgery, Jo continued to have all these symptoms indicating spinal cord sensitisation was ongoing, despite tissue healing. The unrelenting nature of the symptoms despite tissue healing was an indication that her pain was de-coupled from the tissue healing processes.

DON'T MISS THIS

Possible contributors to ongoing spinal cord sensitisation

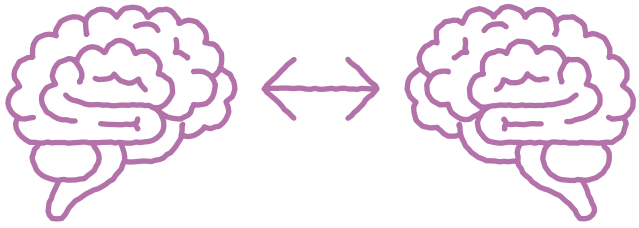
There are many clues in Jo's story that suggest contributors to ongoing descending facilitation that would maintain sensitisation in the spinal cord. At the start, Jo relates how, when the accident happened, she "was panicking" about her horse bleeding, "worried that he was hurt". This gives us some insight into the emotions around the event, which initially generated a strong descending inhibitory response – as she says, she had no pain at the time! However, her words give us a clue as to the importance of her relationship with her horse, and how important riding him was to her. And yet after the injury, she stopped riding, and this important relationship was lost. Not only did she stop riding, but she also stopped working. Jo has told us that being a paramedic was important to her, she was proud of her job, it was her identity, now she lost this too. These losses may have resulted in descending facilitation whenever she thought about her thumb, noticed she couldn't use her hand, or considered what it all meant. And then, Jo was given unclear messages about how long it might take to get better, even that it might never get better. She was told that she has almost no ligaments left and given many messages about the fragility of her thumb. All of these messages would have contributed to threat, and therefore to pain, and may have reduced her descending inhibitory mechanisms.

Brain

When the injury occurred, Jo's brain accessed all its powerful analgesic mechanisms: she felt no pain and she reduced her own dislocation as she prioritised her horse's wellbeing. Her training kicked into gear, and she made sure that she and her horse were OK. Once safety was established, her brain would have re-evaluated the situation and, instead of descending inhibition, descending facilitation would have dominated, allowing more nociception to reach the brain. The system turned up the pain to capture Jo's attention and motivate her to do something about her thumb. Jo's brain would have accessed all her prior knowledge and experience in the hippocampus (the memory centre). Her system likely tapped into all she knew about these injuries and compared them to all she has seen in her career, to decide how much pain to generate. It was painful initially, but she expected that, and she expected that, if she looked after it, it would get better. However, over time, as she did not get better, her brain would have continued to try to solve the problem of pain, and perhaps not surprisingly given her life experience working in trauma, her brain turned up the pain volume.

Before

I am strong and fit, and I don't think I have hurt myself too badly - I am more worried about if my horse is hurt!



After

I don't know how to cope anymore. Nothing helps and there must be something seriously wrong!

What evidence do we have that Jo's brain may have been turning up her pain? Jo tells us that "*it was clear I had to resign from my job, with no idea of how to support myself and massive medical bills exceeding the support of my medical insurance*" – she was feeling helpless and lost, she had tried everything she knew and was doing everything she was being told to do, and yet it wasn't working. This can result in a spiral of pain, disability, fear, disuse and more pain. She couldn't think straight, her cognition was impaired, she stopped engaging in life generally, her life shrank to a single focus on getting better. All of these other subtle cognitive and motivational symptoms suggest the involvement of brain-level processes. And while her function improved, the pain did not, in fact it spread, up her arm, and started to affect her mood, her personality, her cognition.

Synergistic systems

Jo wasn't sleeping well, she collapsed into bed after work but was constantly tired. She described being in a fog, not eating, not exercising, feeling financially stressed, and feeling physically stressed trying to do her job, but feeling unable to cope. The lack of sleep was critical for Jo: it would have upregulated the sympathetic nervous system, with loss of parasympathetic activity and further sensitised her nervous system.

DON'T MISS THIS

The 3 I's of Pain

Pain interrupts and interferes, and it interrupted and interfered with Jo's life in multiple ways. When pain continues like this, it not only interrupts and interferes; it also changes people's identities – we can clearly hear from Jo that she was no longer the person she used to be (38).

A blur of ongoing pain and suffering... and then there is hope

> *I dislocated my thumb again trying to pick up a cup, and the discussion was no longer about rehabilitation but about more surgery. I felt fragile, lonely, totally reliant on other people for even the most basic tasks and like my life had shrunk. "Be more careful, it could happen again," said the surgeon. I was taking heavy analgesia to get through the day, and it made me spacey and confused. I asked my physiotherapist and surgeon about the pain – it's in my arm and hand now – and their answer is to prescribe more painkillers and more exercises, inject steroids into joints, and offer to surgically fuse my thumb as a whole so it won't move.*
>
> *Through a colleague, I got a referral to a specialist pain clinic. "I have some ideas of what could be causing your pain, and some things we can try," says the pain specialist. For the first time, I felt hope and relief. It is all so hard to remember through the fog, and I don't remember much of what we talked about, but I remember crying because I was so relieved. I wasn't alone anymore – I had help and some answers. That's all I really remember: being believed, knowing that there was hope and I wasn't making it up. She believed me when I talked about my pain, and she had answers for where it came from. She wasn't just giving me more drugs, more exercises I couldn't do, or suggesting more surgery.*
>
> *With my eyes closed, she did a test to show me how well my brain was connected to my hands, and it was miles off normal. She measured how closely I could tell where two points were touching – when I opened my eyes after she tested they were 5 centimetres apart. It was there and visible – the damage and the pain was real and shown in two marks on my wrist and elbow.*

Assessing the pain mechanisms

The first consultation was initiated by asking Jo what she hoped to gain from the session. It was important to initiate a trusting therapeutic relationship and ensure that everyone was on the same page in terms of the goals of treatment. Jo indicated that she wanted to understand what was wrong, why was she still in pain? And she wanted to know whether there was any hope at all that she might be able to use her hand again, that she might regain her life.

Using open questioning Jo was invited to tell her story from the beginning and in the telling we could establish the "O, P, Q, R, S, T, U, V, W" of her pain. Key information which gave insight into the nociplastic and neuropathic mechanisms of her pain are outlined in the Table below.

Table 3.3:
Key insights from Jo's "O, P, Q, R, S, T, U, V, W" of her pain

Gather information on the...	Jo's information	What it tells us
Onset	Still painful well after tissue healing time	Pain is no longer nociceptive
Provoking and palliating activities	Everything and nothing	Suggests central sensitisation
Quality of the pain	Burning, tingling and electrical shooting pain	Suggestive of neuropathic pain
Region or radiation	Spread into her whole hand, up her arm and into the bicep	This referral pattern does not reflect the thumb or hand innervation. Suggests nociplastic changes
Severity	Severe – Jo was totally overwhelmed by pain	Pain was completely derailing her life
Treatment	Analgesia (central acting opioids) not effective	Suggests that opioid receptors are not available for the drugs to work. Also suggests that the opioid pathway is not involved in the mechanism of pain. Neuropathic and nociplastic pain have poor responses to opioids.
Understanding beliefs and impact	Jo believes her thumb is unstable, it will never get better, and the pain means she can't use it. But Jo also doesn't understand why the pain is spreading up her arm and getting worse, not better.	Jo has been given repeated messages about how severe her injury was, how uncertain her recovery is, how vulnerable it is. She has been told not to do things, not to work, not to ride, not to use the hand for fear of dislocating again. All of these messages will have increased the threat factor, and are increasing the impact on her function.
Values	Jo is desperate to get back to being herself, to be a paramedic, to ride her horse, to reengage with friends and family.	Jo had gotten stuck in a spiral of pain, avoidance of activities, isolation, and more pain. Treatment needed to focus on restoring meaningful life roles, not just reducing pain.
What else?	Jo was very tearful, and afraid of what the future held. She was anxious and depressed. Jo was not sleeping.	Synergistic systems – particularly stress and the autonomic nervous system – were exacerbating her pain.

Based on Jo's history, there was clear indication that a physical examination was needed to check for indications of neuropathic pain (allodynia, hyperalgesia and sensory loss). When doing the physical examination of Jo's hand and arm, it was clear that there were no signs of inflammation and her surgical scar had healed well, in fact her hand and arm looked remarkably normal. However, she had allodynia up to her elbow, with primary and secondary hyperalgesia to careful pricking with a straightened-out paperclip. These findings, coupled with her history, were suggestive of nociplastic pain, in particular the condition called Complex Regional Pain Syndrome (CRPS) type 1. The Budapest criteria were used to confirm that she had the CRPS-1 (Table Y.1) (39).

Table 3.4: Jo's scoring on the Budapest criteria confirming her diagnosis of CRPS-1

A: The person with pain has continuing pain which is disproportionate to any inciting event	☒
B: The person with pain has at least one sign in two or more of the categories	☒
C: The person with pain reports at least one symptom in three or more of the categories	☒
D: No other diagnosis can better explain the signs and symptoms	☒

Category		Sign (you can see or feel a problem?	Symptom (the person with pain reports a problem)
1: "Sensory"	*Allodynia* (to light touch and/or temperature sensation and/or deep somatic pressure and/or *hyperalgesia* (to pinprick)	☒	☒ *Hyperesthesia** does also qualify as a symptom
2: "Vasomotor"	Temperature asymmetry and/or skin colour changes and/or skin colour asymmetry	☐ If you notice temperature asymmetry it must be >1°	☒
3: "Sudomotor/ oedema"	Oedema and/or sweating changes and/or sweating asymmetry	☐	☒
4: "Motor/ trophic"	Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair/nail/skin)	☒	☒

Allodynia – pain from a normally non-painful stimulus
Hyperesthesia – abnormal increase in sensitivity to normal stimuli
Vasomotor – relating to constriction or dilation of blood vessels
Sudomotor/oedema - A medical term used to describe something that stimulates the sweat glands.
Motor dystonia – disorder in motor coordination

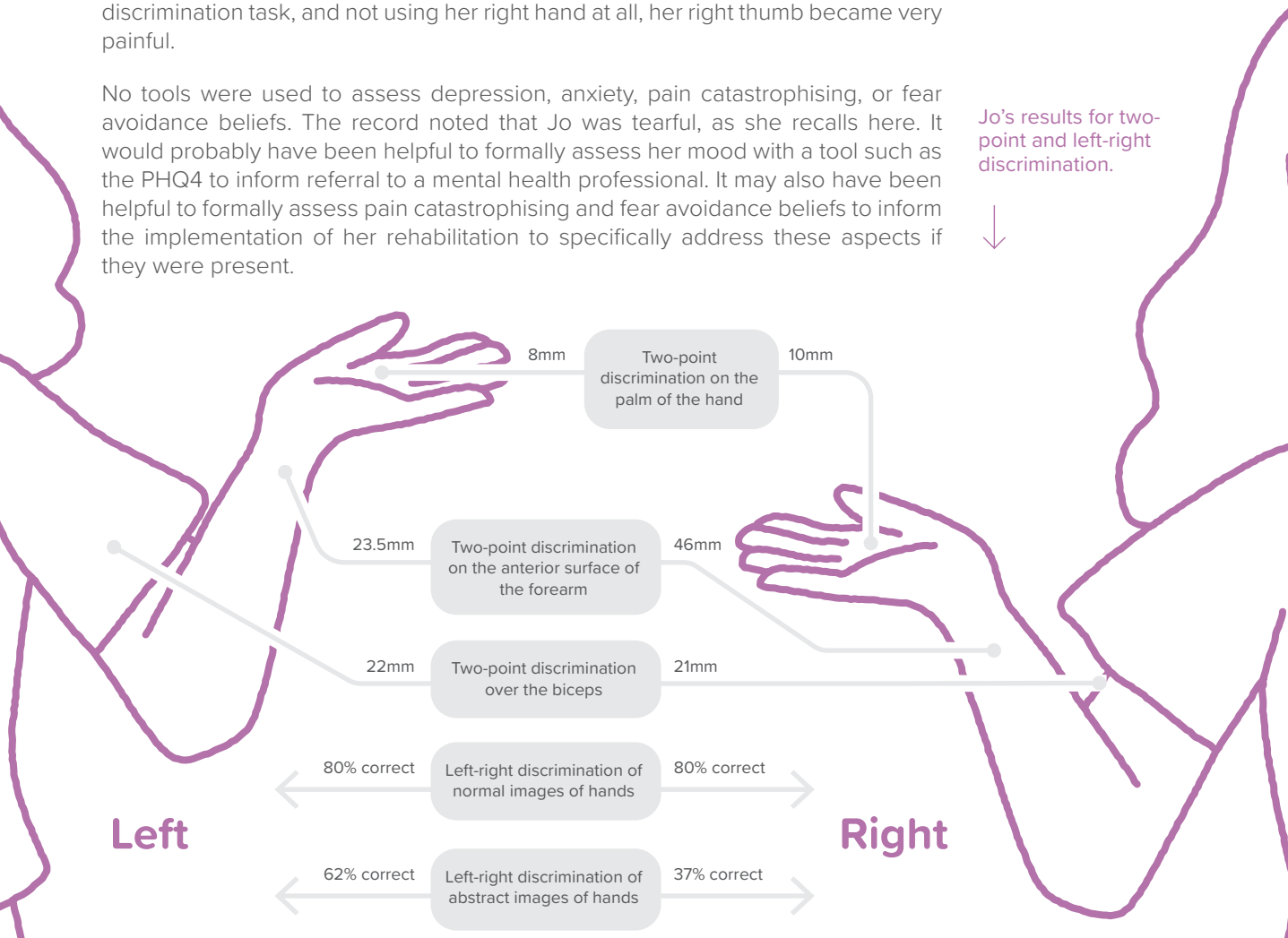
However, was this only nociplastic pain? Because Jo's pain was spreading from her hand up her arm and into her shoulder, she could have been developing widespread pain from central sensitisation. The Central Sensitisation Inventory was used to establish whether Jo had global sensitisation. On this tool, she scored 35, indicating mild central sensitisation. This score suggests that while she has some widespread sensitisation .

Finally, additional sources of nociceptive pain were explored in the physical examination. Examination of range and muscle strength, although impaired, did not reproduce her pain. The assessment of neurological integrity (dermatome and myotome) was also normal, as was the neurodynamic assessment. However, assessment of full range of shoulder abduction, extension and external rotation reproduced pain in Jo's bicep which she had specifically described as "one point of pain where it feels like it's boring into my arm". On palpation, it appeared that she was developing fascial tethering or cording, possibly as a result of long-term lack of movement.

Now that we had a diagnosis of her pain as CRPS-1, a nociplastic chronic pain, with some nociceptive input, we needed more information on the specific mechanisms which might be contributing to her symptoms. We assessed her two-point discrimination and her left-right discrimination between her left and right hands (Table Y.2) – both tests indicated that Jo had altered somatosensory representation of her painful right hand. Jo also commented that while she was doing the left-right discrimination task, and not using her right hand at all, her right thumb became very painful.

No tools were used to assess depression, anxiety, pain catastrophising, or fear avoidance beliefs. The record noted that Jo was tearful, as she recalls here. It would probably have been helpful to formally assess her mood with a tool such as the PHQ4 to inform referral to a mental health professional. It may also have been helpful to formally assess pain catastrophising and fear avoidance beliefs to inform the implementation of her rehabilitation to specifically address these aspects if they were present.

Jo's results for two-point and left-right discrimination.



With this additional information from the assessment, we needed to include treatments that would target:

- The peripheral nervous system by targeting the fascial tethering.
- The central nervous system sensitisation by
  - Understanding pain
  - Reducing fear
  - Restoring somatosensory representation
  - Restoring meaningful life roles
  - Targeting mechanisms pharmacologically
- The synergistic systems by
  - Addressing sleep
  - Reducing stress

Complex Regional Pain Syndrome Type 1

CRPS-1 is a nociplastic pain condition typified by severe regional pain that is disproportionate to tissue healing, with associated sensory, vasomotor, sudomotor or trophic changes (40). In the ICD-11, CRPS-1 is classified as one of the chronic primary pain conditions, MG30.04. This extremely painful and distressing condition develops in between 0.2-4% of people who have had an injury (39, 41).

The strongest predictor of developing CRPS-1 post trauma is severe pain (≥5, on a 0-10 pain rating scale) in the first week after injury (42). The condition affects women 2-4 times more often than men and is most commonly reported following upper limb fractures, trauma or surgery (39). The risk of developing CRPS-1 also increases with depression and kinesiophobia (fear of movement). As CRPS-1 is recognised as a nociplastic pain condition, it is perhaps not surprising that risk of developing the condition also increases in people who have other nociplastic pain conditions such as fibromyalgia and headaches (39).

CRPS is such a debilitating pain condition that 50% of people with it have considered suicide.

CRPS-1 is a debilitating condition. Nearly 50% of people with CRPS have considered suicide; 15% have attempted suicide (43). People suffering from this painful condition have described it as a "war-like" experience with daily battles with the enemy, pain (44). In addition to having to manage their pain in an ongoing battle, they also report intense fear that the pain will spread to other parts of their body and struggles engaging with healthcare professionals who do not believe or understand the severity of their condition. Based on this experience of living with CRPS-1 as living through a war, many organisations and support groups refer to sufferers as 'warriors' fighting battles with CRPS-1 (44).

Restoring what had been lost

> *We talked about trying to start regaining the parts of my life that I missed – running, riding my horse, being a paramedic again. I hadn't thought that I was going to able to do any of those things again – all the things that were the most important to me and who I am. I felt brave enough to try again, and when I felt more like myself, I felt more in charge of my recovery. I had tools to manage my pain that weren't just the haze of heavy analgesia – she showed me how to better manage multi-modal analgesia, the importance of exercising and eating, and helped me feel stronger. My treatment involved using an app to help my brain to tell which was my right and left hand. The first time I tried the app,*

my score was less than 15%. That meant that in fewer than 15% of the times I showed my brain a right or a left hand, it just could not tell the difference. After six months, my scores were over 85% consistently, and I could feel the difference in how much less analgesia I needed to get through the day, and I didn't need to sleep for 14 hours a day. The pain in my arm was just fascial tethering – and after a few weeks of rubbing my arm with a tennis ball and a horse brush, I was pain-free there.

A treatment plan

Having developed a trusting therapeutic alliance through the assessment process, Jo could now engage in a discussion about her pain and treatment options. All the relevant treatment options were offered to Jo, and she chose to start with learning about pain and her own pain in particular.

Pain science education is a form of cognitive reassurance which Jo particularly benefited from because she had been struggling to understand her pain for so long. Structured education, using a range of tools including drawing on pieces of paper and explaining the results of her assessment, helped Jo to understand that her pain was a problem in and of itself, rather than a symptom of something else being wrong. A critical component of this education was explaining to Jo that the "maps in her brain of her body" had become distorted – this is why she was struggling with two-point discrimination and left-right. The explanation, coupled with the evidence of the pen marks on her arm, were a "light bulb" moment for her, confirming that she wasn't going mad or making up this pain, but there was something to explain it.

Pain science education is a powerful treatment for pain. It empowers the person with pain to engage in active rehabilitation.

Once she understood her pain, Jo could begin to engage with methods to "redraw her brain maps", not just of her body, but also the map of her life. To redraw the map of her life we discussed normalising her daily routine, sleep hygiene, and getting back to doing the things she loved, including riding her horse. With facilitation, Jo developed a daily activity schedule which included regular rest periods when she practiced relaxation and mindfulness techniques, time to do her rehabilitation exercises, time to work, and most importantly, time to play, including running and riding her horse. This was her map to regain her life.

To redraw the "map of her body in her brain" Graded Motor Imagery training was initiated (41). The first step in this treatment is left right discrimination. Jo started left-right discrimination training using an app she downloaded onto her phone (Recognise®). She practiced recognising left or right hands for 5 to 10 minutes every hour initially. Over time she slowly reduced this to five times a day with extra doses for breakthrough pain.

Finally, Jo was offered manual therapy for the fascial tethering, which involved hands-on physiotherapy treatment. The "pain boring into her arm" immediately felt better after this treatment and then Jo was given specific mobilising exercises to do daily.

At this first treatment session, Jo had told us that she would be leaving to work in a distant town for two months. This meant that we focused a lot of the treatment on what Jo could be doing for herself, giving her structure on how to progress her own treatment every two weeks and clarity about what to expect. We also discussed pharmacological treatment options with Jo.

DEEP DIVE

Graded Motor Imagery

In the chapter on phantom limb pain, we discuss the use of Graded Motor Imagery (GMI) in more detail. Broadly, the treatment approach is based on the understanding that the representations of the body in the primary and secondary somatosensory cortices of the brain (your sensory homunculus) and the representations in the pre-motor and motor cortices (your motor homunculus) are use-dependent. Remember we discussed this in Section 1? With many nociplastic pain conditions, these maps change, getting larger, moving, and losing specificity. The GMI three-step treatment approach targets these maps – in the sensory and motor homunculi – and aims to make the representation and activation of the affected area more precise. Let's break this down. Step 1: refining the maps in the somatosensory cortices by practicing left/right recognition. For Jo, this meant looking at pictures of left and right hands, because that's where she had pain – in her hand – and practicing recognising whether the picture was of a left hand, or a right hand. (If someone has foot pain, they need to look at pictures of feet! i.e. the pictures must be of the affected anatomical area). When Jo was able to recognise right hands (the affected side) with the same accuracy and speed as she could recognise left hands (the unaffected side), she was ready for Step 2: refining the maps in the pre-motor cortex by practicing imagined movements or doing visualisation exercises. Sometimes imagining movement can make pain worse. Practicing imagined movements in different contexts is then important to "refine" the representation of the affected area in the map in the pre-motor cortex. When Jo was able to imagine movement without her pain getting worse, she was ready for Step 3: mirror visual feedback. In this step, the painful limb (in this case, the right hand) is hidden behind a mirror and the unaffected side (in this case, the left hand) is placed in front of the mirror. When Jo looked into the mirror, it looked like she was looking at a right hand, even though it was just a reflection of her left (unaffected) hand. She then performed bilateral hand exercises. This means that the brain is getting reassuring visual feedback showing accurate execution of the movement instructions it is giving, helping it to "refine" the representation of her hand in/on her motor cortex map.

It is clear that chronic nociplastic and neuropathic pain requires a different pharmacological approach. Jo told us that the opioids were not helping, and this is reflected by the research showing that opioids are not effective for nociplastic pain. As outlined in Section 1, we turn to the membrane stabilising drugs like anti-epileptic drugs to target the spontaneous firing of neuropathic pain and associated sensitisation of nociplastic pain. We also turn to the anti-depressants which target the central nervous system such as the tricyclic amitriptyline and the SNRIs duloxetine and venlafaxine. These drugs increase the CNS concentration of nor-adrenaline and serotonin that increase descending inhibition with resultant decrease in pain.

All medications also have side-effects. However, not all medications cause dependence, and some side-effects like drowsiness can be used to the advantage of the person using them. We know that Jo was struggling to sleep. If Jo had taken some of these medications earlier in her pain journey, she may have had better sleep, and an improvement in her mood as well. The correct application of medication targeting specific receptor pathways can help people on their road to recovery. However, when we prescribe incorrect medication for prolonged periods of time, they may very well prevent the person from getting better and place them at an increased risk of drug dependence.

Once we had reviewed her medication, Jo chose to adjust it, with the guidance of the doctor, to using 1g paracetamol 6 hourly.

DEEP DIVE

Corticosteroids for CRPS

The unique pathophysiology of CRPS offers the opportunity for two interventions in the acute phase that could drastically alter the course of the condition. Since CRPS has been shown to increase pro-inflammatory mediators, clinicians have studied the effectiveness of corticosteroids as a treatment modality to decrease the inflammatory response in the acute phase of the disorder (45). Some researchers have suggested that CRPS may also represent an auto-immune disorder, which further points towards the efficacy of glucocorticoids (46). CRPS is also known to involve bone demineralisation (47). The increased osteoclast activity may also release pro-inflammatory mediators from the bone, and therefor bisphosphonates have also been effectively used in the treatment of CRPS. Let's have a look at these two treatment pathways.

Corticosteroids are potent anti-inflammatory drugs that are used in numerous disease profiles where the body's natural pro-inflammatory response becomes harmful. Prednisone is an oral glucocorticoid agent (48). It has potent systemic effects and should never be prescribed long term without considering its numerous side-effects. Prednisone has been used at various dosages in the first 6 months of people presenting with CRPS (45). We know that the earlier we treat CRPS with prednisone, the better the treatment response. One of the treatment guidelines with good clinical evidence, suggest that adult patients with CRPS should be started on a 28-day taper regimen starting at 60mg prednisone per day (45). This dose is decreased by 5mg per day up to 20mg, after which it is continued at 15mg per day for one week, 10mg per day for one week and ends on 5mg per day for one week. The elderly, adolescents and diabetic patients start on a slightly lower dose of 40mg per day before the taper. This high dose, 28-day taper has been shown to improve all the symptoms associated with CRPS included in the Budapest Criteria. Treatment response is best if started in the first 6 months – the sooner, the better!

Bisphosphonates inhibit bone resorption and are commonly used in osteoporosis and other metabolic bone diseases (49). They act by inhibiting osteoclast activity. There are various oral or intra-venous bisphosphonates available. One of the studies used oral alendronate 40mg daily for 56 days (49). This double-blind placebo-controlled trial with cross-over design, showed a significant reduction in CRPS symptoms after 4 weeks. The placebo group crossed over to alendronate at 16 weeks and displayed significant improvement on the drug. There is good quality evidence to suggest that bisphosphonates as well as prednisone can have a major effect on the symptoms of CRPS if the treatment is initiated early in the disease progression.

Two months later, Jo's pain was significantly reduced. She was sleeping well and waking refreshed. She had been riding her horse, been to the gym, and was engaging socially. Her left-right discrimination and two-point discrimination were still not normal but had improved. Jo also found that, when she had exacerbation of her pain, she could use the left/right discrimination app for effective analgesia. She progressed to imagined movements in the Graded Motor Imagery programme and continued to build her fitness and activity levels.

Conclusion

> *It has been a few years now. I live a wonderful full life, I have a career that I love and am happier beyond what I could have ever imagined. I don't think I will ever be pain free, but I never feel limited by my pain.*

As we have heard from Jo, Complex Regional Pain Syndrome can completely derail someone's life. The good news is that we can make a significant impact on pain and, if the diagnosis is made and treatment initiated within the first two years of onset, we have a good chance of having significant effects (41). In our experience, if we can start treatment early, this is one chronic nociplastic pain condition we aim to cure. As we see here, a cure is getting someone back to living their wonderful full life!

4 Chronic Pelvic Pain

"Putting out little fires everywhere": navigating chronic pelvic pain

Em
Corina Avni
Romy Parker
Meg Merand
Nicole Chilimigras

Introduction

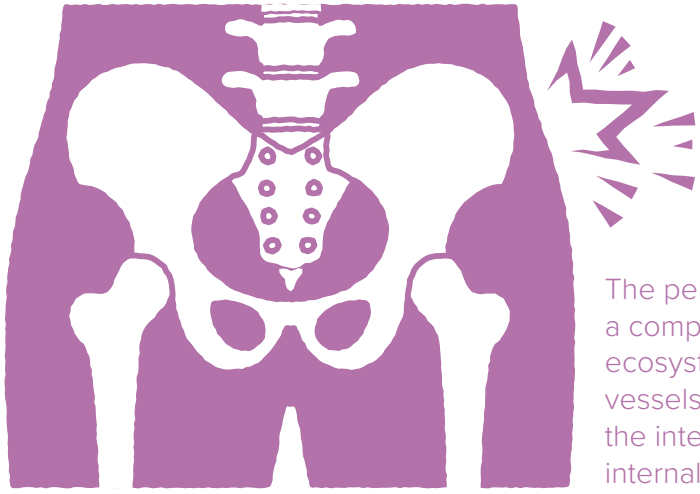
I am a 29-year-old single female part-time lecturer living in the Western Cape, South Africa. Life has not been overly easy so far, with multiple struggles – some physical, some mental, and some social. My case is complex, and my symptoms have changed over time; I have not always been able to find an empathetic healthcare professional to assess and manage my symptoms, which include:

- *Ongoing constant symptoms of urinary tract infections (UTI), including needing to go and empty the bladder all the time with small volumes and poor flow, and a burning urethra worse before and after emptying; there is slight relief during passing urine. If I do have a UTI, then the pain after emptying is significantly worse. These symptoms are flared by sexual activity, orgasm, tight clothing, stress, and high levels of (sexual) frustration.*
- *Hip pain with a labral tear right hip with arthroscopy in 2020; a traumatic experience due to no opioid pain relief after the procedure and excessive hip pain requiring me to be in bed for months. I now have concerns that there is a labral tear on the left.*
- *General body tension with a sensation of my muscles "feeling out"*
- *Headaches – migraine and tension-type headaches*
- *Jaw tension and pain – temporomandibular joint disorder (TMD)*
- *Recurrent thrush - vaginal*

Other history of note is that I am extremely sensitive, in recovery (Narcotics Anonymous), and have prominent levels of toxic shame. I used to have an eating disorder (bulimia) and used to smoke cigarettes. I lost my virginity at 16 and have never been pregnant. Sexual activity has flared my symptoms sporadically; at present, I am on a self-imposed 1-year sex sabbatical/ban as sexual activity now flares symptoms every time. I have metabolic syndrome, asthma, polycystic ovarian syndrome (PCOS), and ADHD.

Epidemiology

Chronic pelvic pain is described as cyclic or non-cyclic pelvic pain lasting for at least three months or six months (depending on which definition is used) with or without dysmenorrhea (painful menses/periods); dyspareunia (painful sexual function, superficial or deep); dysuria (pain with micturition/bladder emptying); and/or dyschezia (pain with defaecation/bowel evacuation) (50). Chronic pelvic pain (CPP) is a complex condition with various potential causes, making clarity about its epidemiology challenging.



The pelvic bones encircle a complex interconnected ecosystem of muscles, blood vessels, lymph, nerves and the intestines, bladder and internal sex organs.

The prevalence of CPP varies widely across different populations and studies, with reported rates ranging from 2-24% in 2006 (51), to 5.7-26.6% in 2014 (52). It affects women more commonly than men and is estimated to affect 15-20% of women worldwide, across all ages, including adolescents and postmenopausal women (53). Whilst exact reasons for the higher prevalence of CPP in females are not fully understood, the burden of gynaecological conditions e.g., polycystic ovarian syndrome (PCOS), or endometriosis, combined with differences in hormonal and immune function and activity are believed to be significant factors (54). The prevalence of CPP varies depending on the specific diagnosis and population studied, and the criteria used to define CPP. A study conducted in Egypt reported prevalence rates of 26.6 % for CPP, 55.3% for dysmenorrhea, and 40.5% for dyspareunia (55).

DON'T MISS THIS

Chronic pelvic pain is an umbrella term

CPP refers to many presentations and diagnoses. Common presentations of CPP include pain associated with bladder, bowel, and/or sexual activity; as well as pain felt in the pelvis associated with movement or sustained positions e.g., walking or sitting. Common diagnoses include bladder pain syndrome, urethral syndrome, interstitial cystitis, vulvodynia and vestibulodynia, endometriosis, anal and/or rectal pain, irritable bowel syndrome, chronic low back pain, coccyx pain, hip pain, pelvic girdle pain, pudendal neuralgia, myofascial pain syndrome, and chronic prostatitis/chronic pelvic pain syndrome (CP/CPPS).

Several risk factors are associated with the development of chronic pelvic pain, including a history of adverse childhood experiences (56-58), psychological factors including anxiety, depression, distress, stress, pain catastrophising, fear, and injustice (59-62), prior pelvic surgeries, certain gynaecological conditions e.g., endometriosis, and to a lesser extent PCOS (63, 64), chronic infections (65, 66), and other nociplastic pain states such as migraines and tension-type headaches, temporomandibular joint disorder, and interstitial cystitis/bladder pain syndrome (67).

We can identify several of these risk factors in Em's description. As we recognise that chronic nociplastic pain is influenced by a range of biopsychosocial factors, it may be that people living in Africa who have negative socioeconomic conditions, poor healthcare access, and who suffer from specific health issues prevalent in different regions, may be at greater risk of developing CPP.

DON'T MISS THIS

Chronic pelvic pain affects every aspect of people's lives

As we can hear from Em, CPP significantly impacts quality of life. People with CPP suffer from physical limitations, sexual dysfunction, psychological distress, and impaired social functioning with subsequent reduced productivity and increased healthcare use (68). A recent study in the USA found that CPP placed a high burden on services including diagnostic assessments, treatments, and surgeries. CPP places many demands on financial, mental, and physical resources (4). A 2017 cross-sectional study of the burden of bladder pain in five European countries compared 275 people with bladder pain to 548 matched controls, and found that people with bladder pain had significantly impaired mental and physical health-related quality of life ($p < .001$), lower overall work productivity ($p < .001$), and were significantly more likely to have used healthcare resources and providers in the preceding six months (69).

DEEP DIVE

Chronic Overlapping Pain Conditions

CPP is one of the conditions included in the Chronic Overlapping Pain Conditions (COPC). When we consider Em's story, we can clearly see that she suffers from several overlapping chronic pain conditions or comorbidities. While chronic pelvic pain conditions comprise approximately half of the common COPCs (irritable bowel syndrome, endometriosis, chronic low back pain, interstitial cystitis, and vulvodynia) (Figure 1), the other conditions present outside the pelvis. These include fibromyalgia (chronic widespread pain), headaches (migraine and tension-type), temporomandibular joint disorder (TMD), and myalgic encephalitis/ chronic fatigue syndrome (ME/CFS) (4, 68). As we hear from Em, we can also recognise that CPP (like most nociplastic pain conditions) is also often comorbid with negative psychological factors e.g., anxiety, depression, and pain catastrophising (60, 61, 70, 71). These comorbidities are thought to be partly mediated by dysregulation of the autonomic nervous system (72-74).

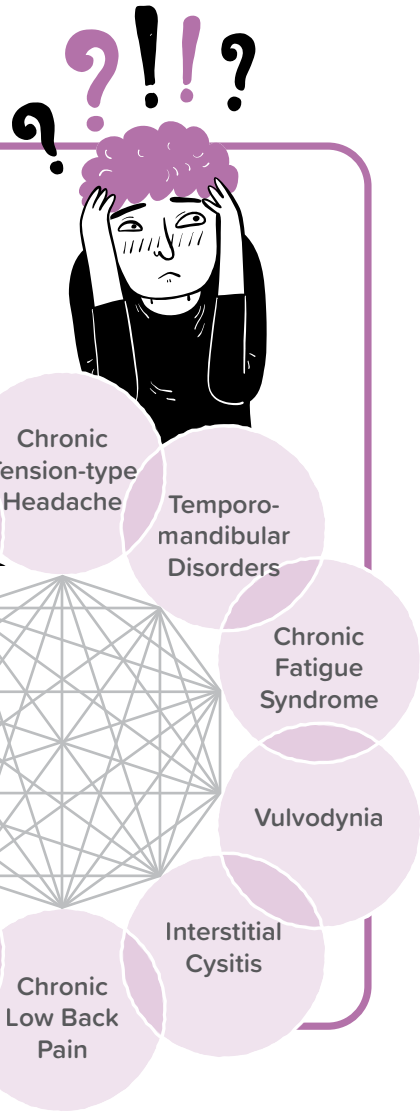


Figure 3.3: Chronic overlapping pain conditions and pelvic pain (4). ⟶

Em has been struggling for most of her life

> *I have had a long history of UTIs since age 4 or 5 years old. These were investigated and nothing of note was found, ending with a "hypersensitivity of the bladder" conclusion from specialists at the time. Long-term partner relationships seemed to result in recurrent UTIs, at least one a month and a round of antibiotics, most often ciprofloxacin. I was put on a three-month course of Nitrofurantoin (Macrodantin) which seemed to help for a year or so. Later I have had a UTI with almost all new sexual partners and suffered with lengthy periods of constant vaginal thrush which was not helped by any medical interventions. A few months ago, I had a cystoscopy (a scope of the inside of the bladder) with Hydromorphone (Hydrostat - opioid) and urethral dilation (stretching or widening of the urethra) for urinary symptoms – it flared instead of easing them. I have been on Nitrofuratoin (Macrodantin), Canephron, Citra-soda and D-Mannose, with no lasting relief. After many UTI infections precipitated by sexual activity, the pain now flares even without infection. This makes having a normal sexual life exceedingly difficult and stressful.*

Pain assessment

As we discussed in Section 1, Chapter 3, on the principles of assessment, it is critically important to gather all the information about Em's medical history after initiating the session. When someone presents with CPP, additional information needs to be gathered on associated symptoms, such as bladder or bowel symptoms, menstrual abnormalities, or sexual dysfunction. In addition, previous medical diagnoses, treatments, and surgeries related to the abdomino-pelvic region need to be reviewed. When exploring the **O, P, Q, R, S, T, U, V, W** of pain with someone with CPP, the healthcare professional carefully explores the **P** (provoking and palliating factors) such as activities or positions, including sexual positions which may aggravate or ease their pain.

DON'T MISS THIS

Working through a trauma-informed lens

'Trauma-informed' refers to a way of providing care and support that considers the impact of trauma on individuals and prioritises sensitivity, understanding, and empowerment in responding to their experiences. It involves creating an environment that promotes safety, trust, and respect for individuals who have experienced trauma, whether in a single event or in ongoing adversity. Trauma is highly prevalent in South Africa and many other low-resource (or poor) settings. People suffering from chronic nociplastic pain, including chronic pelvic pain, have often suffered adverse childhood events (ACEs) and past trauma (or may be living with persistent trauma). Remember that post-traumatic stress disorder (PTSD) exists on a spectrum and that vulnerable individuals can be easily triggered. As healthcare professionals we must be aware of this and ensure that we work with a trauma-informed lens (75).

Once all relevant information had been gathered, including a full understanding of how CPP was interrupting, interfering, and affecting Em's identity, a physical examination was performed. For someone with CPP, this physical examination assesses the pelvic region and surrounding structures including an external examination of the abdomen, pelvis, and genitalia. An internal pelvic examination may be conducted to evaluate the pelvic organs, assess muscle tone, and identify any abnormalities or signs of inflammation – please see "Pelvic Floor Physical

Therapy for Vulvodynia: A Clinician's Guide" for a detailed description of how to conduct such an assessment (76).

The physiotherapist conducted a series of assessments including evaluating Em's breathing patterns, posture and some specific physical examinations. The results of this assessment were:

1. Breathing patterns – Em was breathing apically with decreased diaphragmatic activation and excursion (movement)
2. Posture – acceptable standing and sitting, although a tendency to lose lumbar curve and adopt a posterior pelvic tilt (stability reliant on force rather than form closure) – slightly less active and engaged or tendency to lack of anti-gravity postural control.
3. Multiple areas of painful restricted movement, possibly indicating a background default of tension, rigidity, and guarding (lack of movement/variability were identified using skin rolling (a form of connective tissue manipulation)
4. Internal vaginal examination – Sensitivity (burning) to light touch with a cotton earbud at the vaginal opening (introitus), normal pelvic floor muscle contraction, partial relaxation with tendency to contract unless reassured/calmed/slow movement, tendency to breath-hold during examination.

DEEP DIVE

Pelvic floor muscle (PFM) examination

PFM activity is examined via digital palpation and graded according to voluntary and involuntary contraction and relaxation. Grading is based on the following scale:

1. Voluntary contraction is absent, weak, normal, or strong.
2. Voluntary relaxation is absent, partial, or complete.
3. Involuntary activity (contraction and relaxation) is absent or present.
4. It is common to feel fear and anxiety before and during a pelvic examination, with people using strategies such as breath-holding and tensing to cope. The fear, anxiety, and associated coping strategies can increase pain and provoke other symptoms (77). A PFM examination should only be conducted or performed by clinicians with specialist training, and with additional, comprehensive, informed, signed consent. Training includes using a range of techniques during the examination to facilitate the process.

Depending on the suspected underlying causes, various diagnostic tests may be indicated. These include laboratory tests to evaluate for infections, inflammation, hormonal imbalances, or other specific markers. Imaging studies, such as ultrasounds, MRI scans, or CT scans, have not yet been used in Em's case to visualise the pelvic organs and identify any structural abnormalities; they are also indicated to exclude tissue-based pathology. In Em's case, a specialised test (cystoscopy), was necessary to visualise the bladder directly – please see Consensus Guidelines for the Management of Chronic Pelvic Pain for further information on imaging for CPP (78).

A recent visit to a new GP with a special interest in sexual function resulted in a range of tests including:

- The GP noted that, being new to Em's case, it was important to listen to her concerns, and exclude medical causes before discussing chronic or neuropathic pain. The GP emphasised the importance of not dismissing possible organic causes for CPP without prior testing and assessment. This process of assessment is empowering for the person with pain who is reassured that nothing has been missed and that their pain is being taken seriously.
- The GP diagnosed Em as having primary vestibulodynia (a form of localised vulvodynia) childhood trauma and negative sexual experiences, with associated vaginismus (involuntary contraction of the pelvic floor muscles in response to attempted vaginal penetration). She noted her depression and widespread pain; as well as PCOS.
- The GP was concerned about the specificity of Em's current chronic medication. To inform her pharmacological management and with Em's consent and understanding of why the tests were being suggested, the GP performed and ordered additional tests. A screen for sexually transmitted infections was performed to rule out any pelvic infections which had not previously been assessed for. These included swabs for gonorrhoea, chlamydia, ureaplasma, mycoplasma, trichomoniasis, and blood tests for HIV, syphilis and hepatitis B and C. Blood tests were also requested to explore hormonal imbalances. The GP also conducted a physical examination and noted a urethritis (inflammation of the urethra). A urine assessment ruled out infection in the urine. All swab and blood tests were negative for infection.

Once the physical assessment was complete, we asked Em to complete the Central Sensitisation Inventory to provide more information on pain mechanisms. To assess the synergistic systems, we focused on sleep and asked her to complete the Insomnia Severity Index. To help us evaluate contributing and vulnerability factors we used a range of questionnaires aimed at identifying psychosocial contributors to chronic pain (attitudes, beliefs, and conditions known to be comorbid). Em completed the DASS21 for depression, anxiety, and stress, the positive and negative affect schedule (PANAS), the pain catastrophising scale (PCS); the pain self-efficacy questionnaire, and the injustice experience questionnaire (IEQ). We have summarised the results of these tools and how to interpret them in Table X.1.

Table 3.5: Results from the assessment tools

Instrument	Score	Interpretation	
Central Sensitisation Inventory (79)			
Part A	70/100	Extreme	
Part B	4/10	Several co-morbid conditions	
Insomnia severity index (80)	23	Severe	
Adverse childhood experiences (81)	3	Clinically significant for increased risk for serious health problems	
DASS-21 (82)			
Stress	17	Mild	
Anxiety	13	Moderate	
Depression	14	Moderate	
Pain Catastrophising Scale (83)			
Total	42	Severe	
Helplessness	21/24	Severe	
Rumination	12/16	Severe	
Magnification	9/12	Moderate	
PANAS (positive and negative affect scale) (84)			
Positivity	21	Low	
Negativity	36	High	
Pain self-efficacy questionnaire (PSEQ) (85)	8	Acceptable	
Injustice experience questionnaire (IEQ) (86)	32	High	

 A significant finding which must be considered in clinical reasoning and treatment planning

 A result which should be considered in clinical reasoning and treatment planning but might not be a primary target

 Does not appear to be contributing to pain

Mechanisms of pain

Em has chronic pain (pain on most days for more than three months) that is:

- nociceptive – when she has an ongoing UTI and bladder infection,
- nociplastic – she has widespread pain and a score classified as "extreme" on the CSI.Chronic pelvic pain is a complex condition with multiple potential underlying mechanisms. Here are some known mechanisms that can contribute to CPP:

Chronic pelvic pain is a complex condition with multiple potential underlying mechanisms. Here are some known mechanisms that can contribute to CPP:

DON'T MISS THIS

Em's interdisciplinary team

The assessment of someone with chronic pelvic pain requires an interdisciplinary approach. For Em, multiple urologists and gynaecologists, GPs, a psychiatrist, psychologist, neurologist, sexologist, and physiotherapist with a special interest in pelvic function have made up the team to date. As we have highlighted throughout this book, this collaborative approach ensures a comprehensive evaluation and helps tailor a treatment plan that addresses the specific needs of the person with pain.

Peripheral nervous system

Inflammatory processes within the pelvis can lead to CPP through peripheral sensitisation. Inflammatory conditions, such as urethritis, activate peripheral nociceptors which may result in nociceptive pain. As we discussed in Section 1, when nociceptors fire, they become sensitised. If the inflammatory processes continue over time or frequently recur, with the peripheral nerves being sensitised each time, the peripheral nerves can then become "stuck" in a sensitised state resulting in nociceptors firing even when there is no frank inflammation i.e., nociplastic pain resulting in pain even with minor stimulation.

Dysfunction of the pelvic floor muscles can also contribute to CPP. Conditions which involve spasm of the pelvic floor muscles, e.g. vaginismus (involuntary muscle contraction in response to penetration), can lead to persistent pain in the pelvic region as a consequence of the repeated stimulation and therefore sensitisation of the peripheral nociceptors.

DEEP DIVE

Pelvic floor muscle activity

The pelvic floor muscles (PFM) are innervated by the pudendal nerve (the only peripheral nerve in the body to carry both somatic and autonomic fibres), thus representing an interface between the somatic and visceral nervous systems. Involuntary activity of the PFMs is significantly influenced by autonomic nervous system activity. This allows changes in bladder activity to affect the PFMs (from the viscera to the musclescan affect bladder function (from the muscles to the viscera) – there is bidirectional feedback .

Can you remember the last time you had to speak in public, or heard a loud and unexpected noise e.g., a car backfiring that may have been mistaken for a gunshot? If so, did you notice that:

1. your muscles tensed,
2. your heart started to pound,
3. your breathing changed (you either stopped breathing or took little shallow breaths),
4. your mouth may have become dry,
5. you either needed to empty the bladder repeatedly (frequency/urgency) or you couldn't empty until the threat was gone (think of people with 'shy' bladders in public toilets)!

These disparate physiological effects are due to autonomic activity and demonstrate the bidirectional feedback between the muscles and the viscera. Your sympathetic system is activated during the stress response and influences everything from alertness, to breathing pattern, cardiovascular function (blood pressure, heart rate and heartrate variability), digestion, and bladder activity. Normal sympathetic activity governs musculoskeletal tone and the storage functions of the bladder and bowel (and sustained or extreme stress can disrupt the normal process), whereas parasympathetic activity governs visceral movement or variability e.g., heart rate, pee, poo, and pleasure. Sexual function (pleasure) is governed by parasympathetic activity, although orgasm is sympathetic (surprise!).

Spinal Cord

Chronic pelvic pain is associated with central sensitisation (remember this from Section 1?). Em has clear allodynia – pain to a stimulus that is normally non-painful. Her allodynia was particularly obvious on the internal vaginal examination when she had pain from touching with a cotton earbud. As you will remember from Section 1, allodynia is an indicator of central sensitisation in the spinal cord.

In Section 1 we also discussed the importance of descending inhibition from the brain to the spinal cord level. We would expect that consensual sexual activity (penetrative or non-penetrative events with orgasm), would result in a release of neurotransmitters activating the descending inhibition of incoming nociception and thus decrease pain. However, Em suffers from increased pain after all forms of sexual activity, suggesting that her descending inhibitory mechanisms are impaired. She may also have increased descending facilitation.

Long-term exposure to nociception can lead to sensitisation of neural circuits in the spinal cord, resulting in increased excitability and aberrant nociceptive processing. This plasticity can contribute to the maintenance of pain in CPP conditions.

Brain

The brain receives and processes nociceptive signals from the pelvic region. As we discussed in Section 1, various regions of the brain, including the somatosensory cortex, insula, and anterior cingulate cortex, engage in the perception and processing of pain. People suffering from CPP have changes in brain activity and connectivity in these regions that suggest central sensitisation (87-91).

Em scored 70 (extreme) on the central sensitisation inventory, has pain at multiple sites and has noticed that her pain gets worse with stress. People with CPP commonly have central sensitisation such that nociceptive processing in the brain is altered. Brain-level changes related to central sensitisation can involve altered activation patterns and connectivity in areas such as the somatosensory cortices, insula, and anterior cingulate cortex. These changes can lead to heightened pain sensitivity, decreased pain inhibition, and the development of widespread pain.

Dysregulation of the autonomic nervous system is a common feature of chronic pelvic pain. An increase in sympathetic nervous system activity can increase pain, inflammation and change bladder function.

We learn pain via our brain's ability to reorganise and adapt, an ability termed neuroplasticity. Neuroplasticity contributes to the development and persistence of CPP. Persistent noxious stimuli e.g., recurrent UTIs and thrush, result in persistent nociceptive messages from the periphery which, over time, can lead to long-term changes in the structure and function of the brain, including altered synaptic connections and neural pathways. These changes can reinforce and perpetuate the experience of pain even after the initial cause has resolved.

Synergistic systems

When considering Em in terms of synergistic systems, it is important to recognise the interconnectedness and interactions among different body systems that contribute to symptoms and overall well-being. As we have discussed, Em presents with dysregulation of the ANS, leading to increased sympathetic and decreased parasympathetic activity, contributing to increased pain sensitivity, increased inflammation, and changes in bladder function.

Recurrent urinary tract infections (UTIs) and vaginal thrush suggest potential immune system involvement. The immune response and inflammation associated with these conditions can contribute to pain and ongoing symptoms. Addressing immune system function and potential underlying causes may be important in managing these recurring infections.

Em's history of PCOS and recurrent vaginal thrush suggests involvement of the reproductive system and the endocrine system. Hormonal imbalances associated with PCOS may contribute to pain and inflammation in the pelvic region. Em's experiences of negative sexual encounters and primary vestibulodynia highlight the complex interplay between psychological factors, trauma, and the reproductive system, in the context of chronic pain.

Em's history of depression, anxiety, stress, and adverse childhood experiences underscores the significant role of psychological and emotional factors in chronic pain. These factors involve not only the nervous system (including the autonomic nervous system), but also the endocrine, and immune systems, influencing pain and impacting overall well-being.

Em has worked hard to get help

> *I have seen multiple doctors (GPs, urologists, gynaecologists etc.), and have had a variety of interventions. Some were partially successful (Nitrofuratoin (Macrodantin) 3-month course, Urizone 1-day antibiotic course, Betadine douche, Canephron) and others less so (cystoscopy, urethral dilation, D-mannose, Candizole cream, Fluconazole course, Lomexin ovules). Recently, I have found significant relief with pelvic physiotherapy, specifically connective tissue manipulation (skin rolling) and pain science education along with behavioural advice, which has allowed me to calm my nervous system.*
>
> *In terms of medication for pain management, due to the chronic headaches I was advised by a neurologist I consulted to not take any NSAIDs as the frequency of my headaches meant I was also taking NSAIDs frequently which would result in refractory or withdrawal headaches . As such, I do not really use any pain relief measures besides ice. Using an ice pack to the urethra/vulva helps the worst acute pain moments.*

People with chronic pain conditions see an average of 11 different healthcare professionals before getting a diagnosis. Chronic pelvic pain is no different, Em has consulted multiple specialists in her search for help.

Pain Management

Chronic pelvic pain often requires multiple healthcare encounters and consultations with various specialists, including gynaecologists, urologists, pain specialists, and physiotherapists. The management of CPP can be complex and should be interdisciplinary to optimise the benefits. Treatment approaches which have shown promise in targeting the brain, including cognitive-behavioural therapy (CBT), mindfulness-based techniques, and neurofeedback, can reduce pain and improve quality of life. In addition, medications which target brain receptors and neurotransmitters, such as certain antidepressants and anticonvulsants, can also be considered in the treatment plan. It is important to note that the field of CPP epidemiology is continually evolving, and new research may provide additional insights into its prevalence, risk factors, and impact.

Em and her team recognised that understanding and focusing on the nervous system mechanisms involved in CPP was essential for developing effective treatment for her. Em and her team discussed the relationship between physical symptoms and psychology with special emphasis on the role of autonomic nervous system activity, the stress response, anxiety, and involuntary muscle tension. Em felt it would be useful to be referred to a sexologist. Collaborating with her team, Em decided on a conservative approach to her pain which included:

- Cognitive Behavioural Therapy, using a decatastrophising worksheet, to target brain mechanisms. This technique aims to challenge and reframe catastrophic thoughts and beliefs about pain. It can help people develop a more balanced and realistic perspective on their symptoms and improve coping strategies. Em may benefit from exploring some of her unhelpful, 'dangerous' thoughts regarding pain, dysfunction, sexual frustration, and relationship concerns.
- Expressive writing to improve health, a process of disclosure. Expressive writing involves writing about one's thoughts, feelings, and experiences related to their pain. It can serve as a therapeutic tool to process emotions, reduce distress, and improve overall well-being (93, 94). Em may also find expressive writing helpful in processing negative attitudes and emotions, thus also addressing brain mechanisms.
- Forgiveness therapy ("Forgive for Good") is a therapeutic approach that focuses on helping individuals let go of past resentments and forgive themselves and others. It can be beneficial in addressing psychological factors, reducing emotional distress, and promoting healing. Em has a high sense of injustice which may be contributing to a feeling of victimisation, or not being heard, amplifying brain-based pain mechanisms.
- Mindfulness-based strategy of diaphragmatic breathing to target the spinal cord, brain, and autonomic nervous system. Breathing techniques can help regulate the autonomic nervous system by improving vagal tone (parasympathetic nervous system activity), promote relaxation, and reduce muscle tension. Mindful breathing may contribute to overall pain management and stress reduction (95, 96).
- Pain science education to increase understanding, reduce fear and anxiety, increase self-efficacy and improve knowledge, skills and ability to manage pain. Em has already benefitted from a better understanding of the complex interactions and multisystemic relationships involved in complex comorbid chronic pain conditions.
- Connective tissue manipulation (skin rolling) to target the synergistic systems and peripheral nervous system. This technique – indicated in the assessment and management of pudendal neuralgia and autonomic, bladder, and/or sexual function – involves manual manipulation of loose connective tissue to alleviate tension, improve blood flow, and restore normal tissue mobility (97-101). Em's multisystem presentation shifted slightly after three sessions of skin rolling – she reports her bladder pain as less intense, less often, with only minor flare once a day (opposed to much of the day being experienced as a pain flare). Her right hip felt significantly better (more movement, less stiffness and restriction). However, she was more aware of the left hip and reported being more sensitive to temperature changes (face flushed with heat e.g., open fireplace).

Conservative therapy can be misinterpreted as passive treatment, or no treatment. In Em's situation, conservative therapy is very active, she has had to fully engage with her treatment!

- Myofascial release via internal vaginal examination to target the peripheral nervous system and synergistic systems. Myofascial release techniques, performed internally during a vaginal examination, aim to release tension and restrictions in the pelvic floor muscles and surrounding tissues. These techniques have been shown to address musculoskeletal dysfunction and alleviate pain (76, 102). Em benefitted from the mindfulness associated with voluntary PFM relaxation. The next steps in this treatment involve topical treatment to calm the hypersensitive vaginal vestibule before attempting penetrative therapy.
- Visceral manipulation to target the synergistic system. Visceral manipulation techniques involve gentle manual therapy applied to the organs within the pelvis to improve their mobility, release tension, and restore normal function (103, 104). Em enjoyed the technique and felt a deep sense of relaxation afterwards with less pelvic pressure and irritation. However, as this was performed at the same session as an internal vaginal examination, she experienced residual discomfort and burning, rendering her overall sense of well-being as less than satisfactory.
- Pelvic stretches to target the peripheral nervous system, spinal cord, brain, and synergistic systems. Specific pelvic stretches, particularly bilateral stretches, can help lengthen and stretch the deep posterior pelvic floor muscles. These stretches aim to improve muscle flexibility, reduce muscle tension, and restore normal PFM activity and function. Em has started stretching, as well as increasing her exposure to movement, and limiting sustained positions e.g., hours spent sitting at a desk.

DEEP DIVE

What is a sexologist?

Sexology is the general term for the scientific study of human sexuality and sexual behaviour. The people who study it are generally referred to as sexologists. Not all sexologists are sex therapists only some sexologists choose to pursue a clinical career as a sex therapist by working directly with patients; others may pursue careers such as researching sexual behaviour or sexual health, or become a sex educator helping in expanding sexual knowledge in the public domain, or a medical doctor specialising in sexual health and treating diseases associated with sexual behaviour, like sexually transmitted infections and other physical symptoms. Another group of individuals working in sexology act as public policy activists regarding sexually related issues, such as legalising prostitution, LGBTQI&A rights and building on the general rights of marginalised individuals allowing everyone to have fulfilling sexual relationships.

A few universities offer undergraduate or postgraduate degrees in sexology or human sexuality. It is common that people who become sexologists have backgrounds in sociology, psychology, biology, medicine, public health (nursing) or anthropology. Sexologists generally have a master's or doctoral degree, although some have another type of advanced professional degree. Although a board certification is not required to call yourself a Sexologist, many students in this field seek credentials from professional organisations such as the American Board for Sexology, or the International Society for Sexual Medicine. To be certified, you typically need to show a relevant advanced academic degree, relevant work experience in the field, and completion of a certain number of training hours. These requirements however may vary based on the certification.

Taken from here.

- Referral to a sexologist to target brain mechanisms. Considering the integral role that CPP has played in Em's identity and worldview, referral to a sexologist can help address the sexual and intimate aspects of her experience. The sexologist can provide specialised support, guidance, and interventions to address sexual function and emotional well-being. The sexologist noted that Em was deeply invested in her CPP as a sense of identity – she has had it for so long, and it defines so much of her life – what or who would she be without it?
- Em is already using topical ice as it brings relief as reducing temperature also slows firing of nociceptors.

The GP's plan for Em's urethritis targets infective and non-infective drivers of peripheral nervous system contributions to combat the loss of descending inhibition in the spinal cord.

Treatment for infection is not indicated as the STI screens were all negative. Targeting of peripheral hormonal mechanisms has been initiated by starting a hormonal cream. Em has recently started this treatment and evaluation is ongoing. The cream is a combination of Emla 5g (topical anaesthetic cream), Gabapentin 4% (membrane stabiliser) in Nutraderm, Bi-Est (80/20), Testosterone 0, 125% (targeting hormonal imbalances). If Em's symptoms have not improved with this treatment, then treatment with the antibiotic, doxycycline 100 twice daily for one week will be trialled (as per CDC guidelines). Treatment for candida may be indicated after completion of the course of antibiotic.

It is important to remember that the treatment approach for CPP should be individualised and may involve a combination of these strategies. The specific management plan will depend on the underlying causes identified by thorough assessment and the unique needs of the person with pain. Close collaboration between the person with pain and healthcare professionals from various specialties, such as gynaecology, urology, pain management, and psychology, is essential to develop an effective and holistic treatment plan.

Em starts working with a holistic physiotherapist

> *I am currently seeking help from pelvic function physiotherapy with a holistic approach to pain. Education about pain has been helpful, as has Qi Gong, and this has enabled some hope for a potential reduction in symptoms. I have also recently seen an empathetic GP with a special interest in sexual function, and she has ordered some tests and has referred me for psychosexual support.*

Socio-psycho-biological approaches are essential to effectively manage chronic pelvic pain. After all, pain is about a person, in their context.

Lessons learnt

There were several key lessons to learn from Em's story, starting with: the person's narrative is essential. Every person is different, and whilst their presenting symptoms might be the same or seem similar, they have their own unique set of drivers (causes) of multisystem dysfunction e.g., three people might all present with urinary frequency/urgency – one might have an overactive bladder (OAB), one might have anxiety-driven autonomic nervous system dysregulation, and one might have a bladder infection. Assess the person, not the symptom.

It is imperative that all healthcare professionals work through a trauma-informed lens. Remember to recognise the need for sensitivity, understanding, and empowerment in responding to the experiences of the person with pain whilst creating an environment that promotes safety, trust, and respect. Motivational interviewing should be part of the skill set of a clinician who works in the chronic nociplastic pain setting. Motivational interviewing enhances assessment and treatment by eliciting and enhancing motivation for behaviour change.

Assessment must integrate the biopsychosocial (or socio-psycho-biological) approach. Chronic pain is complex with multisystem drivers; do not get stuck in a biomedical model – exclude pathology and keep assessing!

Effective chronic pain management needs multimodal therapy in an interdisciplinary team. No one clinician has the solution for all people with pelvic pain. Some people may benefit from stress management, others, dietary modifications, and yet others will need to decrease sedentary behaviours in favour of more movement. A thorough assessment and mechanism-based clinical reasoning allows for individualised care for phenotypes and pathophysiology. Each person is different and deserves bespoke care for their particular presentation and drivers; many people notice that stress aggravates symptoms, others report a lack or excess of movement to be more significant in their pain experience.

Do not "throw the baby out with the bathwater" – do not assume there is no tissue pathology and that it's all psychosocial. A thorough assessment to exclude biological pathophysiology is essential whilst addressing concomitant psychosocial factors. Treatment should address and exclude biomedical and biomechanical aspects, but also include relevant support for psychosocial contributors to pain e.g., sleep hygiene, good self-care, and dietary recommendations (fluid and fibre).

5 Conclusion

We hope these stories have offered you some guiding principles for walking the road to recovery for people with chronic pain - recovery which fosters engagement in their meaningful life roles. Further, we hope you have gained specific insights into practical management steps. We believe five principles are core for successful interdisciplinary teams that include people with chronic pain.

First, it is important to validate the experience of the person with pain. As healthcare professionals we bear witness to people's suffering, and it is important that we consciously use our communication skills to validate people's pain experiences. Validating their pain experience must also be done while holding to the message that chronic pain may not be caused by a problem in their tissues. This is a skill which takes both training and practice. If you have not yet had training that focused specifically on communication skills, we strongly recommend that you obtain such training and dedicate time and effort to becoming an expert communicator – you'll be surprised by how powerfully skilled communication can improve your effectiveness as a clinician. Active listening, validation and effective communication are skills that can be learned, and that allow us to be truly person-centred.

Second, a fundamental first step to recovery from chronic pain is making the shift from understanding pain as an accurate measure of tissue damage to understanding that pain can arise as a response to an event that is inaccurately perceived as a threat by an overprotective, sensitised system (nociplastic pain). Understanding that nociplastic pain is about multiple factors allows recognition of the usefulness and effectiveness of treatment modalities besides drugs and surgery. Importantly, however, people reach this understanding in different ways and with different timelines. Our role as clinicians is to facilitate a conversation that allows the person with pain to recognise their current beliefs about pain, question some of those beliefs within a psychologically safe space, discover their own new insights, and make their own cognitive leaps and paradigm shifts. Again, skilled communication is fundamental to facilitating this delicate and yet transformative process. These three stories illustrate the importance and power of coupling cognitive shifts with active behaviour change. I learn, I do, I understand.

DON'T MISS THIS

Education and behaviour change

Huyaam learned about pain, but it was when she became more active, started exercising and changing her behaviour that she really 'got it'!

For Jo, just learning about her pain and that her hand was OK completely and rapidly changed both her pain and her ability to engage with life.

Em has become curious, now that she has learnt about pain. Learning about the complexities of pain has helped her to understand why it is important for her to work with different members of the team and to use multiple active treatment strategies.

Third, it is no quick task to distinguish new symptoms of the same chronic nociplastic mechanisms from new symptoms of a different and evolving pathology such as cancer or infection. Do not throw the baby out with the bathwater! Just because someone has chronic nociplastic pain does not mean that they cannot develop a new, *nociceptive* cause for pain. This awareness means that constant attentiveness is required from both the clinician and the person with pain. Lean on your colleagues in the interdisciplinary team and other clinical specialties, and remain calmly vigilant. Any new symptoms must be fully assessed.

Fourth, as a healthcare professional, you may often need to fight the urge to "do something" or "prescribe something" when the best path may actually be to listen and hold the line. The conversations we have with our patients are often the most potent interventions.

And lastly, a deliberately person-centred approach places the person with pain at the centre of the care team. They know themselves and their lives best; they are well placed to lead decisions and planning around their care. Indeed, a person with pain who is empowered and enabled is the person most likely to achieve meaningful and lasting recovery.

DON'T MISS THIS

Free resources

In this section we have highlighted a few open-access resources. Here they are, all in one place, for ease of access.

Pain in 5 minutes

Tame the beast

Pain and Me

Why things hurt

PEEP

Living with OA

Positive Living

De-catastrophising tool

Forgiveness methods

Pelvic stretches

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