

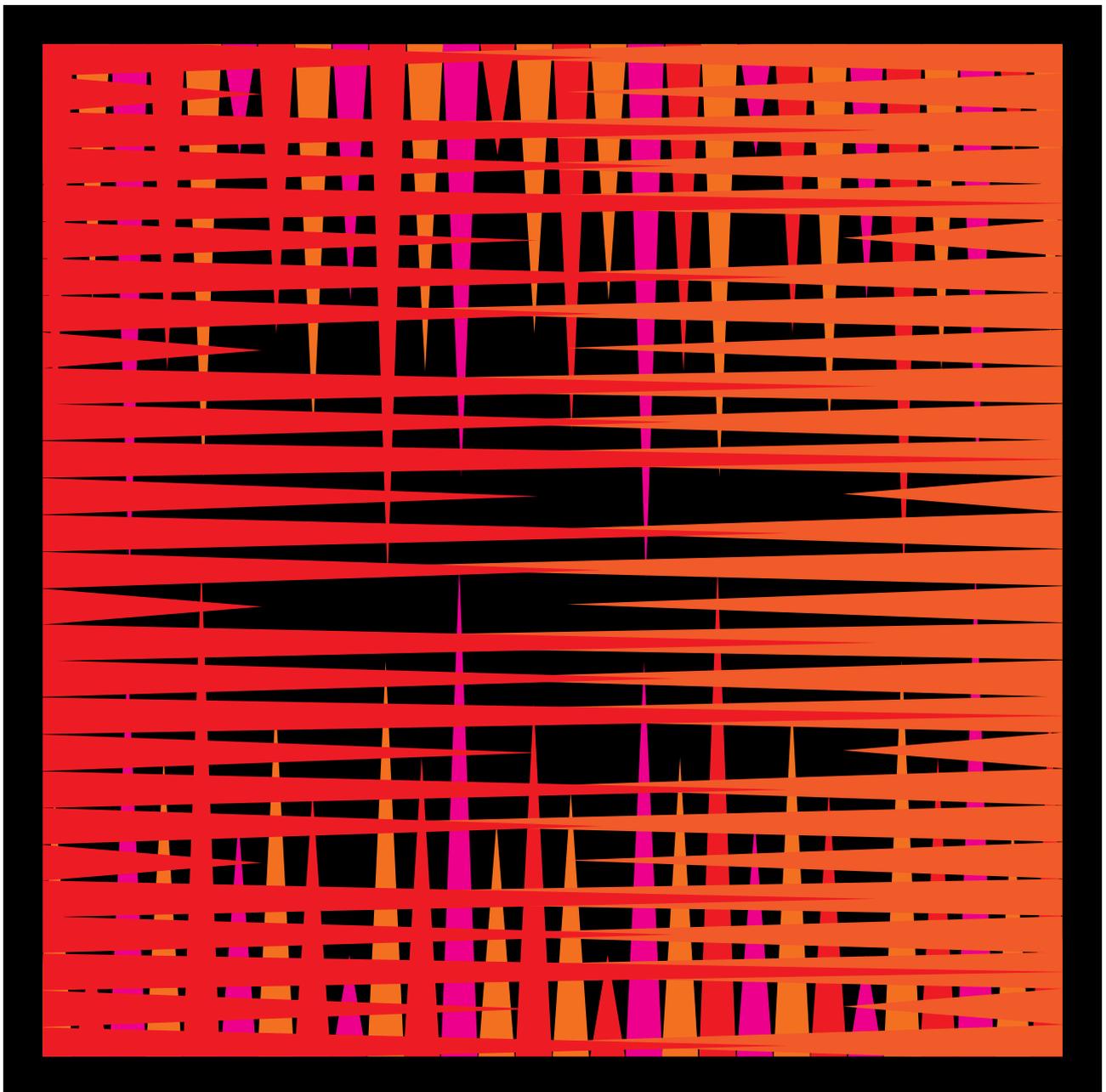
FOR HEALTH PROFESSIONALS

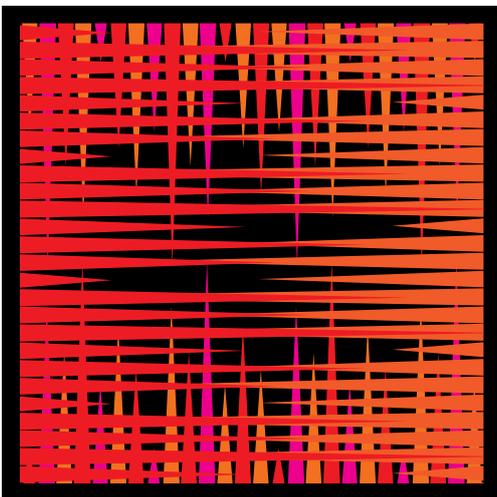


AUSTRALIA

# PRACTICE

Pain and multiple sclerosis (MS)





## **Pain and multiple sclerosis (MS)**

Pain in people with MS can be the direct result of demyelination and axonal loss. Other MS symptoms such as spasticity or weakness, as well as disorders that affect the general population, may also lead to pain in people with MS.

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## 1.0 Pain

Pain is a complex symptom experienced by individuals in many different ways. Pain is defined as “an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage” by the International Association for the Study of Pain (IASP).<sup>2-4</sup> Pain, therefore, has both a physical and psychological component. Some common pain-related definitions:

- **Dysaesthesia** is an unpleasant abnormal sensation.<sup>2</sup> For example, pain such as burning, numbness, itching or pricking. Dysaesthetic pain in MS is atypical pain caused by damage to the central nervous system (CNS).
- **Affective pain** is the emotional response to the perception and interpretation of a pain stimulus. The experience of pain varies greatly between people and is influenced by environment, culture, psychological status, and previous pain experiences.<sup>5</sup>
- **Hyperalgesia** is increased response to stimulus that is normally painful.<sup>2</sup>
- **Allodynia** is a painful response to a stimulus that does not normally cause pain.<sup>2</sup>
- **Pain threshold** is defined as the least experience of pain which a subject can recognise.<sup>2</sup>

### 1.1 Classification of pain based on pathophysiology

**Nociceptive pain** is transmitted to a conscious level of awareness after nociceptors (sensory neurons for pain) are activated. Nociceptors are located in the skin, musculoskeletal system (generating somatic pain) and in the viscera (generating visceral pain). Nociceptive pain warns a person of potential tissue damage and elicits protective, coordinated reflexes and behavioural responses.<sup>6</sup>

**Neuropathic pain** originates in the nervous system (nerves, spinal cord, or brain) when it is damaged by disease or injury. It can be caused by a lesion or dysfunction in either the peripheral or central nervous system (CNS).<sup>2</sup> If the cause is located in the CNS (as is the case in MS) it is termed central neuropathic pain (CNP) or central pain.<sup>2,7</sup> Clinical characteristics of neuropathic pain are a burning, shooting, stabbing or pricking sensation, allodynia and/or hyperalgesia.<sup>6,8</sup>

### 1.2 Classification of pain based on duration

**Acute pain** is short-term pain that warns of tissue damage in order to protect life. Acute pain is usually well-localised.

**Episodic pain** is a transient form of acute pain (e.g., pain that may be experienced during an MS exacerbation).

**Chronic pain** is defined by the IASP as constant or intermittent daily pain, persisting for greater than three months,<sup>9</sup> usually after the tissues are expected to have healed. There may or may not be a persistent irritant that continues to cause pain. Once pain becomes chronic it no longer has a protective role, with the pain continuing despite a lack of obvious, ongoing tissue damage. It is thought that once nociceptive pain becomes chronic there is also a neuropathic pain component, with synapse changes that are established through persistent use of pain pathways.<sup>5</sup>

**Paroxysmal pain** is sudden, severe pain occurring without warning or injury. Symptoms may last for seconds or minutes (e.g., Lhermitte’s sign, trigeminal neuralgia, burning sensations, and itching). O’Connor *et al.* recently proposed a classification of pain for patients with MS (table 1).<sup>1</sup>

Table 1. Proposed classification of pain conditions associated with MS (Adapted from O’Connor *et al.* 2007)

Pain classification	Examples
Continuous CNP	• Dysaesthetic extremity pain
Intermittent CNP	• Lhermitte’s sign • Trigeminal neuralgia
Musculoskeletal pain	• Painful tonic spasms • Low back pain • Muscle spasms
Mixed neuropathic and non-neuropathic pain	• Headache

## 2.0 Incidence and impact of pain in MS

Pain is a common symptom experienced by people with MS. Several studies report that the incidence of pain within a one-month period is between 53 and 79%.<sup>10–12</sup> The point prevalence for pain in MS is lower at 43–54% (excluding pain related to headache).<sup>13–15</sup> Prevalence estimates vary due to the different definitions of pain and the assessment measures used. The exclusion of specific types of pain such as headaches, optic neuritis and painful tonic spasms is also a contributing factor to the variations in prevalence.<sup>1</sup>

Chronic pain is experienced by between 64 and 69% of people with MS.<sup>16,17</sup> Of these people, 60% are reported to have experienced chronic dysaesthetic pain and 70% have experienced episodic pain. Prevalence tends to increase with age and number of years since disease onset.<sup>18,19</sup> Several studies have noted a higher pain prevalence in females with MS (in comparison to their male counterparts) and in people who have moderate-to-severe mobility restriction, as measured by the Expanded Disability Status Scale (EDSS).<sup>20–23</sup> However, it is important to note that pain affects people with

MS at all stages of the disease, including 11–23% of people who have been newly diagnosed with MS.<sup>14,16,24</sup>

For people with MS, pain can significantly interfere with participation in the activities of daily living<sup>25</sup> and can also adversely affect health-related quality of life.<sup>16,25</sup> A study conducted by Warnell *et al.* found that among people who experience pain in MS, 40% have difficulty working, 44% have difficulty sleeping, and 34% have troubled relationships.<sup>21</sup> Results from studies that compare people with MS without pain to those with pain suggest a link between pain in MS and anxiety,<sup>16</sup> depression,<sup>16,22</sup> and lower mental health scores (using the Mental Health Inventory).<sup>11</sup> The strongest predictors of pain severity are the presence of multiple pain sites, depression, higher disability level, and pain that interferes with the activities of daily living and enjoyment.<sup>22</sup> The subjective impact of pain seems to be lower than one would expect, with only 32% of people with MS reporting pain amongst their most severe symptoms,<sup>14</sup> and 12% as their most severe symptom.<sup>26</sup>

## 3.0 Pathophysiology of pain in MS

### 3.1 Nociceptive pain

Nociceptive pain or ‘musculoskeletal pain’ is a consequence of injury, strong sensation, or distortion of bodily tissues other than nerve tissues. Nociceptive pain may protect the body from further injury by eliciting a reflex response to rapidly remove the body part from the object inflicting injury, or by employing secondary protective behaviours (such as limping or not using an arm properly). Nociceptive pain is not directly related to MS. It is not related to damages in the myelin sheath. It arises from stimuli to nociceptors located in the skin, musculoskeletal system, and in the viscera.

The noxious stimulus is registered by nociceptors in the skin, joints and viscera. The stimulus is then carried by nerve fibres (A-delta and C) to the spinal cord and brain. C fibres carry mechanical, chemical, and thermal stimuli, whilst A-delta fibres carry high intensity mechanical stimuli. The afferent fibres (those conveying impulses towards the CNS) enter the spinal cord and then cross and ascend in the anterolateral tracts such as the spinothalamic tract. The fibres primarily travel to

the thalamus where they communicate with the cortex and limbic systems, where the emotional, memory and learning response to pain occurs. The central pathways are responsible for localisation and recognition of the stimulus, and the behavioural response to pain.<sup>27,28</sup>

### 3.2 Central neuropathic pain (CNP)

CNP or ‘nerve pain’ in MS is believed to be a consequence of damage to myelinated nerves in the CNS, and can be propagated by two mechanisms:

1. The generation of ectopic impulses at demyelinated lesions in response to neural damage.<sup>29</sup>
2. Interruption of inhibitory impulses from the brain, which removes the modulation of afferent A-delta and C pain pathways.<sup>28</sup> The absence of inhibitory impulses means that stimuli from peripheral receptors, which are normally below the threshold to generate pain, can now register pain.



Symptoms such as Lhermitte's sign and painful tonic spasms are thought to be caused by ectopic impulses resulting from demyelination and axonal damage in MS. These ectopic impulses can spread to surrounding normal neurons.<sup>30,31</sup>

Dysaesthetic extremity pain is thought to be caused by MS lesions in the nociceptive spinothalamic pathways of the spinal cord, affecting the inhibitory functions of gamma aminobutyric acid (GABA) interneurons. Disinhibited nociceptor input leads to constant central pain sensation.<sup>30,32</sup>

### 3.3 Theories of pain perception

The 'gate control' theory of pain was first described by Melzack and Wall in 1965.<sup>34</sup> They hypothesised that pain is modulated by a metaphorical gate mechanism in the dorsal horn of the spinal cord, which controls the transmission of nerve impulses from the periphery to the brain. Nerve impulses from A-delta and C nociceptive fibres activate transmission cells in the dorsal horn, 'opening the gate' and allowing transmission of noxious information to the brain

when pain sensation is perceived. The gate is 'closed' by activating A-beta sensory fibres in the periphery (registering touch, pressure, and temperature). Pain perception can be modulated by the effect of non-painful stimuli such as heat and transcutaneous electrical nerve stimulation (TENS),<sup>33</sup> or by central descending inhibition.<sup>34</sup> Anxiety and depression are thought to increase pain perception through descending activation of dorsal horn cells.

Prolonged or repetitive noxious stimulation of C fibres leads to sensitisation of neurons in the dorsal horn. When the inhibitory systems in the dorsal horn are dampened a theoretical process of pain sensitisation known as 'wind-up' occurs. Dorsal horn cells then develop reduced thresholds, which are prolonged after discharges and increased spontaneous activity with expansion of peripheral fields.<sup>27,35,36</sup> This process is perpetuated in chronic pain causing allodynia and hyperalgesia.<sup>37</sup>

## 4.0 Clinical characteristics of pain in MS

CNP and nociceptive pain have been estimated to occur in 27.5% and 21% of people with MS, respectively.<sup>8</sup> MS-related CNP is described by a range of sensations including itching, tingling, crawling, burning, numbness, spasm, throbbing, sharpness, and stabbing.<sup>22</sup>

It is not uncommon for people with MS to experience CNP in several areas of the body, but it primarily occurs in the lower extremities (96%), back (70%), and upper extremities (52%).<sup>10</sup> Similar findings have been reported by Ehde *et al.* in people with MS and pain of any type, with pain experienced in an average of 6.62 distinct sites, most commonly affecting the legs (74.6%), lower back (59.3%), neck (51.7%), and shoulders (49.2%).<sup>23</sup>

Neuropathic pain in people with MS is characterised by heat hyperalgesia (sensitivity) and allodynia to touch or cold.<sup>8,10,38</sup> People with MS who experience neuropathic or musculoskeletal pain tend to have lower pain thresholds than those who do not experience pain.<sup>10</sup>

### 4.1 Nociceptive pain in MS

#### ■ Lower-back pain, neck pain, and headache

can occur as a result of irregular, asymmetric movement patterns and postures, and changes in muscle strength, tone (spasticity) or length (contracture).<sup>39</sup> These changes can place excessive strain on structures such as discs and ligaments. Walking, for example, can be asymmetrical and involve compensatory movement patterns that exert excessive strain on the lumbar spine.

#### ■ Pain related to spasticity and muscle spasms

can include muscle aching, cramping, pulling or stiffness. These symptoms are often worse at night or early in the morning.<sup>40</sup> Lumbar spasticity is also a possible cause of lower-back pain, due to increased muscle tension and its effect on lumbar spine joints. For further information about spasticity and MS refer to the *Spasticity and multiple sclerosis* handout.



- People with MS may experience **pain associated with fractures**. They are susceptible to fractures as a result of: vitamin D deficiency and low bone mineral density relating to lack of sun exposure, reduced weight-bearing activity, and repeated corticosteroid treatment during MS exacerbations.<sup>18,41</sup>
- There are several possible causes of **headache** in people with MS. Headache may occur due to brain stem or cervical demyelinating plaque(s), due to altered biomechanics or posture with a cervicogenic origin. Headache can also occur secondary to medication or have multifactorial causes. The incidence of headache in people with MS is 12–27%.<sup>16,22</sup> Rolak and Brown found that 22% of people with MS experience migraine headaches, and that migraine accounted for 41% of all headaches in MS.<sup>42</sup> People with MS treated with immunological modulating medications may experience an increase in the frequency and intensity of headaches of more than 40%.<sup>43,44</sup>
- **Pressure-area pain** can develop as a secondary consequence of immobility, particularly when sensation is impaired.<sup>39</sup>
- **Chronic back pain** is present in up to 16% of people with MS.<sup>20,22,24</sup> It can be of central origin,<sup>8,10</sup> a result of degenerative joint disease,<sup>20</sup> or a result of other musculoskeletal causes. Furthermore, chronic back pain can be aggravated by prolonged standing or sitting.
- **Painful tonic spasms** are extensor or flexor spasms of the limbs characterised by sudden, painful and repetitive increases in muscle tone with a set pattern. They involve both the upper or lower limbs and last less than two minutes.<sup>29,45</sup> Painful tonic spasms can be chronic or remitting and are also called nocturnal spasms because they occur primarily at night and contribute to sleeping difficulty. The incidence of painful tonic spasms in people with MS has recently been reported to be 11%, although supportive evidence was not provided.<sup>46</sup> Painful tonic spasms can be preceded by somaesthetic aura (such as migraines), and triggered by emotions, movements (such as touch), and hyperventilation.<sup>47–49</sup> Spissu *et al.* note that the pain may precede the spasm rather than be caused by the muscle spasm. This has implications regarding the origin of the pain being neuropathic, or mixed. Associated lesions are found in the basal ganglia, internal capsule, cerebral peduncle, medulla, and spinal cord.<sup>47</sup> It is important to note

that spasms are not always reported as painful.

#### 4.2 Acute and intermittent neuropathic pain in MS

- **Trigeminal neuralgia** – also known as tic douloureux – is severe episodic facial pain and allodynia that can be triggered by chewing, talking, brushing teeth or even a breeze touching the face.<sup>18,50</sup> The pain is often described as ‘stabbing’ and may last from a few seconds to a minute. The prevalence among people with MS is between 1 and 2%, of which 11–31% are affected bilaterally.<sup>51</sup> Lesions have been found at the trigeminal nerve root entry or in the pontine tegmental pathway.<sup>52,53</sup> Trigger points may be on the face or scalp, and can interfere with hygiene and nutrition.<sup>18</sup> Note that trigeminal neuralgia can be confused with pain of dental origin.
- **Lhermitte’s sign** is described as a transient, short-lasting sensation usually triggered by neck flexion.<sup>54</sup> It is a sharp feeling described as an ‘electric shock’, lasting less than two seconds, which radiates from the neck, down the back, and into the legs. It can also be felt in other parts of the body.<sup>54</sup> It has been associated with lesions in the cervical spinal cord,<sup>55</sup> which are thought to cause sensitivity to stretching.<sup>56</sup> The point prevalence is between 9 and 13%, and 40% of people with MS have experienced it, usually for four-to-six weeks during an MS exacerbation.<sup>13,54,56</sup>
- **Optic neuritis** can involve retro-orbital pain, which is aggravated by eye movements. Medical opinion suggests that the pain tends to resolve following recovery of visual acuity.<sup>6</sup> Among people with MS, 10% have experienced optic neuritis at some point.<sup>24</sup>
- **Glossopharyngeal neuralgia** is paroxysmal pain in the throat, posterior pharynx, base of tongue and tonsil area, which may be provoked by yawning or chewing.
- **Acute radicular pain** is intense pain similar to nerve-root pain, but without nerve-root pathology. Demyelination plaques at the dorsal root of the spinal cord are a possible cause of acute radicular pain.<sup>57</sup>



### 4.3 Chronic neuropathic pain in MS

- **Dysaesthetic extremity pain** is a burning, throbbing, stabbing, or aching pain, which is frequently experienced in the legs and feet bilaterally, and is often worse at night.<sup>8,20</sup> Among people with MS who have dysaesthetic extremity pain 66–95% also experience loss of temperature sensation.<sup>20</sup> The point prevalence of dysaesthetic extremity pain is 17%, making it the most commonly reported form of pain in MS.<sup>13–15</sup>
- **Visceral pain syndrome** affects a very small percentage of people with MS. This syndrome involves symptoms of abdominal cramping, referred cutaneous pain, aching, and bloating, the mechanism of which is unknown.<sup>29</sup> The source of the pain needs to be investigated to eliminate other conditions, such as persistent urinary tract infection or constipation. Painful bladder spasms have been proposed as a likely cause.<sup>6</sup>

## 5.0 Physiotherapy assessment of pain in MS

### 5.1 Acute pain

Physiotherapists are generally well-skilled to assess acute pain with regards to site, intensity, duration, aggravating factors, relieving factors, 24-hour behaviour, and affective description of pain. Pain in people with MS can be measured using the same tools as those commonly used by physiotherapists for the wider population (e.g., visual analogue scales [VAS] and numerical rating scales). Additional assessment of MS-related symptoms, such as fatigue and spasticity, should also be completed.

### 5.2 Chronic pain

In addition to measuring pain, it is important to understand how the person with MS believes pain interferes with their quality of life and their ability to perform activities of daily living. It is also essential to identify what component of disability is due to behavioural and psychological factors. The following assessment tools can be used to measure these aspects of pain:

- Modified versions of the interference scale, within the Brief Pain Inventory (BPI), have preliminary support regarding validity and reliability for assessing chronic pain in people with MS.<sup>58</sup>
- Disability measures used specifically for the assessment of chronic pain (e.g., Oswestry Disability Questionnaire) have not been validated in the MS population. The Expanded Disability Status Scale (EDSS) is commonly used in MS literature and is shown to be a valid and reliable measure of physical disability in MS.<sup>59</sup> The Disease Steps is a simple disability measurement tool for clinical health professionals.<sup>60,61</sup>
- The Tampa Scale for Kinesiophobia (TSK) measures fear avoidance of physical activity.<sup>62</sup>
- The Multiple Sclerosis Impact Scale (MSIS-29) has shown good validity and reliability for measuring the physical (20 items) and psychological (9 items) impact of MS.<sup>63,64</sup>
- The use of a bio-psychosocial, health-related quality-of-life-measure may assist health professionals in identifying life domains in which pain is limiting participation and satisfaction.<sup>65</sup> The Assessment of Quality of Life (AQoL)<sup>66</sup> and World Health Organization Quality of Life with 100 questions (WHOQOL-100)<sup>67</sup> both assess an individual's perception of their position in life in the context of the culture and value systems in which they live, and in relation to their goals, expectations, standards, and concerns. WHOQOL has the greatest evidence base including validity for chronic pain;<sup>68</sup> the recently developed AQoL-2 also asks pain-related disability questions.

## 6.0 Pain management in MS

For people with MS, rehabilitation, with a focus on physical and psychological goals, impacts upon quality of life and a person's ability to function in everyday living. This differs from a pain-reduction goal that is more appropriate for acute pain.

The following sections will explore the roles of physiotherapy, occupational therapy, psychological intervention, pharmacotherapy, as well as medical and multidisciplinary management of pain in people with MS. Input from an MS nurse (1800 042 138) is also essential to this approach. Multidisciplinary management is an important component of managing chronic pain in people with MS.

### 6.1 Multidisciplinary management of chronic pain

Most people who experience chronic pain require treatment by more than one health professional (e.g., physiotherapist and psychologist). Such a multidisciplinary approach requires good communication for positive reinforcement of management strategies, coordination, and common goals. Multidisciplinary therapy based on exercise improves physical function and can have modest effects on chronic lower back pain.<sup>69</sup> Limited evidence exists showing that multidisciplinary management of all MS symptoms results in lower pain scores on SF-36.<sup>70</sup> Multidisciplinary programs can be individual or group-based. The IASP, British Pain Society, and Australian Pain Society (APS) have each released position statements or guidelines on the components of Multidisciplinary Pain Management Programs.

People with MS who experience unremitting chronic pain should be referred to pain medicine specialists, and multidisciplinary pain clinics. Assistance for people with MS in accessing local pain clinics may be obtained by contacting the MS Society in the relevant state or territory (1800 042 138) or a local health department.

### 6.2 Physiotherapy

The IASP recommends that the role of a physiotherapist in pain management include:

1. Assessment of factors that contribute to pain, the pain-activity cycle, and overall function.
2. Development of a program directed at modifying the effect of factors that contribute to pain, promotion of tissue healing, and reduction of the factors that may lead to recurrence of pain and dysfunction.

The aims of physiotherapy intervention include maintenance of functional and occupational abilities, as well as prevention of inactivity or physical restriction due to pain. Traditional physiotherapy methods for acute pain-relief include massage, TENS, heat and cold therapy, dry needling, and spinal manipulation. Although people may report short-term relief from chronic pain, there is little evidence for long-term pain reduction through passive treatment methods (based on chronic lower-back pain studies).<sup>71</sup>

Specific exercise prescription is an effective therapy for chronic pain management since it focuses on increasing functional ability and reducing disability, which contributes to quality of life.<sup>72</sup> The focus in chronic pain and disability should be on self-management through active, rather than passive, methods. For people with higher levels of disability, education of their carers is also of value.

It is important to note that many people with MS-related pain (44–55%) report that physical activity temporarily increases their pain and sensory symptoms.<sup>17,73</sup> This symptom aggravation has been found to be short-lived and is thought to be associated with nerve conduction fatigue, or stimulation of sensory inputs. Physical activity should not be precluded for the maintenance of physical function and independence.<sup>73</sup>

#### 6.2.1 Management of acute pain

Presently, minimal evidence exists demonstrating the effectiveness of physiotherapy for acute pain management in people with MS. The best evidence available is for treatment of specific injuries in the general population.

The effects of MS symptoms such as heat sensitivity, fatigue, numbness, or allodynia need to be considered, and a thorough neurological assessment of all MS symptoms is indicated. If a person has allodynia to touch or cold, then the use of therapies involving ice or touch may be ineffective. There is also a risk of injury due to decreased sensation, so sensory testing is important.



The physiotherapist should minimise aggravating movements or positions and avoid positions that may cause pain due to neural tension. For example:<sup>74</sup>

- Minimise Lhermitte's sign during an MS exacerbation by using a collar and avoiding neck flexion
- Minimise painful tonic spasms by reducing sensory stimulation of the affected limb(s)
- Prevent increased spasticity and spasms.

### 6.2.2 Management of chronic pain

Physiotherapy management for all types of chronic pain currently follows the principles described for chronic nociceptive pain.<sup>75,76</sup> There is insufficient evidence to indicate specific physiotherapy treatment methods for particular pain syndromes in MS or for chronic pain, generally. However, there is evidence suggesting that physiotherapy exercise can positively impact on disability and quality of life in people with MS.<sup>77</sup>

The management of chronic pain involves the use of cognitive behavioural strategies to reinforce behavioural changes, teach pacing of activity levels, SMART goal-setting (Specific, Measurable, Achievable, Realistic, and Timely goals), and providing positive reinforcement.<sup>76</sup> Physiotherapy aims to break the progressive cycle between pain, inactivity, and disability in MS by focusing on maintaining physical activity and function. A physiotherapy pain management program based on APS and IASP guidelines may include retraining muscular stability, pain education, posture, gait, body mechanics, paced increase in activity (exercise for distraction), and increase in functional exercise (specific to activities of daily living).

Exercise is an important component of chronic pain management. Aerobic exercise can be prescribed, when possible, to assist with pain control, and improved mental health through the release of endorphins. Exercise programs should be tailored to individual needs and adjusted if the person experiences excessive MS fatigue or MS flare-ups. For more information about prescribing exercise for people with MS refer to the *Strength and cardiovascular exercise for people with multiple sclerosis* handout.

### 6.2.3 Supporting evidence

Pain management techniques used by people with MS primarily include manipulation and exercise.<sup>78</sup> There exists little evidence in support of the effectiveness of

specific physiotherapy treatments for pain in MS. The evidence is discussed below.

- Passive range of movement exercises may be used when there is joint swelling due to lack of active movement. Although there is no evidence in the literature for this in relation to chronic pain, in practice, it is used for oedema control.
- It has been suggested that physiotherapy involving physical activities can stimulate sensory pathways and the brain to distract attention from the pain, and maintain physical wellbeing.<sup>7</sup> However, this is unsubstantiated.
- Clinical evidence has demonstrated that endurance or cardiovascular exercise can decrease pain intensity in chronic lower-back pain.<sup>72</sup> Exercise therapy shows strong evidence in the improvement of anxiety, depression, and health-related quality of life in people with MS. However, current studies do not specifically examine pain.<sup>79</sup>
- Heat therapy has been reported to reduce pain and muscle spasm, as well as increasing tissue extensibility. Heat therapy is indicated in acute muscular pain, muscle spasms, joint contractures and tendonitis. The use of heat in people with MS should be used with caution due to the possibility of heat insensitivity.<sup>33</sup> The increase in MS symptoms should be only temporary, but excessive or prolonged heat can cause an increase in MS symptoms.<sup>80</sup>
- Hydrotherapy at 33 °C may dampen the stretch reflex in spastic muscle groups in MS.<sup>81</sup> The impact of hydrotherapy on pain in MS has not been formally investigated.
- Cryotherapy (cold therapy) reduces pain, inflammation, oedema, and muscle spasm locally in the area of application. Cooling impairs the conduction velocity of nociceptors and may, therefore, block pain signals. Cryotherapy is generally indicated for acute pain, chronic pain, and muscle spasm; it must be used with caution in people with MS since cold insensitivity may put the person at risk of tissue damage.<sup>33</sup> Cooling may decrease symptoms of MS, particularly fatigue, but there is currently no formal research into cooling and pain symptoms.



- The results of a small randomised controlled trial and a small pilot study using TENS for the treatment of chronic back pain in people with MS revealed that pain reduction was not statistically significant, although clinical differences were observed.<sup>82,83</sup> These studies did not determine if the back pain was of nociceptive or central neuropathic origin, and TENS did not increase the reported pain (i.e., stimulation of the peripheral nerves was not perceived as hyperaesthesia or allodynia). Another pilot study found that TENS reduced spasticity,<sup>84</sup> while a randomised controlled trial found that eight hours of TENS per day (with parameters set at 100 Hz and 0.125 ms pulse width) led to a significant reduction in muscle spasm and pain, but not spasticity.<sup>85</sup>

### 6.3 Psychological intervention

Psychological assessment and intervention is indicated for the management of chronic pain by the APS. Psychological management may include components of cognitive behavioural therapy, challenging unhelpful thoughts, problem-solving, planning, stress-management, dealing with relationships, coping strategies, hypnosis, relaxation methods, and distraction techniques. Psychologists can be effective in treating anxiety, depression, and post-traumatic stress, all of which impact on the perception of pain.

Depression has been linked to other chronic pain conditions but the relationship between depression and MS-related chronic pain needs further study. Depression has been identified as a predictor of pain in people with MS<sup>22</sup> and chronic pain is linked to depression in the general population.<sup>86</sup> People with MS who have high levels of pain and negative affective memory bias (the tendency to recall more negative information) are also more likely to experience depressive symptoms compared with people with MS who have high levels of pain and positive affective memory bias. Therefore, it is postulated that a decrease in pain or negative affective memory bias is achieved through therapy, and this may also affect depression levels.<sup>87</sup>

People with MS who react to pain by catastrophising (less than 10%) have higher levels of pain intensity, interference with activities of daily living, and poorer psychological functioning as measured by SF-36.<sup>88</sup> This relationship supports the need for comprehensive bio-psychosocial assessment and intervention in chronic pain.

### 6.4 Pharmacotherapy

There are few randomised controlled trials on pharmacological management of pain in people with MS. The best evidence available comes from the results of randomised controlled trials involving other CNS conditions, such as stroke and spinal cord injury, and peripheral neuropathic pain in the wider population.<sup>30,89-92</sup>

Many pain medications have side effects similar to MS symptoms (e.g., impaired coordination, double vision, dizziness, urinary retention, weakness, sleeping difficulty, and slurred speech). The drugs used most frequently in the management of nociceptive and neuropathic pain include:

- Carbamazepine, which has an effect on transmission of demyelinated fibres due to the action site of anticonvulsants<sup>93</sup>
- Baclofen, which has fatigue as a common side-effect
- Tricyclic antidepressants (TCAs), which have adverse effects including drowsiness, constipation, urinary retention, and hypotension. TCAs can cause sedation, cognitive impairment, balance problems and postural hypotension<sup>94</sup>

Determination of common side effects of medication in treating pain, and good communication with prescribing professionals is recommended.

Cannabinoids, such as tetrahydrocannabinol (THC), are an alternative drug group that have been trialled in the management of pain in people with MS. A recent meta-analysis, involving six studies of cannabis-based treatments for neuropathic pain in MS, demonstrated a clinically and statistically significant reduction in pain.<sup>95</sup> *Wissel et al.* found THC to decrease spasticity-related pain,<sup>96</sup> *Rog et al.* found improved sleep quality,<sup>97</sup> and *Svendson et al.* found improved quality of life.<sup>98</sup> The side effects have been found to be variable and Phase III trials are required to determine the long-term effect of this treatment. It should be noted that cannabinoids are currently not licensed for use in Australia.



### 6.4.1 Pharmacological management of chronic pain

In Australia, the pharmacological management of chronic pain follows a step-wise, evidence-based approach. According to the Therapeutic Assessment Group (TAG) guidelines (NSW) for the rational use of opioids in chronic or recurrent non-malignant pain, non-opioid analgesics are recommended for first-line management. Second-line management involves combination therapy using non-opioids together with weak opioids. Chronic or neuropathic pain requires adjuvant therapy using TCAs or anticonvulsants. Strong opioids are recommended for third-line management.<sup>99</sup>

Interferon-related side effects such as headache and pain are usually treated with non-steroidal anti-inflammatory drugs (NSAIDs); they have not been shown to be effective for these headaches.<sup>100,101</sup>

### 6.4.2 Pharmacological management of CNP

There are evidence-based recommendations for neuropathic pain from the IASP and APS, mainly based on studies of peripheral neuropathic pain. First-line management involves the use of TCAs, gabapentin or topical lidocaine; second-line management involves combination therapy using opioid analgesics or tramadol together with first-line medications, and third-line management uses antiepileptics and antidepressants.<sup>91</sup>

There are several randomised controlled trials on medication used for specific CNP syndromes in MS. These are listed below.

- Trigeminal neuralgia
  - Anticonvulsants such as carbamazepine,<sup>51,102</sup> phenytoin,<sup>103</sup> gabapentin,<sup>50,104</sup> and lamotrigine<sup>6,39,46,105-7</sup>
  - Combinations of lamotrigine or carbamazepine with gabapentin have been shown to be effective in MS<sup>108</sup>
  - Antispastic medications such as baclofen<sup>46,109</sup>
  - Anaesthetics such as lignocaine<sup>31</sup>
  - TCAs<sup>46</sup>
  - Misoprostol has shown some efficacy in people resistant to anticonvulsants but may inhibit the immune system.<sup>110</sup>
- Painful tonic spasms
  - Anticonvulsants such as phenytoin, carbamazepine<sup>111</sup>, and gabapentin<sup>6,18,45,104</sup>

- Anaesthetics such as lignocaine<sup>31</sup>
- Antispasmodics such as baclofen<sup>6,18</sup>
- Cannabinoids<sup>96</sup>
- Acute radicular pain
  - Intravenous methylprednisolone has been ineffective for acute radicular pain in Guillain-Barré<sup>112</sup>
- Optic neuritis
  - Corticosteroids such as (oral or intravenous) methylprednisolone<sup>6,18,29</sup> and carbamazepine<sup>46</sup>
  - Baclofen or anticonvulsants<sup>113</sup>
  - NSAIDs<sup>6</sup>
- Lhermitte's sign
  - Anticonvulsants such as carbamazepine<sup>6,46</sup>
  - Lidocaine<sup>31</sup>
- Dysaesthetic extremity pain
  - First-line management involves TCAs including amitriptyline,<sup>114</sup> nortriptyline, and desipramine<sup>6,29,46</sup>
  - Second-line management involves intravenous lignocaine<sup>31</sup> or anticonvulsants such as carbamazepine, phenytoin, gabapentin,<sup>113,115</sup> or lamotrigine<sup>6,39,46,116</sup>
  - Third-line management with TCAs<sup>46</sup>
  - Opioids have evidence in other chronic pain conditions<sup>117</sup>
- Visceral pain syndrome
  - Antibiotics or anticholinergic agents such as oxybutynin.<sup>29</sup>

### 6.5 Occupational therapy

A referral to occupational therapy for adaptive equipment can assist people with MS to maintain their functional independence, despite their pain-induced physical limitations. Occupational therapists can prescribe postural support for seating, wheelchairs, and bedding. In many cases a workplace ergonomic assessment may be required.

### 6.6 Further treatment options

Medical management of neuropathic pain is usually coordinated through a neurologist. People with MS who have unresponsive chronic pain should be referred to a pain medicine specialist for review and consideration of surgical options. However, the evidence for these interventions for people with MS is very limited.



Examples of more invasive treatments include:

- Intrathecal baclofen pump implantation<sup>32,118</sup>
- Dorsal cord stimulation via TENS implantation<sup>119</sup>
- Radiofrequency for trigeminal neuralgia<sup>120,121</sup>
- Microvascular decompression, which has been shown to be effective in some people with MS who have trigeminal neuralgia.<sup>122,123</sup>

### 6.7 Alternative and complementary therapies

Alternative and complementary therapies are used by many people with MS. Over 50% of people with MS in the US responded to a survey regarding complementary and alternative medicine in the US and reported using modalities such as herbal remedies, chiropractic manipulation, and massage (for which there is no evidence).<sup>124</sup> Further research is required to establish the effect of these therapies on pain in MS. Alternative therapies that have been shown to decrease anxiety and depression may be helpful for pain management since, in theory, they may be able to modulate pain levels.

Other forms of alternative or complementary therapies include yoga, meditation, tai chi, reflexology and acupuncture.

- Yoga, meditation, and tai chi have been associated with chronic pain reduction, as well as increased function and coping in older adults.<sup>125</sup> Tai chi can reduce pain, improve activity tolerance, and improve quality of life in the general population.<sup>126</sup> Tai chi can also improve tension headaches.<sup>127</sup> One randomised controlled trial found that yoga did not alter mood, but did decrease fatigue among people with MS.<sup>129</sup> Pain was not assessed.
- Reflexology was shown to decrease paraesthesia and spasticity among <sup>71</sup> people with MS who received reflexology therapy for 11 weeks, according to the results of one randomised controlled trial.<sup>128</sup>
- Acupuncture has been shown to be effective in the management of chronic lower-back pain, but there is insufficient evidence for acupuncture in MS.<sup>130,131</sup>

## 7.0 Summary

- Chronic pain affects approximately 64% of people with MS in Australia, with 12–30% reporting pain as their most severe symptom.
- The most commonly reported pain by people with MS is CNP.
- People with MS can experience the same pain syndromes as people who do not have MS.
- Pain in MS can be directly related to demyelination and axonal damage, secondary to other MS symptoms, or secondary to medications.
- Precautions can affect treatment decisions for people with MS and pain. For example, sensitivity to heat contraindicates the use of heat packs, and specific types of allodynia have a risk of burn using electrophysical agents, cold or heat.
- Pain management should involve a multidisciplinary rehabilitation team, incorporating physiotherapy, psychology, occupational therapy, pharmacology and other disciplines appropriate to the individual's needs.
- Depression and negative affective bias (catastrophising) is reported to affect pain intensity in people with MS. This highlights the important role of psychological interventions to treat depression in people with MS who experience pain, particularly of a chronic nature.
- The treatment goal for people with MS undergoing physiotherapy for chronic pain is to maintain physical and occupational abilities and to prevent inactivity or restriction due to pain.
- Common physiotherapy techniques for managing chronic pain include endurance and cardiovascular exercise, TENS, and heat. There is very limited research available to support these or other physiotherapy techniques in people with MS.

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### **MS Practice//For Health Professionals**

MS Practice is an initiative of MS Australia (MSA). MS Practice is an online resource designed to support allied health professionals in the symptom management of people with multiple sclerosis (MS). The series addresses the various symptoms associated with MS, providing health professionals with evidence-based information and clinical practice recommendations to enhance the quality of care and outcomes for people with MS. The MS Practice topics were identified by the MSA Physiotherapy Network.

### **Pain and multiple sclerosis multiple sclerosis**

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### **MS Australia**

MS Australia is a not-for-profit organisation that has been supporting people with MS since 1956. Through state-based MS Societies, MS Australia strives for a world without MS through quality research and service excellence for people with multiple sclerosis, their family and friends, and healthcare professionals.

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### **Disclaimer**

This handout is intended to provide information to support current best practice for the management and treatment of physical impairments in people with MS. While the information is available to all health professionals, there are details that are most relevant to physiotherapists, exercise physiologists, and people who are qualified to provide exercise opportunities for people with MS. MS Australia has made every effort to ensure that the information in this publication is correct. MSA does not accept legal responsibility or liability for any errors or omissions, or for any physical or financial loss incurred whilst participating in the exercises or activities outlined in the MS Practice handouts. Be sure to seek advice from the sources listed.



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