CHAPTER 2

LITERATURE REVIEW

The literature review in this study will explore the literature related to elderly with neck pain and a foundation for understanding the potential contribution of sensory perception to elders with neck pain. The first sub-section will review the prevalence of neck pain in the elderly population. The second sub-section will focus on pain mechanisms and its measurements. The third sub-sections will review alteration of the sensory system in older persons and the last sections changes in pain perception in patients with neck pain.

2.1 Neck pain in elderly population

Neck pain is the second most common musculoskeletal complaints after back pain in the elderly population (6). Women report more neck pain and longer duration of pain than men (2, 5, 6). The prevalence of neck pain has been reported to be 20% in this age group (6). The mean prevalence estimates of neck pain in the elderly population varies periodically with time: 38.7% for point prevalence, 8.8-11.6% for one-year prevalence (2, 28) and 17% for lifetime prevalence (only elderly women) (1). Additionally, Fejer et al (5) demonstrated that older persons with neck pain reported less neck pain than adult populations in the one-year prevalence. In Japan, the prevalence of neck pain was found to be slightly higher in the 70-79 years age group than the 60-69 years old (1). Furthermore, its prevalence was found to vary in communities (1). In a population-based study of pain, intensity of neck pain reported by elderly subjects was more intense than moderate and mild (2). Approximately 48% of those elders with neck pain reported having intense pain while 39% and 12% of those reported having moderate and mild pain, respectively. Also, the temporal pattern of neck pain was more persistent. About 41% of elderly subjects reported pain lasting more than 6 months.

It has been demonstrated that neck pain has substantial effects on psychosocial functions and physical function. Hartvigsen et al (6) found that 7% of elders with neck pain had impaired physical activities. Approximately 11% of elders with neck pain had received treatment for neck pain in the past year from a general medical practitioner or physiotherapist. Likewise, studies on general populations also reported that patients with neck pain had mental distress (i.e. anxiety and depression) and social function (4, 7-9, 29) and those with comorbid pain experienced more disabling neck pain than those who did not have comorbid pain. Furthermore, it has been suggested that neck disability is positively correlated with pain scores (8, 9, 30) and negatively correlated with isometric neck muscle strength (30).

2.2 Pain mechanisms and measurements

Pain is defined as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage" (31). One way that pain begins is from the injury site. A noxious stimulus from the injury site is thought to be detected by a specific peripheral receptor such as Aδ mechanical nociceptors, C polymodal nociceptors, or C fiber mechanical nociceptors. Each sensory receptor is connected to the first primary nociceptive afferent neuron that transmits the impulse to a higher centre. The larger fibers transmit impulses faster than smaller fibers. Two different types of fibers that carry pain impulse are Aδ and C fibers, which their characteristic and physiologic properties are described in Table 1 (32). Primary nociceptive afferent neurons synapse with second-order neurons in the spinal cord and send its process across the midline into the anterolateral aspect of the spinal cord white matter. Then the input from afferent fibers is sent into thalamus via spinothalamic tract (33). From thalamus, second-order neurons synapse with third-order neurons that project to the primary somatosensory cortex (33). Finally, efferent input is sent back to the injury site via ascending pathways.

Table 1 Characteristics and physiologic properties of primary nociceptive afferent fibers (32)

Type	A-delta fiber	C fiber
Anatomy	Free endings Myelinated 1-5 µm fiber diameter Punctuate fields	Free endings Unmyelinated 0.5-1.5 µm fiber diameter Diffuse receptive fields
Stimulus	High threshold Mechanical Thermal - heat (>45°, >53°C) - cold (<25°C)	High threshold Mechanical Thermal Chemical Polymodal
Physiologic properties	Fast 10-30 m/sec conduction First pain (sharp, pricking) Well localized	Slow 0.5-2 m/sec conduction Second pain (dull, burning) Poorly localized Sensitized, Cross-sensitized

Tissue injury or damage leads to an inflammatory response with release of pain substances and may induce changes in response characteristics of the peripheral and central nociceptive neurons and fibers. In general, peripheral sensitization contributes to the pain hypersenstivitiy (lower activation thresholds or increased responses to noxious stimuli) at injured or local sites (32). When intense or prolonged peripheral noxious stimuli at the dorsal horn of the spinal cord are occurred, they can also increase excitability of central sensory neurons. This is termed central sensitization, that is pain is experienced in response to stimulation that are at an uninjured tissue or remote site (34).

Quantitative sensory testing (QST) is a method commonly used to assess peripheral and central sensitization in patients with pain in both research and clinical setting (35). QST can also be used as an outcome measure to determine changes in somatosensory function related to treatment. Pain threshold, the lowest intensity of stimulus at which pain is felt, is clinically the simplest measure of pain sensitivity. Hypersensitivity is characterized by a reduction in pain threshold to experimental stimulation such as mechanical, electrical and thermal stimulation (32, 34). Electronic digital algometry is often used to determine mechanical (pressure) pain threshold (10-13) whereas Thermotest device is often used to determine thermal (heat and cold) pain thresholds (10-13, 18, 36).

Supra-thresholds response is another clinically relevant quantitative sensory testing measure that determine the pain-modulatory ability of the central nervous system (37). It measures amount of pain that imposed by stimuli above the threshold level. It has been suggested that supra-threshold stimulation is to be more sensitive and the strongest QST measure in association with clinical pain intensity compared with measures of pain thresholds for evaluation of generalized pain perception (37, 38). Edwards et al (39) also reviewed that overall supra-threshold pain response is more clinically relevant than responses to threshold-level noxious stimuli. Rating supra-threshold to heat is commonly used for assessment of pain in subjects with clinical conditions (37, 40-43). It has been suggested that low heating rates may be mediated by the activation of C-fiber nociceptors whereas high rates of heat noxious stimuli are apparently mediated by the activation of Aδ nociceptors (44, 45). The magnitude of pain is also suggested to increase with increasing rates of temperature changes (45). However, this relationship is still controversial. Pertovaara et al (46) reported that the magnitude of pain is independent of the rate of temperature rise. Yucel et al (43) investigated the effect of the rate of temperature increase on the intensity of the evoked pain before and after hyperalgesia induced by topical capsaicin. The authors found that in the primary hyperalgesic area, the slow heating rate (1°C/s) was perceived more painful than fast heating rates (5°C/s and 8°C/s). Additionally, the authors demonstrated that secondary hyperalgesia to heat was present for temperatures that were normally perceived as painful (45°C and above). No differential effect on the heating rates by the capsaicin application was found. From these results, it has been suggested that C-fibres play an important role in the primary hyperalgesia and both Aδ and C fibres are mediating the increased thermal sensitivity in the secondary hyperalgesic area. However, the underlying mechanisms remain unclear. Likewise, Serra et al (47) reported heat hyperalgesia to a 47 °C thermal stimulus in the secondary hyperalgesic areas using a contact heat stimulation thermode with probe size of 1 cm.

Pain thresholds measured by QST can be influenced by many factors such as body regions, age, gender and clinical pain (48, 49). However, it has been suggested that QST measurements are more associated with body regions than age and gender (49). Women report greater sensitivity to experiment noxious stimuli (i.e. lower pain tolerance and higher pain rating) than men, especially for heat pain (39, 49, 50). Associations of pain sensitivity/thresholds and clinical pain intensity and psychological factors have also been suggested. Robinson et al (42) demonstrated that greater scores on fear of pain and anxiety (State-Trait Anxiety Inventory, STAI and Anxiety Sensitivity Index, ASI) were related to greater supra-threshold response. The psychological measures were significant and strong predictors of pain ratings at all sites tested (trunk, lower and upper extremities). It has been suggested that psychological influence might be more consistent across sites for Aδ fiber mediated processes. Influences of psychological factors on supra-threshold response have also reported by other studies (51, 52).

2.3 Alterations in the sensory system in older persons

There is evidence of age-related changes in the structure and function of the nociceptive system. Lin et al (53) demonstrated that age is the most significant factor that influences sensory sensitivity and the processing of sensory stimuli compared to other factors such as gender, body height, body weight and body mass index. A review of Gibson et al (15) also suggested that changes in primary afferent nociceptive fibers and the central nervous system are potential explanations for the changes in pain perception/thresholds with advancing age.

2.3.1 Changes in primary afferent nociceptive fibers with ageing

It has been proposed that there are functional, structural and biochemical changes in peripheral nerve with ageing (54). Several studies demonstrated that the number and density of myelinated and unmyelinated fibers decrease with advancing age (55-58). Electrophysiologic studies also showed that older persons had lower nerve conduction velocity values than younger subjects (59, 60). Additionally, there may be a reduction of major neurotransmitters (i.e. substance P and CGRP) in primary afferent nociceptive fibers (61).

2.3.2 Changes in the central nervous system with ageing

In addition to changes in the peripheral nerves with age, changes in structure, neurochemistry and function in the central nervous system have also been documented with advancing age. Quiton et al (62) investigated age-related changes in nociceptive processing in human brain and found that older persons had significantly smaller pain-related fMRI responses than younger subjects in cortical regions of interest involved in nociceptive processing (i.e. anterior insula, primary somatosensory cortex and supplementary motor area). Proportions of grey matter in anterior insula and primary somatosensory cortex and, a loss of myelin, serotonergic and noradrenergic neurons in spinal dorsal horn have also found to be significantly smaller in older persons (63, 64). Additionally, there is a reduction in neurotransmitters and receptors in spinal, thalamus, limbic system and the cerebral cortex (e.g. substance P, β-endorphin, GABA, noradrenaline, dopamine or opioiod) (15, 65-68).

From changes in structure and function in the peripheral and central nervous system with age, numerous studies have investigated differences in pain perception between older and younger persons. However, the age effects on pain sensitivity remain unclear and poorly understood. Most evidence supports decreased pain thresholds to mechanical (pressure) stimuli and increased pain thresholds to thermal stimuli with advancing age. As mentioned earlier, pain thresholds could be attributed by many factors including psychological distress. However, the prevalence of psychological disturbances with age was variously reported as being either decreased, increased or unchanged (19-22). Thus, psychological disturbances may or may not be necessary to be attributed to pain thresholds in older persons. Influence of psychological factors should be taken into account when investigating pain in older persons.

2.3.3 Age-related changes in pressure pain thresholds (PPTs)

Lautenbacher et al (17) conducted a comprehensive study of age-related changes in pain perception using a pressure algometer (a probe size of 0.25 cm^2 and 0.75 cm^2 and an application rate of 1000 kPa/s) and showed that older subjects had significantly lower PPTs over the volar end-phalanx of the middle and ring finger of both hands compared to younger subjects ($p = 0.003$). Likewise, Pickering et al (18) investigated the impact of age on experimental nociception thresholds using a pressure alogmeter (a probe size of 0.28 cm^2 and an application rate of 1.1 N/s) and found that older persons tended to have lower PPTs than younger persons over the middle phalanx of the second, third, fourth and fifth fingers. In contrast, Edwards et al (36) assessed age-associated differences in responses to various forms of experimental noxious stimulation using a pressure algometer with a probe of 0.503 cm^2 and an application rate of 30 kPa/s. The authors did not find any differences in PPTs between older and younger subjects over the upper trapezius and masseter muscles. Marini et al (69) compared PPTs of 18 head and neck muscles between a group of young subjects (aged 20 to 30 years) and a group of elderly subjects (aged over 65 years) using Fischer algometer. The results showed that the elderly group had increased PPTs than the younger group. The discrepancies between the PPT results of the previous studies may be due to differences in stimulus duration, site, areas as well as psychological influences (15).

2.3.4 Aged-related changes in thermal pain thresholds

2.3.4.1 Heat pain thresholds (HPTs)

Lautenbacher et al (17) investigated age-related changes in HPTs in younger subjects (mean age 27.1 years) and older subjects (mean age 71.6 years). The results showed that HPTs were likely higher in older subjects compared to younger subjects, using a thermode with an application rate of 4°C/s. However, the differences in HPTs between the two groups did not reach statistical significance. In a review by Gibson et al (15, 16), older persons have increased HPTs compared to younger persons, using a contact thermode device with a short heat stimulus duration (between 4°-17°C/s). Nevertheless no change in HPTs has been noted, using a contact thermode device with longer heat stimulus duration (0.5°-1°C/s) (18, 36). Duration of thermal stimuli has also been suggested to be associated with age (15).

2.3.4.2 Cold pain thresholds (CPTs)

At present, there has been no research investigating differences in cold pain thresholds between older and younger persons but only cold detection. Lautenbacher et al (17) investigated age-related changes in somatosensory thresholds (cold, warmth, vibration) in younger and older persons and showed that cold detection were significantly higher in older persons compared to younger persons using a contact thermode with a decreasing rate of 1°C/s. In contrast, Chakour et al (70) investigated cold detection between the elderly and younger groups using a contact thermode at a rate of 1°C/s and found no significant differences between two groups. However, it was noted that in Chakour et al’s study, increased cold detection were found in older persons compared to younger subjects. Further studies are needed to determine age-related influences on CPTs.

2.3.5 Age-related changes in supra-threshold pain ratings

There has been little research investigating supra-thresholds in older people. A review of Gibson et al (16) demonstrated a corresponding decrease in the subjective pain rating of high-intensity noxious heat stimuli in older persons. Harkins et al (41) evaluated the effect of age on visual analogue scale rating of experimental pain in the forearm region in young, middle-aged and elderly groups. Intensity of six levels of painful contact heat stimuli (43°C, 45°C, 47°C, 48°C, 49°C and 51°C) with a rate of 17°C/s was measured. The result showed that the middle-aged and elderly groups had less pain rating than the younger group at 43°C, 45°C and 48°C. The elderly group also had slightly higher pain rating than the younger group at temperatures of 49°C and 51°C. This may suggest that heat pain intensity recruitment is affected by age.

2.3.6 Altered pain thresholds in older persons with pain

Sensory hypersensitivity has been commonly demonstrated in many patients in association with pain or injury. However, hypersensitivity has not, as yet, been extensively investigated in older persons with pain. Lee et al (23) assessed pain sensitivity and the inflammatory response to pain in patients with knee osteoarthritis (OA) (mean age = 59.0 ± 7.5). Pressure pain thresholds were measured using a pressure algometer with a probe of 0.5 cm^2 and an application rate of 30 kPa/s. The results demonstrated that patients with OA had significantly lower pressure pain thresholds over the quadriceps and trapezius muscles as well as the first metacarpophalangeal joint compared to controls without pain ($p < 0.005$). This suggests widespread mechanical hypersensitivity in patients with knee osteoarthritis. In contrast, Uthaikhup et al (24) reported that widespread sensory hypersensitivity was not a feature of elders with headache associated with neck pain. In Uthaikhup et al's study, the PPTs at forehead, upper neck and tibialis anterior muscle were not different between elders with and without headache. Schenk et al (71) also reported similar pressure pain thresholds over the lower back between subjects (aged between 45-62 years) with and without recurrent low back pain. The findings of Uthaikhup et al's and Schenk et al's studies are not consistent with studies conducted in the general populations, which have demonstrated the presences of central sensitization in patients with headache and lower back pain (25-27). Age-related changes in peripheral and central nervous system may be attributed to changes in pain sensitivity (thresholds) in elders with pain. Investigation of pain sensitivity in elders with pain is still required.

2.3.7 Psychological factors in older persons with pain

Psychological distress is frequently reported in older persons with pain conditions. Uthaikhup et al (21) investigated relationship between physical and psychological well-being in elders with chronic headache (migraine, tension-type and cervicogenic headache) compared with controls without headache. They found significantly higher depression scores in elders with headache than in the control group ($p < 0.05$). However, depression scores in elders with headache were below threshold values for depression. In addition, elders with chronic frequent headache had also significantly higher depression scores than the infrequent headache group ($p = 0.037$) and control group ($p < 0.001$). Similarly, Wang et al (22) found that depression was significantly higher in elders with more frequent or severe headache. A review of Herr et al (19) also demonstrated the close association between chronic pain and depression and anxiety in the older population. Therefore psychological disturbances should be assessed in studies investigating pain in old persons.

As pain perception measured can be altered by psychological distress, influence of psychological factors (e.g. depression and anxiety) has been often determined in studies investigating pain in older persons. A review of Herr et al (19) suggested that the assessment of mood, in particular depression is an essential component of the pain assessment in older persons with chronic pain. Kose et al (20) investigated pressure pain thresholds and its correlation with depression and anxiety status in geriatric nursing home residents with and without cognitive impairments. The results showed no correlations between pressure pain thresholds and psychological disturbances (depression and anxiety) in the group with cognitive impairment. In the group with normal cognitive impairment, PPTs were found to be correlated with depression and anxiety. Thus influences of psychological distress on pain thresholds will be assessed and controlled if necessary in this study.

2.4 Alterations in the sensory system of patients with neck pain

Alterations in the sensory system of patients with neck pain have been demonstrated in many studies (10-14). Most studies suggest that patients with chronic neck pain have a significant reduction in pressure and thermal (heat and cold) pain thresholds over local areas (the cervical spine) (10-14) as well as other remote site (tibialis anterior) compared to healthy controls (12, 13). This has been proposed as a result of sensitization of peripheral and central nervous system (10-14). It has been suggested that nociceptor activity at a local site can initiate central hyperexcitability (34). Thus ongoing or maintained nociceptive inputs from the periphery can then lead to a chronic pain state (72).

2.4.1 Pressure pain thresholds (PPTs)

A number of studies have investigated pressure pain thresholds in patients with neck pain. For example, Johnston et al (13) investigated relationships between sensory features and neck pain in female office workers using quantitative sensory measured. Eighty-five office workers and 22 controls without neck pain were recruited for the study. Office workers were categorized based on Neck Disability Index (NDI) scores: no disability (NDI score ≤ 8/100), mild pain and disability (NDI score 9-29) and moderate/severe pain and disability (NDI score ≥ 30/100). The duration of neck pain was 4.3 ± 6.9 yrs for workers with no disability, 10.7 ± 8.7 yrs for workers with mild pain and disability and 8.2 ± 8.7 yrs for workers with moderate/severe pain and disability. PPTs were measured using a digital algometer with a circular prove of 1 cm^2 and a pressure application rate of 40 kPa/s over levator scapulae, posterior neck, semispinalis capitis, upper trapezius and tibialis anterior muscles, and median nerve trunk. The results showed a pattern of lower PPTs over each site in female office workers with mild and moderate/severe pain and disability compared with workers with no disability or controls, even though the group differences were significantly found only in the tibialis anterior muscles and median nerve ($p < 0.01$). Decreased PPTs over the local site (levator scapulae) may reflect a sign of primary hypersensitivity whereas decreased PPTs over the tibialis anterior muscles represent a site of secondary hypersensitivity, which is suggestive of a feature of central sensitization. Similarly, Javanshir et al (12) and Touche et al (14) revealed lower PPTs over C5-C6 (local site) as well as non-symptomatic regions or remote site in patients with chronic idiopathic neck pain compared to healthy controls. Scott et al (11) investigated sensory sensitivity in patients with chronic whiplash and idiopathic neck pain. PPTs were measured using algometer with a circular probe of 1 cm^2 and a pressure application rate of 40 kPa/s over the articular pillars of C2-C3 and C5-C6 and tibialis anterior muscle. The results showed significantly lower PPTs over C2-C3 and C5-C6 in both idiopathic neck pain and whiplash groups compared to controls. However, significantly lower PPTs over tibialis anterior muscle were found only in whiplash group. From the study results, the authors suggested that patients with whiplash injury had additional widespread hypersensitivity to mechanical pressure stimuli, which was not present in patients with chronic idiopathic neck pain. Results of Scott et al’s study are also supported by findings of Chien et al’s study (10). Overall, studies suggest localized hypersensitivity to mechanical stimuli in patients with neck pain both idiopathic or whiplash origin. The presence of generalized hypersensitivity in patients with whiplash neck pain has been established but in those with idiopathic neck pain is still controversial and needed to be further investigated.

2.4.2 Heat pain thresholds (HPTs)

Alteration in heat pain thresholds in patients with neck pain has been shown in several studies. Johnston et al (13) determined relationships between sensory features and neck pain in female office workers. The results showed that female office workers with mild pain and disability had significantly decreased HPTs over posterior neck region compared with female office workers with no disability and controls ($p = 0.001$). There were no differences between workers without disability and controls or between workers with mild and moderate/severe pain. However, the results are in contrast to Scott et al's (11) and Javanshir et al's (12) findings, which demonstrated no significant differences in HPTs between patients with idiopathic neck pain and controls over cervical spine. Scott et al (11) also revealed lower HPTs at cervical spine, tibialis anterior and deltoid insertion sites in patients with whiplash injury compared to those with idiopathic neck pain and controls. This result is similar to findings of Sterling et al's study (73). Sterling et al (73) investigated HPTs over cervical spine in patients with whiplash injury and found that patients with whiplash injury had significantly lower HPT than controls who had no pain. On the other hand, Chien et al (74) however demonstrated no significant difference in heat pain thresholds between the whiplash and control groups. The discrepancies of the HPTs among the previous studies may be due to differences in variances of level of pain-related disability and sources of pain. Furthermore, as a study of Johnston et al (13) recruited only women with neck pain whereas the other studies recruited both men and women, the HPTs measured may also be influenced by gender, which women are found to be more sensitive than men (49).

2.4.3 Cold pain thresholds (CPTs)

Studies demonstrated that patients with neck pain were more sensitive to cold stimuli over cervical spine (12, 13, 75) and tibialis anterior muscle (remote site) (12) than controls. This is also evidence suggesting alterations of peripheral and central sensitization in patients with neck pain. Johnston et al (13, 75) demonstrated that female office workers with mild pain and disability had significantly increased sensitivity to cold stimuli over posterior neck region compared to female office workers without disability and controls ($p = 0.008$). Likewise, Javanshir et al (12) reported decreased CPTs over cervical spine and also tibialis anterior muscle in patients with idiopathic neck pain compared with controls. However, Scott et al (11) and Chien et al (10) found no significant differences in CPTs in patients with idiopathic neck pain but in those whiplash injury over cervical spine and tibialis anterior muscle compared to the control group. Again, the discrepancy may arise from variances of level of pain-related disability, sources of pain and gender differences.

2.4.4 Influences of psychological factors on pain thresholds in neck pain patients

It is evident that neck pain is associated with psychological factors such as depression and anxiety. Several studies investigated the correlations between pain thresholds, current level of pain, neck disability and psychological factors (11, 14). Touche et al (14) found that pressure pain thresholds were negatively correlated with current level of pain intensity at masseter muscles (r = -0.62 for a dominant side, $p < 0.001$ and r = -0.51, $p = 0.02$ for a nondominant side). Current level of pain intensity was also found to be positively correlated with neck disability (r = 0.57, $p = 0.004$) and depression (r = 0.64, $p = 0.01$) (14). In addition, Scott et al (11) revealed significant correlations between pressure pain thresholds at C2-C3 and C5-C6 and NDI scores (r = -0.23 and -0.3, respectively, $p < 0.05$) and between cold pain thresholds at tibilais anterior muscle and cervical spine (r = 0.4) and NDI scores (r = 0.26 and 0.4, respectively, $p < 0.05$) (11). Patients with idiopathic neck pain tended to show higher scores of anxiety than whiplash group and controls. Touche et al (14) found that patients with idiopathic neck pain showed greater levels of both anxiety and depression compared to controls. However, anxiety was not found to be significant correlated with sensory measures in patients with neck pain (11, 14). Although correlation between anxiety and sensory measures were not found, a measure of anxiety should not be disregarded as its influence on pain sensitivity has been reported (76).

Summary statement

Neck pain is a significant problem in the elderly population. In general, studies conducted in the general populations have demonstrated increased sensitivity to mechanical and thermal stimuli in patients with chronic neck pain. However there is no comprehensive study investigating changes in pain sensitivity in elders with neck pain. Given that there are changes in peripheral and central nervous system with age, findings found in younger/middle-age population (18-59 years) may not be valid to the old age group. Additionally, pain sensitivity can be influenced by psychological factors and pain experience. Thus, research specific to this age group is required. A better understanding of pain mechanisms in older persons with neck pain will help enhancing appropriate treatment and management for elders with neck pain.