Whiplash-associated disorder: musculoskeletal pain and related clinical findings

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The aim of this paper was to review the physical and psychological processes associated with whiplash-associated disorders. There is now much scientific data available to indicate the presence of disturbed nociceptive processing, stress system responses, muscle and motor changes as well as psychological factors in both acute and chronic whiplash-associated disorders. Some of these factors seem to be associated with the transition from acute to chronic pain and have demonstrated prognostic capacity. Further investigation is required to determine if these processes can be modified and if modification will lead to improved outcomes for this condition. The burden of whiplash injuries, the high rate of transition to chronicity, and evidence of limited effects of current management on transition rates demand new directions in evaluation and management. The understanding of processes underlying this condition is improving and this lays the foundation for the development of more effective management approaches.

Keywords: WAD, MCV, Musculoskeletal pain

Introduction

Whiplash-associated disorders (WADs) are a common, disabling, and costly condition that occur usually as a consequence of a motor vehicle crash (MVC). While the figures vary depending on the cohort studied, current data indicate that up to 50% of people who experience a whiplash injury will never fully recover[1] and up to 30% will remain moderately to severely disabled by their condition.[2,3] The associated costs secondary to whiplash injury, including medical care, disability, lost work productivity as well as personal costs are substantial.

Whiplash is one of the most debated and controversial painful musculoskeletal conditions. This is in part due to the often compensable nature of the injury and that a precise patho-anatomical diagnosis is not usually achievable, at least with current imaging techniques. However, it is now generally acknowledged that there is an initial peripheral injury of some kind to the neck following whiplash injury.[4] Irrespective of whether or not a 'peripheral lesion' is present, it is important to consider processes that may underlie the initiation of whiplash pain and particularly the maintenance of symptoms in those who do not recover. This may allow for the development and testing of interventions to target these processes and improve outcomes.

In recent times, there has been much investigation of these processes by various research groups. These processes are not necessarily causally related to the presentation and outcomes following injury but are features of this pain condition that may shed light on mechanisms underlying ongoing pain and disability following the injury. The aim of this paper is to review the potential processes involved in whiplash pain. It will particularly focus on the transition from acute to chronic pain.

Nociceptive Processing Mechanisms in WAD

There is now overwhelming data demonstrating the presence of sensory disturbances in patients with chronic WAD. These include decreased pain thresholds to various stimuli including mechanical pressure,[5,6] thermal stimulation,[6] electrical stimulation,[7] and vibration.[8] Decreased pain thresholds or sensory hypersensitivity have been demonstrated both locally over the neck as well as at more distal or remote sites such as the upper and lower limbs where there is no tissue damage. The absence of tissue damage at the site of testing suggests that a central sensitization of nociceptive pathways is the cause of the pain hypersensitivity.

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These findings have been confirmed via studies assessing sensory responses following induced muscle pain with injection of hypertonic saline. Following injection to supraspinatus and tibialis anterior muscles, patients with WAD reported higher pain scores, longer duration of pain, and larger areas of local and referred pain compared with healthy controls.[5] Several patients also reported pain spreading to the whole leg and on the contra-lateral side, which was not the case in healthy subjects. These data suggest that pain hypersensitivity is not limited to the injured and surrounding areas (primary and secondary hyperalgesia), but may be generalized to the whole central nervous system. The extensive spread of referred pain is strongly suggestive for central hyper-excitability, possibly involving disinhibitory processes and expansion of receptive fields.[9]

Augmented central nociceptive processing may occur anywhere along the neural pathways and the location of the hyper-excitability cannot be determined from these studies. Nevertheless, some studies have utilized the nociceptive withdrawal reflex to analyze spinal cord hyper-excitability. Patients with chronic WAD displayed lower reflex thresholds than healthy subjects.[10–12] These findings provide objective electrophysiological evidence for generalized spinal cord hyper-excitability.

It is important to recognize that central hypersensitivity is not specific to whiplash, but has been observed in different chronic pain syndromes, such as endometriosis,[13] fibromyalgia,[14] osteoarthritis,[15] tension-type headache,[16,17] temporomandibular joint pain,[18] and post-mastectomy pain.[19] This suggests that similar processes may underlie various painful conditions and differences between them require further investigation.

Recent data demonstrate that sensory disturbances observed in chronic WAD are in fact present soon after the injury. In the acute phase post-injury (up to 4 weeks), local cervical mechanical hyperalgesia (decreased pressure pain thresholds) is found in both individuals with lower and higher levels of pain and disability,[20,21] but this resolves quickly in those with good and fair recovery. In contrast to local hyperalgesia, which occurs irrespective of pain and disability levels, the presence of generalized hyperalgesia has been shown to be more apparent in those individuals reporting higher pain and disability[21] and subsequent poor recovery.[6] Additionally cold hyperalgesia and to a lesser extent heat hyperalgesia have also been found to predominantly occur in injured people with higher initial levels of pain and disability and subsequent poor functional recovery.[6] Recently the presence of negative sensory responses or hypoaesthesia (or elevated detection thresholds) occurring concurrently with hypersensitivity has also been found in patients with acute WAD.[22] Similar to findings of sensory hypersensitivity, the hypoaesthetic changes were widespread and occurred in response to a variety of stimuli including vibration, thermal and electrical stimulation.[22] While they occurred in the majority of participants in the acute injury stage, the hypoaesthesia persisted only in those initially classified as at high risk of poor recovery (higher pain and disability and sensory hypersensitivity).[23] Concurrent positive and negative sensory changes to various stimuli that are widespread and generalized suggest that disturbances in both excitatory and inhibitory central nervous system processes are present.

Importantly some of the sensory phenomena demonstrate capacity to predict individuals at risk of poor recovery. In particular, the early presence of cold hyperalgesia is emerging as a consistent prognostic factor. Initial studies demonstrated that in addition to initial moderate pain, decreased neck movement, older age, and post-traumatic stress symptoms, cold hyperalgesia predicted higher levels of pain and disability at both 6 months and 2–3 years post-injury.[3,24] Cold pain tolerance measured using the cold pressor test has also shown predictive capacity.[25] More recently, it has been shown that when injured people are classified based on the presence of moderate or greater initial pain and sensory hypersensitivity, 86% of those deemed at high risk of poor recovery did indeed develop persistent symptoms at 6 months post-injury.[23] Further research using trajectory modeling has validated cold hyperalgesia as a predictor of a clinical pathway to chronicity.[26]

In summary, current evidence would suggest that some central nervous system nociceptive processes are augmented from soon after injury in those individuals who do not recover but develop chronic moderate to severe pain and disability. The reasons as to why this group manifests more profound changes in pain processes are not clear but there are numerous possibilities including but not limited to: the nature, extent and duration of the original injury providing peripheral nociceptive input to the central nervous system,[27] stress-related responses;[28] psychological augmentation,[29] poorer health prior to the injury[30] or a genetic predisposition.[31] Irrespective of the cause of the changes, the data indicate that consideration of these processes in the early management of WAD may be useful in improving outcomes. The most optimal way to modulate these processes is yet unknown.

Stress System Responses

In addition to subjecting soft tissues to a biomechanical strain, an MVC event is also an acute stressor which activates physiological stress response systems.

In recent times, models have been put forward that link stress system responses[28] and sympathetic nervous system activation[32] and the various physiological changes seen in WAD including both sensory and motor manifestations.

There is some evidence available indicating that autonomic disturbances are present in chronic WAD. Impaired peripheral vasoconstrictor responses have been demonstrated in both acute and chronic whiplash[6] but the relationship of these changes to the clinical presentation of whiplash or outcomes following injury is not clear. Gaab *et al.*[33] have shown reduced reactivity of the hypothalamic–pituitary–adrenal axis, a closely interacting system to the autonomic system, in a small sample of participants with chronic WAD. Autonomic nervous system dysfunction has been found to be present in other painful musculoskeletal conditions such as chronic low back pain,[34] fibromyalgia,[35] and cervicobrachialgia.[36] Individuals with post-traumatic stress disorder (PTSD) also show evidence of autonomic and hypothalamic–pituitary–adrenal dysfunction[37] which may have some relevance for WAD where recently it was shown that a significant proportion of injured people also have a probable diagnosis of PTSD.[38]

One key component of the adrenergic system is the catechol O-methyltransferase (COMT) enzyme. COMT is the primary enzyme that degrades catecholamines, including adrenaline, noradrenaline, and dopamine. Variants of the COMT gene have been associated with experimental pain sensitivity[39] and with vulnerability to both chronic pain[39] and anxiety disorders.[40] McLean *et al.*[41] recently showed that individuals with acute whiplash injury and with a COMT pain vulnerable genotype reported more severe neck pain, headache, and dizziness as well as more dissociative symptoms in the immediate post-injury period in the emergency department. These individuals also estimated that they would take longer to recover both physically and emotionally.[41] While this study was cross-sectional in design and evaluated only patients with acute whiplash, its findings are interesting and if replicated in larger cohort studies could have important implications for consideration of the development of chronic whiplash pain.

In summary, investigation of stress system responses and their role in both non-recovery and the clinical presentation of WAD is in its infancy. Nevertheless, due to the traumatic nature of its onset, this may be an important factor to be considered in this condition.

Changes in the Muscle and Motor Function

There has also been a substantial body of research investigating the motor, muscle, and sensorimotor changes in individuals following whiplash injury. Changes include loss of movement,[42] altered muscle recruitment patterns[43], morphological changes in neck muscles,[44] disturbed eye movement control,[45,46] loss of balance and joint repositioning errors,[47,48] and decreased muscle strength[49] with most of these changes being identified in the early acute post-injury stage as well as in individuals with chronic WAD. It should be noted that many of these movement and motor disturbances are not unique to whiplash-related neck pain but are also found to be present in individuals with non-traumatic neck pain of insidious onset,[43,50] thus it could be extrapolated that they are not involved in the initiation and maintenance of whiplash-related pain and disability, rather are a sequelae of as yet unexplained nociceptive processes. The exception to this is recent interesting findings of magnetic resonance imaging muscle data. Structural muscle changes in the form of fatty infiltration in the neck muscles of females with chronic WAD have been identified.[44,51] The muscle changes are not present in asymptomatic individuals or in those with idiopathic or non-traumatic neck pain[52] and are not related to symptom duration or body mass index.[44] It has been recently demonstrated that the fatty infiltrates manifest at approximately 1 month post-injury but only in those participants with poor functional recovery at 6 months (moderate to severe levels of pain and disability).[53] The muscle changes did not occur in those with lower levels of pain and disability. However, before definitive conclusions can be drawn regarding the importance of these quantifiable muscle changes, an improved understanding of the underlying mechanisms for alterations in paraspinal muscle structure and function as well as their contribution to the development and maintenance of painful signs and symptoms is required.

Few measures of motor or muscle function have demonstrated the capacity to predict poor recovery following injury. Decreased cervical range of movement is the physical factor most commonly investigated for its predictive capacity. An earlier review found only limited evidence for the prognostic capacity of this factor[54] and this is supported by more recent reviews where the general consensus is that this factor is not a strong predictor of poor recovery.[55,56]

Most of the documented motor deficits (movement loss and altered neuromuscular control) seem to be present in whiplash-injured individuals irrespective of reported pain and disability levels and rate or level of recovery.[57] Additionally, apart from cervical movement loss, motor deficits do not appear to have predictive capacity.[24,45] Furthermore, treatment directed at rehabilitating motor dysfunction and improving

general movement shows only modest effects on reported pain and disability levels.[58,59] Together these findings suggest that motor deficits, although present, may not play a key role in the development and maintenance of chronic or persistent symptoms following whiplash injury. This is not to say that management approaches directed at improving motor dysfunction should not be provided to patients with whiplash. Rather the identification of motor deficits alone may not equip the clinician with useful information to either gauge prognosis or potential responsiveness to physical interventions.

Psychological Presentation of WAD

The psychological presentation of whiplash can be as equally diverse as the physical presentation, with some individuals showing marked distress and others seeming resilient to the injury.[38,60] Psychological factors such as high levels of pain catastrophizing,[61] fear of movement,[62] lower pain self-efficacy,[63] and distress[64] have been shown to be associated with more pain and disability in acute WAD. Depressive symptoms are also a common feature of acute whiplash injury[65] and may be associated with prior mental health problems and poorer general health,[65], as well as poor post-injury adjustment.[66]

Different psychological factors may be involved in the etiology and development of chronic whiplash pain when compared to other painful musculoskeletal conditions.[60] For example, the role of fear of movement seems to be a less important factor in whiplash[24] than in low back pain.[67] One possible explanation for the possible limited role of kinesiophobia in whiplash could be that anxiety-related factors play a more prominent role than in low back pain.[68] Because neck pain starts or is attributed to an often stressful motor vehicle crash, this distinguishes it from most cases of low back pain and could give rise to more or different forms of anxiety. The sudden, traumatic onset could also lead to stronger somatic beliefs and related fears regarding recovery.[68]

The effect of the psychological stress surrounding the crash itself as opposed to or in addition to distress about neck pain complaints may have a significant influence on outcome. PTSD is a common sequela of severe injuries following an MVC.[69] Yet, it is only recently that evidence has emerged that it may also play a role in less severe road accident injuries including whiplash. A recent prospective cohort study of 155 participants identified three distinct trajectories for post-traumatic stress measured using the PTSD diagnostic scale. These were: (1) resilient: mild symptoms throughout the 12-month study period (40%); (2) recovering: initial moderate symptoms declining to mild levels by 3 months (43%); and (3) chronic moderate/severe: persistent moderate/severe symptoms throughout 12 months (17%).[38] Furthermore, this study demonstrated that 22% of the cohort had a probable diagnosis of PTSD at 3 months post-MVC with this figure dropping slightly to 17% by 12 months post-injury.[38] This is the first study to demonstrate that the incidence of PTSD in WAD is similar to that identified for more serious traumatic motor vehicle injury, such as following hospital admission and traumatic brain injury.[70] It is likely that individuals who follow this trajectory will require specific psychological interventions to prevent this course. However, such management approaches are often not provided to people with whiplash.[24,71] These findings indicate the need for additional psychological evaluation of these patients[72] and clinicians should be aware of this factor in their assessment of whiplash injured people.

Relationships between Physical and Psychological Features of WAD

While potential processes have been outlined in this paper as separate entities, it is clear that there will be interactions and relationships between these processes. To date this has not been well explored but is an important area for future research. However, there are data available to suggest associations between these factors.

Sterling *et al.*[11] demonstrated moderate associations between pain thresholds (pressure and cold) at some sites, particularly at more remote sites such as in the lower limb, and both psychological distress (GHQ-28) and catastrophisation (pain catastrophising scale) in individuals with chronic WAD. Similar results have been found in acute WAD, where cold pain threshold and catastrophisation show moderate correlations.[73] Notably there appears to be no relationship between psychological factors and the intensity of electrical stimulation required to elicit a flexor withdrawal response in biceps femoris neither in patients with chronic whiplash[10,11,72] nor in controls.[15,27,74] These findings indicate that psychological factors may play a role in central hyperexcitability. However, they do not support the assumption that psychological factors are the only or main factors responsible for central hyper-excitability in whiplash patients. In particular, spinal cord hyperexcitability appears to not be affected, at least significantly, by psychological factors.

The relationships between sensory changes and post-traumatic stress symptoms have also been explored. Using trajectory modeling analyses, distinct trajectories or clinical pathways for both pain and disability and post-traumatic stress were identified.[38] Interestingly cold hyperalgesia (cold pain thresholds of less than 13°C) predicted membership to both more severe pain and disability trajectories and

PTSD trajectories.[26] This suggests that common mechanisms may underlie the development of chronic pain and PTSD symptoms following whiplash injury. Additionally dual analyses revealed that the developmental trajectories of pain and disability and PTSD were mostly in synchrony. For example, individuals are more likely to show higher pain/disability and higher PTSD symptoms or low pain/disability and low PTSD symptoms rather than contradictory membership to say low pain/disability and high PTSD.[26] Together, the findings of these studies suggest close relationships between reported pain/disability levels, post-traumatic stress symptoms, and the sensory presentation of WAD and that all factors should be considered in the assessment and management of WAD.

Recent findings have also illustrated a relationship between symptoms of post-traumatic stress and physical characteristics of WAD. Physical measures of hyperalgesia (cold and mechanical) predicted both a moderate to severe post-traumatic stress symptom trajectory as well as a more severe pain-related disability trajectory[26] indicating relationships between the physical and psychological manifestations of acute to chronic WAD. Current post-traumatic stress symptoms have also been shown to be associated with less activity later in the same day in chronic WAD.[75] More interestingly, the relationship between initial pain intensity soon after injury and the presence of muscle fat at 6 months post-injury was mediated by symptoms of post-traumatic stress.[53]

Thus data are emerging to show that the physical and psychological processes associated with WAD not only co-exist but are also inter-related. Further research is required to clarify this understanding. The results of more thorough investigation along the lines outlined above may provide direction as to the high priority factors to target. For example, should stress responses be targeted or nociceptive (peripheral and central) processes or psychological processes or a combination of these factors? This is not clear as yet.

Conclusions

As discussed in this paper, there is growing evidence of both complex biological and psychological manifestations of WAD and these factors likely contribute to the significant chronicity rate and recalcitrance to treatment associated with this condition. It is becoming clear that a biobehavioral approach that considers all aspects of an individual's presentation will be necessary if gains are to be made in the management of this condition. There is still much work to be done. It remains unknown as to whether or not these processes can be modulated and if modulation will lead to improved outcomes.

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