Published in final edited form as:
Spine (Phila Pa 1976). 2011 December 1; 36(25 Suppl): S309–S315. doi:10.1097/BRS.0b013e318238842a.

The role of tissue damage in whiplash associated disorders: Discussion paper 1

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Abstract

STUDY DESIGN—Non-systematic review of cervical spine lesions in whiplash-associated disorders (WAD).

OBJECTIVE—To describe whiplash injury models in terms of basic and clinical science, to summarize what can and cannot be explained by injury models, and to highlight future research areas to better understand the role of tissue damage in WAD.

SUMMARY OF BACKGROUND DATA—The frequent lack of detectable tissue damage has raised questions about whether tissue damage is necessary for WAD and what role it plays in the clinical context of WAD.

METHODS—Non-systematic review.

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The legal regulatory status of the device(s)/drug(s) that is/are the subject of this manuscript is not applicable in my country. / Corporate/Industry and Federal funds were received to support this work. One or more of the author(s) has/have received or will receive benefits for personal or professional use from a commercial party related directly or indirectly to the subject of this manuscript: e.g., honoraria, gifts, consultancies, royalties, stocks, stock options, decision making position.

RESULTS—Lesions of various tissues have been documented by numerous investigations conducted in animals, cadavers, healthy volunteers and patients. Most lesions are undetected by imaging techniques. For zygapophysial (facet) joints, lesions have been predicted by bioengineering studies and validated through animal studies; for zygapophysial joint pain, a valid diagnostic test and a proven treatment are available. Lesions of dorsal root ganglia, discs, ligaments, muscles and vertebral artery have been documented in biomechanical and autopsy studies, but no valid diagnostic test is available to assess their clinical relevance. The proportion of WAD patients in whom a persistent lesion is the major determinant of ongoing symptoms is unknown. Psychosocial factors, stress reactions and generalized hyperalgesia have also been shown to predict WAD outcomes.

CONCLUSION—There is evidence supporting a lesion-based model in WAD. Lack of macroscopically identifiable tissue damage does not rule out the presence of painful lesions. The best available evidence concerns zygapophysial joint pain. The clinical relevance of other lesions needs to be addressed by future research.

Keywords

whiplash; Cervical spine; tissue damage; Facet Joint; nociception; Psychosocial factors; central sensitization

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INTRODUCTION

Tissue damage frequently cannot be detected in patients with whiplash-associated disorders (WAD). This leads to the question of whether a lesion, responsible for a nociceptive focus, exists and what importance it may have in the determination of symptoms. Furthermore, debate remains as to whether tissue injury is necessary or sufficient to initiate and/or maintain WAD.

In this review, we describe current whiplash injury models in terms of their basic and clinical science. The literature cited was based on the personal libraries and publications of the authors. In this context, there is no pretence of covering the pathophysiology of WAD comprehensively, and consequently mechanisms other than a biomechanical lesion are only marginally mentioned. Our goal is to summarize what can and cannot be explained by injury models, and to guide future research that is needed to better understand the role of tissue damage in WAD.

BIOMECHANICAL CONTEXT FOR TISSUE INJURY

KINEMATICS, KINETICS AND BIOMECHANICS

To better understand whiplash injuries and their prevention, bioengineers have pursued research in two principal domains. Simulated automobile collisions have been performed to predict the presence, timing, and severity of tissue damage and to determine the effects of injury prevention systems. Central to both domains is the quantification of whiplash-induced neck kinetics, i.e. dynamic loads transferred to the neck during the collision, and kinematics which includes intervertebral motions and tissue strains. While some autopsy[1] and cadaveric studies[2,3] have used post-collision anatomical dissection to identify macroscopic neck lesions, other studies defined the potential for tissue damage as non-physiologic neck motions during the collision-exposure.[4,5]

Kinematics and kinetics have been studied using crash dummies, human cadavers, human volunteers, and computer models. Collectively these studies have shown that during rear-end collisions the cervical spine initially undergoes a horizontal shear or retraction.[6–8] Continued retraction accelerates the head and ultimately the cervical spine into extension, followed by acceleration forward and into flexion as a result of head restraint interaction. Total movement of the head and neck largely remains within physiologic limits.[8] However, abnormal motions may occur at one or more spinal levels, particularly during the S-shape phase of neck motion, which consists of flexion at the upper spinal levels and extension at the lower levels.[7,9,10] Studies in cadavers and in normal volunteers have consistently shown that movements of the lower and upper cervical segments during a motor vehicle collision can exceed physiologic limits.[11–13] Abnormal neck postures or axial rotation at the time of the collision increase the risk of structural injury.[14–17]

Evident from this research is that whereas the responses of occupants conform to a general pattern, the magnitudes of the cervical spine dynamics, and their timing, vary for the same subject in different vehicles,[18,19] and between different subjects in the same vehicle,[8] even if the collision severity remains constant. This response variability stems from a diverse range of collision-related, vehicle-related and human-related factors, and exposes the cervical tissues to a wide range of forces and strains. Even greater variability exists in the tolerance to injury of specific cervical tissues,[14,20,21] and the particular combination of tissue exposure and tissue tolerance is hypothesized to determine the genesis, or not, of a tissue lesion in a particular crash.

INJURY PREVENTION

The 1969 Federal Motor Vehicle Standards, FMVSS 202,[22] required automobiles manufactured in USA to incorporate head restraints. However, the standards did not establish requirements for head restraint position. Epidemiological studies found that these traditional head restraints were either ineffective in preventing neck injuries[23,24] or provided up to only 20% reduction in whiplash injury risk.[25–27]

Contemporary approaches to prevention of neck injuries in rear-end collisions have focused on absorbing collision energy and reducing neck motions by modifying seat and head restraint designs.[28,29] Field data evaluating the effectiveness of newer anti-whiplash seat and head restraint designs have shown wide variations. One new seat design initially showed no effect on injury rates, whereas another reduced the risk by 75%.[29,30] The mostrecent assessment of their effectiveness, however, suggests an average reduction in permanent impairment of about 50% across the three main anti-whiplash seats installed in the fleet.[31] These reductions indicate that cervical tissues exposed to lower forces and strains have a lower risk of injury, a finding suggesting that a tissue lesion is responsible for many whiplash injuries.

Some limitations apply to the literature on seat and head restraint effectiveness. Some studies were performed with involvement of the manufacturers,[29,32] with consequent potential conflict of interest. Furthermore, some of the effectiveness studies rely on insurance rather than clinical definitions of injury, and the effect of any bias introduced by these definitions remains unclear.

LESIONS

In cadaveric and post-mortem studies a spectrum of tissue damage has been demonstrated, including: strains beyond physiologic limits in the zygapophysial joint capsules and anuli fibrosi; partial or complete ruptures of capsules, ligaments, and anuli fibrosi; intra-articular contusions; intra-articular fractures; and transarticular synovial joint fractures.[1,3,14,21,33] There is growing evidence from in-vivo animal models of these tissues that their injury can lead to modifications in tissue properties, nociceptor activation, immediate and sustained dysfunction in afferents and spinal neurons, neuroplastic changes and pain.[34–41] A summary of the current injury models and their development state is presented in table 1.

ZYGAPOPHYSIAL JOINTS AND CAPSULES

Although animal studies have focused on various tissues, the greatest body of literature focuses on the capsule of the zygapophysial (facet) joint. In particular, independent studies in different species (rats and goats) provide corroborative evidence supporting the biomechanical findings of injury of the facet capsule derived from the human cadaver and volunteer studies. For example, for comparable maximum principal strains (ranging between ~15–50%) applied to the facet capsular ligament, afferents become saturated and persistent pain is induced.[36,42,43] Those same loading scenarios are also associated with production of collagen fiber disorganization, axonal swelling and altered morphology in the ligament, and permanent modification in the neuronal signaling in the spinal cord.[38–40,44,45]

Using an animal model, it was also demonstrated that removing the contribution of the facet capsule prior to loading the joint resulted in no pain production and reduced spinal glial activation,[46] further supporting this tissue's involvement in WAD. Further, NSAID treatment delivered to the joint following both injury and pain development extinguished the pain.[47]

Of particular interest for WAD is the consistent finding that all of the pathologies listed above are induced in the *absence* of grossly observable evidence of a rupture or tear. Of even greater interest is the finding that higher tissue loading leading to complete and observable capsule rupture results in no prolonged afferent discharge and no persistent pain.[46] These physiological findings present a stark discourse with the biomechanical tenet that more severe loading is more detrimental. They also challenge the belief that lesions that are not clinically detectable cannot be relevant for patients' symptoms.

These observations provide pivotal basic-science evidence that cervical zygapophysial joints can be damaged by whiplash injury and can become sources of pain. They are also consistent with clinical evidence. Indeed, although the current medical imaging technologies do not have sufficient resolution to detect such subtle and small changes, the nociception that excessive capsular strain produces can be tested and detected in patients. Cervical medial branch blocks anaesthetize afferents from the zygapophysial joints.[48] If a patient has pain from some other source, such blocks should not relieve their pain. But a patient with pain stemming from a particular joint should be relieved of his pain if the nerves from that joint are anaesthetized. Crucial for the validity of such blocks is that they must be controlled, in order to reduce false-positive responses.[49]

Studies using double-blind controlled medial branch blocks found that the prevalence of pain stemming from one or more zygapophysial joints was 60% (95% confidence interval (CI) 46–73%) and 54% (95% CI 40–68%) amongst patients with chronic neck pain after whiplash; 27% (95% CI 18–36%) of consecutive patients with neck pain and/or headache after whiplash had pain stemming from the joint C2-3.[50–52] The segmental location of symptomatic joints is consistent with the location predicted by biomechanical studies: joints at C5-6 or C6-7 and at C2-3 are most commonly affected.[13,53,54]

Once diagnosed, a treatment for zygapophysial joint pain is available. A placebo-controlled trial[55] and several observational studies with long-term follow-up[56–58] have shown that percutaneous radiofrequency neurotomy can abolish chronic neck pain stemming from the zygapophysial joints in approximately 70% of treated patients.

ANTERIOR LONGITUDINAL LIGAMENTS AND DISCS

Tears of the anterior longitudinal ligament and rim lesions of the anterior anulus fibrosus have been produced in cadavers subjected to whiplash injuries[3] and observed in post-mortem studies.[1,33] During whiplash, strains in the anulus fibrosus of lower cervical discs can exceed physiologic limits.[7,59] These observations provide a pathologic basis for tears of the anterior disc or the anterior longitudinal ligament being a source of nociception after whiplash injury. Theoretically, lesions of these anterior structures could evoke the same physiological responses that have been demonstrated for the cervical zygapophysial joints. However, this model has not yet been explored outside the cadaver. Nor has discogenic pain after whiplash injury been explored clinically. At present, there are no imaging techniques by which noxious strains of the anterior disc can be demonstrated in vivo. Provocation discography might be used to test for cervical discogenic pain, but its validity for detecting symptomatic tears has not been established. Appropriate techniques might be developed and applied if laboratory studies, in due course, provide convincing evidence that anterior lesions produce nociception in experimental animals.

DORSAL ROOT GANGLION

There is the potential for trauma to the nerve roots and dorsal root ganglion in the neck. Unlike studies of the spinal ligaments, neural impingement is challenging to investigate experimentally. In fact, cadaveric study requires measuring the space in the neural foramen and using that as a proxy for tissue injury.[60] While that cadaveric study suggests a potential mechanism by which nerve root impingement may occur, no study has addressed the specific relationship between decreased foraminal space and the nociceptive physiological responses.

Notwithstanding direct impingement, the cervical nerve roots and dorsal root ganglia are at risk for injury due to rapid changes in the canal pressure that can be established during rapid head and neck motions. Pressure gradients from blood flow resistance have been hypothesized to be generated in the central nervous system during rapid spinal motions, as can occur during whiplash.[61,62] Although the vasculature surrounding the vertebral column regulates blood volume to accommodate any changes in spinal canal size, during rapid head/neck motions, resistance to blood flow can generate pressure gradients both inside and outside of the spinal canal.[18,61–63] These gradients have been shown to induce plasma membrane breakdown of spinal ganglia nerve cells in an in-vivo porcine model of rapid head-neck extension.[18,61,63]

Although suggesting a potential mode of injury to the cell bodies of the neurons, that collection of work provided no direct measure of pain and was not able to explain other types of painful injuries to the nerve root and/or the dorsal root ganglia. Nonetheless, it offers a potential mechanism by which neck, upper limb and/or shoulder girdle pain can result from nerve root injuries and trauma in the neck.

VERTEBRAL ARTERY

A recent retrospective analysis of 500 whiplash patients indicated that the incidence of cervical arterial dissections in this group was significantly higher than in the general population (1.6 vs. 0.0041%).[64] The onset of cerebrovascular symptoms may occur 4 to 12 months following the automobile collision. Altered blood flow rates in vertebral arteries of whiplash patients have been associated with chronic symptoms.[65]

Vertebral artery injury may originate from an intimal tear, most commonly at C1-2, which is the primary site of cervical axial rotation.[66–68] Coupled cervical spine extension and axial rotation beyond the physiologic limit has been hypothesized to cause vertebral artery injury.[66] This hypothesis is supported by biomechanical research,[16] which indicates that elongation-induced vertebral artery injury may occur due to non-physiologic coupled neck motions during an automobile collision. Coupled neck motions may occur due to an offset collision configuration and/or a rotated head posture at the time of the collision. Transient vascular compromise may be due to pinching of the vessel along a turn in its circuitous course, while a tear in the intimal layer may originate due to overstretching of the artery during the collision-exposure.

While some evidence of this tissue's injury mechanism has been demonstrated in the cadaver, no further exploration of this lesion has been undertaken. There is no validated diagnostic tool available to identify arterial dissections caused by whiplash, and these may be difficult to differentiate from those of the general population.

MUSCLES

Pain perceived at regions corresponding to muscles is common in WAD. Direct injury to muscles can occur from the imposed lengthening during reflex neck muscle activation in response to a crash. Biomechanically, muscle fascicle strains of 7% in the sternocleidomastoid muscle and 21% in the semispinalis capitis muscle have been predicted from human subject and modeling studies,[4,69] and these strains are larger than those shown to cause muscle injury.[70,71] Clinically, elevated levels of serum creatine kinase, a marker of muscle injury, have been recorded 24 hours, but not 48 hours, after whiplash injury in patients.[72] Since pain in these patients lasted more than 3 months, these data suggest that lesions to the muscles following a whiplash exposure may be related to the acute rather than chronic phase of whiplash injury.

Some neuromuscular abnormalities of the cervical spine observed in whiplash patients, including repositioning error[73,74] and altered range of motion,[75,76] might also originate from injuries to cervical zygapophysial joint capsules, ligaments, or anular fibers.[77] Animal models have demonstrated that stimulation of spinal ligaments initiated spinal muscle activity.[78] Abnormal signals from mechanoreceptors of injured capsules, ligaments, or anular fibers may cause corrupted neck muscle response patterns and hinder proper neck proprioception of whiplash patients.[77] The neuromuscular control system may stiffen the injured neck to prevent further injuries, thus reducing active neck motion and causing painful muscle spasm. Direct insertion of the multifidus muscles onto the facet capsular ligaments of C4 through C7 may aggravate the lesion of an already injured capsule during otherwise normal head and neck movements.[79,80] Also, reflex activation of the multifidus muscles during the crash may pull on the facet joint capsule and contribute to its initial insult.[81]

So far, no research has produced clinical evidence for a role of the muscles in the determinations of symptoms in WAD. It is largely recognized that the muscles can be areas of referred pain, the primary nociceptive focus being in another structure of the neck.[82] To date, there is no validated diagnostic tool to identify muscles as the primary source of nociception.

CLINICAL CONTEXT

LESION

The demonstration of tissue damage refutes the proposition that damage cannot occur as a result of whiplash injury. Unfortunately, many of the candidate lesions demonstrated in the cadaver or animal models cannot be identified by clinically available diagnostic modalities. Plain radiography cannot detect tears in capsules or discs;[1,3] and it lacks sensitivity for small fractures.[1] Small fractures may be detected by CT scanning, but concerted studies, using high-resolution CT, have not been undertaken in patients with WAD to determine the prevalence of fractures in this population. In human cadavers undergoing rear-end impacts, CT was unable to reliably detect partial ruptures of the ligamentum flavum, anulus fibrosus, anterior longitudinal ligament, or capsular ligaments.[3] Conventional magnetic resonance imaging has not revealed lesions in patients with WAD,[83,84] but this failure may be due to limitations in the resolution of conventional devices and the imaging sequences used. The prospect remains that 3 Tesla devices, or their successors, might provide greater resolution to reveal currently elusive, but still clinically relevant lesions.

Zygapophysial joint pain is the one entity predicted by biomechanical studies that has been fully validated through animal studies, for which there is a valid diagnostic test, and for which there is a proven treatment that can abolish pain. Other candidate lesions have the potential to undergo similar translation from biomechanics to clinical practice, and become recognized as a patho-anatomic basis for WAD; but this process awaits the development, application, and validation of appropriate diagnostic and therapeutic techniques.

OTHER FACTORS

The severity of pain reported, and the disability that ensues is not exclusively a product of the tissue damage. Additional factors apply, such as the psychology and social context of the patient,[85,86] whether or not they are believed,[87] how compensation systems treat them,[88] and central neuroplastic changes leading to hyperalgesia and allodynia.[89]

Animal and human studies indicate that stress exposure may influence neurosensory processing.[90,91] Based on this research, it can be hypothesized that some lesions may produce chronic pain only in individuals with a neurobiological “environment” vulnerable to sensitization. This hypothesis needs to be tested by future research. Animal studies that induce standardized lesions within different neurobiological milieus may provide new information about the interaction between lesion and environment in the development of persistent pain. Large clinical cohort studies examining genetic factors associated with whiplash development may also provide new mechanistic insights: if a genetic factor influencing the function of a particular biologic pathway is associated with WAD outcomes, this would provide evidence that the biologic pathway contributes to chronic pain development.

A challenging hypothesis is that a lesion is not necessary for persistence of symptoms. According to this hypothesis, in some patients the initial lesion may play only a transient initiating role, and instead the neurobiological environment that facilitates sensitization of nociceptive pathways or the psychosocial context may be the dominant factors determining symptom perpetuation. Unfortunately, for many patients with persistent neck pain following motor vehicle collision, no specific lesion driving symptom persistence can be identified using currently available technology. In this setting, opinions differ regarding the proportion of patients in whom an undetectable persistent lesion is present and driving ongoing symptoms. As engineers, basic scientists and clinicians continue to investigate the challenging problem of whiplash prevention, diagnosis and treatment, advances in all of these areas are needed to more completely address this issue. Fortunately, the current landscape includes a growing number of knowledgeable whiplash researchers and practitioners, who are well-past the era when the pain and suffering of whiplash patients was discounted and dismissed. The suffering is real; the search for the causes must continue.

KEY POINTS

1. There is evidence supporting a lesion-based model in whiplash associated disorders (WAD).

2. Zygapophysial joint pain is the one entity predicted by biomechanical studies, validated through animal studies, and for which there is both a valid diagnostic test and a proven treatment.
3. Other candidate lesions have the potential to undergo similar translation from biomechanics to clinical practice, but the evidence is not yet available.
4. The proportion of WAD patients in whom a persistent lesion is the major determinant of ongoing symptoms is unknown; psychosocial factors, stress reactions and generalized hyperalgesia have also been shown to predict WAD outcomes.

Acknowledgments

Funding:

P.C. Ivancic: Centers for Disease Control and Prevention (Grant 5R01CE001257); S. McLean: National Institutes of Health/National Institute of Arthritis, Musculoskeletal and Skin Diseases (AR056328); G.P. Siegmund: Natural Sciences and Engineer Research Council of Canada; B. Winkelstein: National Institutes of Health/National Institute of Arthritis, Musculoskeletal and Skin Diseases (#AR056288), the National Science Foundation (Grant no. 0547451) and the Catharine D. Sharpe Foundation.

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Table 1

Current whiplash injury models and their development state.

Development State	Zygapophysial joint	Dorsal root ganglion	Muscle	Vertebral artery	Spinal ligaments	Disc rim lesion
Theoretical Model	✓	✓	✓	✓	✓	✓
Cadaver/Volunteer						
Injury demonstrated	✓	✖	✓	✓	✓	✓
Animal Model						
Injury produced	✓	✓	✓	✖	✖	✖
Nociception produced	✓	✖	✓	✖	✖	✖
Patient						
Valid diagnosis	✓	✖	✖	✖	✖	✖
Effective treatment	✓	✖	✖	✖	✖	✖

✓ developed; ✖ not developed; NA: not applicable.