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Professional issue

Content not quantity is a better measure of muscle degeneration in whiplash

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ABSTRACT

Whiplash associated disorder (WAD) represents an enormous economic, social and personal burden. Five out of 10 people with WAD never fully recover and up to 25% continue to have moderate to severe pain-related disability. Unfortunately, clear and definitive reasons as to why half of individuals with WAD recover uneventfully and the other half do not, remain elusive. Identifying the factors that can reliably predict outcome holds considerable importance for not only WAD, but arguably for other acute musculoskeletal traumas. The precise pathology present in WAD has been controversial and often biased by outdated models. Fortunately, a combination of new measurement technology that illuminates pain processing, physical and social functioning and post-traumatic stress responses (and possibly markers of altered muscle size/shape/physiology) is providing a clearer picture of the multisystem pathophysiology in individuals with persistent WAD. The aim of this professional issues paper is to illuminate the clinical and research communities with regards to the growing body of knowledge for determining the trajectory of a patient with whiplash.

1. Introduction

Optimistic expectations of the Western World might lead members of modern society to believe that whiplash injuries from a motor vehicle collision (MVC) are unlikely to produce chronic pain related disability, raising questions as to whether it reasonable to think a simple, often low-speed (<10–15 mph), rear-end collision can cause injury? Contrary to such optimistic expectations, third party insurance (TPI) claims related to whiplash in the United Kingdom (UK), for example, have risen by 40% since 2006 (Actuaries, 2012). In 2011 the increase in TPI claims led to a £440 m increase in costs to UK insurers, resulting in a total cost of £2 billion (Actuaries, 2012). These emerging patterns have led many to question the validity of persistent whiplash related pain and disability. Recent UK government bills have reinforced the urgency of understanding the broad context of whiplash:

> "It is difficult to diagnose whiplash injuries objectively and this has deterred insurers from defending claims in court. We recommend that the bar to receiving compensation in whiplash cases should be raised. If the number of whiplash claims does not fall significantly as a result there would, in our view, be a strong case to consider primary legislation to require objective evidence of a whiplash injury…before compensation was paid" (House of Commons Transport Committee, 2011).

The Association of British Insurers (2012) opines that injury is virtually impossible to disprove, making whiplash the 'fraud' of choice for those looking to make away with easy money through illicit compensation schemes. Although there is an obvious and growing concern of a compensation culture related to whiplash, it is not clear that a relationship between compensation-related factors and health truly exists (Spearing and Connelly, 2011). Whilst fraud may exist, clinical research suggests that up to 50% of patients will never fully recover from a whiplash injury following a MVC (Carroll et al., 2008). Such data make it difficult to readily refute an injury model for Whiplash associated disorder (WAD). At the core of this complex and wide-reaching matter is a simple question: does injury following MVC exist?

To answer this question, clear, consistent and accurate measures of injury are required. Unfortunately, measuring whiplash injury is no easy feat. Meaningful identification of salient pathology with existing imaging technologies is not readily available (Elliott et al.,

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2009a, 2009b; Sterling et al., 2011). There are however several aetiological, physiological and psychological processes that would appear to play a role in the initiation and maintenance of long-term symptoms following whiplash trauma (Sterling et al., 2011). The relationships and interactions between these processes are not totally clear but it is imperative that future research elucidates the mechanisms underlying these processes in order to provide a foundation for more informed assessment and management strategies. Given the multi-factorial, multi-stakeholder associations of whiplash, the authors propose that it is absolutely critical that accurate and quantifiable measures of injury – and the response to the injurious event – be explored and developed.

2. Why is the pathology missed?

Although controversial, current evidence suggests the presence of a peripheral lesion in some individuals following whiplash (Curatolo et al., 2011). There also exists evidence that a peripheral lesion may not be required for the genesis (and maintenance) of clinical signs/symptoms (Sterling et al., 2011). Further complicating the issue is the widely accepted position that radiological findings are inconsistently associated with poor recovery (Pettersson et al., 1994, 1997; Borchgrevink et al., 1997; Pfirrmann et al., 2001; Myran et al., 2008; Matsumoto et al., 2010; Myran et al., 2011; Ulbrich et al., 2012). In contrast, a recent set of investigations into the degeneration of muscular tissues in whiplash provides preliminary evidence to suggest otherwise (Elliott et al., 2006, 2008a, 2008b, 2009a, 2010, 2011; Elliott, 2011).

Muscle fatty infiltrates on magnetic resonance imaging (MRI) develop soon after the whiplash event (between 4-weeks and 3-months), but only in those with higher initial pain levels and a subsequent post-traumatic stress response (PTSD) (Elliott et al., 2011). While the genesis of such muscle changes and their ultimate influence on recovery remains largely unknown, the early presence of structural muscle degeneration in tandem with well-established physical and psychological factors and their role in recovery (or non-recovery) from whiplash injury should not be under-estimated (Elliott, 2011; Sterling et al., 2011, 2012).

3. Why does this matter?

As stated, up to 50% of people who experience a MVC will never fully recover (Carroll et al., 2008), and approximately 25% will remain moderately to severely disabled in the long-term (Sterling et al., 2003a, 2003b, 2003c, 2005, 2006; Sterling, 2004; Carroll et al., 2008; Walton et al., 2009). The early (4 weeks post-injury) presence of sensory and motor deficits as well as psychological distress (PTSD) in the 25% with moderate to severe pain and disability is strongly associated with poor functional recovery in the long-term (Sterling et al., 2006).

Despite this available evidence, the prevailing media-driven opinion in the UK (and certainly other western cultures) remains that whiplash is a fraudulent 'crash for cash' condition. Complimentary to such assertions, some authors of recent peer-reviewed works using serial MRI measures of muscle degeneration (Matsumoto et al., 2012; Ulbrich et al., 2012) have appeared to excuse the available literature in this area and as such, demonstrate a lack of current understanding of the neurophysiological and psychological processes associated with the transition from acute to chronic pain. Failing to acknowledge the available evidence could result in an ongoing worldwide public mind-set that *people claiming whiplash injuries should not be entitled to compensation since there is no objective evidence that they have suffered injury.*

4. Example of 'outdated' muscle imaging in whiplash

First, the authors wish to commend Matsumoto and colleagues on their work (Matsumoto et al., 2012). Completing a 10-year follow-up of subjects with whiplash injury secondary to a MVC is not an easy endeavor. However, their conclusion that whiplash injury is not associated with symptomatic atrophy of the posterior cervical muscles in the long term is tenuous and not fully supported by their findings. Whilst Matsumoto et al. (2012) acknowledged the limitations of small sample size, they have omitted a plethora of available evidence (from 2003 on) highlighting risk factors for poor functional recovery following whiplash injury. Such evidence has greatly increased existing knowledge regarding the complex clinical presentation of patients that are at risk for transitioning from acute to chronic pain. Despite this available evidence, Matsumoto et al. (2012) instead performed a binomial transformation of subjective self-report data on neck pain, shoulder stiffness, headache, arm pain and/or numbness. In short, there was no attempt (nor mention of need) to categorize these patients with respect to varying levels of pain and disability.

Second, the MRI measure of muscle cross-sectional area (CSA, which is really a volume) and comparisons between Gradient Echo (GRE) Imaging (initial set of scans) with T2-weighted scans (10 year follow-up) detailed in the Matsumoto et al. study (2012) is not consistent with previous studies using anatomical T1-weighted scans for measuring neck muscle morphometry (Elliott et al., 2008a). As suggested, a fat suppressed acquisition (and/or an inversion sequence, such as a Short T1 Inversion Recovery (STIR)) is possible, but the T1 of fat has to be assumed, which may vary depending on the evolution of fat infiltration (Bydder et al., 1985).

Third, the measures of CSA should (going forward) be accurately categorized as a 3D volume of the entire muscle as 3D acquisition methods have evolved and are not as sensitive to the radio frequency slice profile as is 2D imaging. As such, the reported 'CSA' measures in this study (and admittedly others – (Elliott et al., 2008a)) may have partial volumes. Another issue remains the lack of reporting on how the slices were aligned in plane. Not doing so could create a discrepancy depending how the angle through each muscle was performed. Using some standard reference object or tissue that is not expected to change over time could control for this. Perhaps the most crucial issue is the lack of consideration of changes in muscle composition. Fig. 2 of the Matsumoto et al.

Table 1
Standardized clinical self-report outcome measures that should be used in whiplash.

Clinical self-report measures
Neck Disability Index (NDI)
The NDI is a 10-item validated questionnaire (Vernon and Mior, 1991) that has been widely used in studies of whiplash (Sterling et al., 2005, 2006; Elliott et al., 2006; Elliott et al., 2010; Sterling et al., 2012) and can be scored as a percentage (x/100). Higher scores equal more pain and disability.
Impact Events Scale (IES)
The IES (Horowitz et al., 1979) is a 15-item questionnaire measuring present stress related to a particular event. The IES has been validated in studies investigating emotional responses to acute trauma (Karlehagen et al., 1993; Sterling et al., 2003b) and shown to be predictive of poor outcome in the long-term following whiplash (Sterling et al., 2006; Sterling et al., 2012).
Tampa Scale of Kinesophobia (TSK)
The TSK is a reliable and valid 17-item self-report measure of fear of re-injury due to movement (kinesophobia) (Kori et al., 1990). Clinicians should feel confident in using the TSK-11 with people with neck pain, especially of traumatic origin and longer duration (>6 months) (Walton and Elliott, 2013)
Cold pain thresholds and pain intensity ratings
A pain intensity rating of >5 provides for a positive likelihood ratio of 8.44, suggesting that if this value is reported, clinicians could be suspicious of the presence of cold hyperalgesia (Maxwell and Sterling, 2012)

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(2012) manuscript suggests there are no temporal changes in total CSA, yet the available figure clearly shows a change in muscle composition. The reader must look at the tissue composition (content) not just atrophy (quantity) to understand the dynamic changes of WAD.

To quote the letter from Woodward (2011) in response to the 2010 study involving the same cohort (Matsumoto et al., 2010)… The simpler conclusion from this study is that persons who have neck pain today are more likely to have neck pain in 10 years' time than those persons who do not have neck pain today—an unsurprising observation. The reader cannot (and should not) draw definitive conclusions from this study regarding muscle changes (or lack thereof) and their influence on long-term symptoms following whiplash. The inadequate sample size, questionable MRI methodology for measuring cervical spine muscle morphometry and lack of observations for known risk factors of poor recovery following whiplash question the credibility of the findings.

Table 2
A sample of studies supporting the presence of central nervous system hyperexcitability in whiplash-associated disorders (WAD) – *adapted from* Sterling and Kenardy (2008).

Reference	Study cohort	Findings
(Sheather-Reid and Cohen, 1998)	Chronic neck pain and WAD	Lowered pain threshold to electrical stimulation of the neck
(Koelbaek-Johansen et al., 1999)	Chronic WAD	Widespread pain responses following injection of hypertonic saline
(Curatolo et al., 2001)	Chronic WAD	Lowered pain thresholds for electrical stimulation to the neck and lower limbs
(Sterner et al., 2001)	Chronic WAD	Sensory disturbance in trigeminal distribution
(Ide et al., 2001)	Chronic WAD	Mechanosensitivity to brachial plexus provocation manoeuvres
(Sterling et al., 2002a)	Chronic WAD	Lowered pressure pain thresholds throughout body
(Sterling et al., 2002b)	Chronic WAD	Hypersensitive responses to brachial plexus provocation test
(Moog et al., 2002)	Chronic WAD	Pain on non-noxious stimulation (vibration). Hyperalgesia to heat and cold stimuli
(Sterling et al., 2003c, 2005, 2006)	Acute to Chronic WAD	Cold hyperalgesia, sympathetic disturbances predictive of poor functional outcome
(Banic et al., 2004)	Chronic WAD	Decreased threshold for activation of nociceptive flexor withdrawal
(Scott et al., 2005)	Chronic WAD and idiopathic neck pain	Mechanical and thermal hyperalgesia – present in chronic WAD but not idiopathic neck pain
(Kasch et al., 2005)	Acute to Chronic WAD	Reduced cold pressor pain tolerance associated with poor recovery
(Sterling, 2010)	Acute to Chronic WAD	Lowered nociceptive flexor withdrawal response
(Maxwell and Sterling, 2012)	Chronic WAD	A pain intensity rating of >5 gave a positive likelihood ratio of 8.44, suggesting that if this value is reported, clinicians could be suspicious of the presence of cold hyperalgesia
(Elliott et al., 2009a)	Chronic WAD	Combined factors of sensory, physical, kinesthetic, and psychological features all contributed to a small extent in explaining the varying levels of fatty infiltrate in neck extensor muscles, with reduced cold pain thresholds having the most influence
(Walton et al., 2011)	Acute to Sub-Acute WAD	Lower pressure pain thresholds at the lower limbs
(Daenen et al., 2013)	Chronic WAD	Impaired conditioned pain modulation

5. A way forward

The need to conduct larger scaled patient-centered quantitative studies on whiplash injuries across cultures is urgent. The importance of this need reaches beyond the evidence-base of the medical and rehabilitative professions and impacts forcibly on political, legal and actuarial dimensions of the whiplash phenomena. The potential scientific identity of a 'whiplash lesion' will change the face of how whiplash is thought of by all stakeholders. However, it would be mistaken to think that this would reduce the phenomena to a purely biological concern. This basic science is firmly and comfortably contextualized by the psychosocial dimensions which are becoming increasingly better understood. In light of this complexity and the inherent heterogeneity of the whiplash condition, standardized reporting of whiplash injuries is warranted on an international scale. This information should include serial measures of pain-related disability, physical and social functioning, post-traumatic stress, and pain processing (See Tables 1 and 2). Finally, specialized imaging in high-risk patient populations should be considered (See Appendix). Let's hope all stakeholders involved in the management of the patient with whiplash injury can work together to accurately collect and interpret imaging data to determine the prognostic and objective value of said muscle changes…not only in whiplash but also other systemic and neuromusculoskeletal conditions (Reeder et al., 2012).

Appendix

The demonstration of neck muscle fatty infiltrates on T1-weighted imaging in acute (Elliott et al., 2011) and chronic whiplash (Elliott et al., 2006, 2009a, 2010) is interesting. Such findings were not featured in those with chronic non-traumatic neck pain (Elliott et al., 2008b) and it has been postulated that these muscle changes represent one neurophysiologic basis for the transition to chronic pain in this population. While the mechanisms underlying their temporal development and contribution towards the transition remain unclear, it is possible that newer MRI techniques (3D Fat/Water Separation and Proton-Density Fat Fraction) (Reeder et al., 2012) could help quantify earlier physiologic changes at the level of the muscle cell that may precede observable (and potentially irreversible) muscle changes on T1-weighted sequences at 4-weeks to 3-months post-injury. An earlier detection of such changes could prove crucial for identifying the early presence of altered muscle physiology and its potential role in the development of WAD-related pain and disability.

Fat/Water Separation

Several approaches are possible to measure the water and fat composition of various tissues on MRI. One such measure is the Dixon method (Dixon, 1984), where data is collected at echo times when water and fat are in-phase and when water and fat are out of phase. The data can then be combined to generate a fat and water image. This method works well when there are no field inhomogeneities, which is often not the case. Current methods collect multiple echo time data to improve the estimation of the fat and water images and these have been applied successfully in the liver and musculoskeletal system using an iterative least squares solution (e.g. IDEAL) (Reeder et al., 2004, 2005). The method our research group at Northwestern University currently uses in the

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study of whiplash subjects collects 8 different echo times sufficiently spaced on the unit circle to provide adequate phase information for the variable projection algorithm (VARPRO[1]), generating a globally optimal solution for the water/fat decomposition (Hernando et al., 2008).

A 3D − 230 mm FOV axial gradient echo acquisition can be used to collect the data required for the VARPRO algorithm. The sequence parameters are TR = 23.81 ms, 8 echo times with a spacing of 1.78 ms starting at 1.36 ms. A single slab is placed over the cervical spine with 36 partitions and a partition thickness of 3 mm and slab oversampling of 22% to prevent aliasing in the 3D direction. The in-plane resolution is 1.4 mm using a rectangular field of view of 75% resulting in an acquisition time of 2:06 min.

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