Editorial

Whiplash and Fibromyalgia: An Ever-Widening Gap

Although recognized as a real symptom complex for more than a century, the cause of fibromyalgia (FM) remains elusive. A possible link with a triggering event has been repeatedly suggested and is mostly based on patient report and retrospective studies[1-3]. Opinions regarding an association between trauma such as whiplash injury (WLI) and subsequent FM are emotionally charged and highly polarized. A possible causal link between trauma and FM would carry important societal costs regarding issues of attribution, blame, and compensation. For this reason, any statement regarding an association between a precipitating event and FM must be supported by sound scientific evidence. To date, the most convincing link between WLI and FM was the report that 21.6% of patients who had sustained a WLI and were attending an occupational clinic had developed FM in the year following injury[2].

In this issue of *The Journal*, Tishler and colleagues from Israel report the first prospective study examining the occurrence of FM in 153 subjects who sustained WLI in a motor vehicle accident (MVA)[4]. The control group comprised 48 injured subjects, also following an MVA, who required hospitalization. FM developed in only one patient with WLI and none of the controls during the year following injury. This low rate of progression to chronic pain occurred although participants had been informed that the intent of the study was to examine musculoskeletal consequences related to an accident. The authors are to be complimented on the early recruitment of subjects, which occurred within hours of the injury at the time of presentation to an emergency room, and for the size of this prospective study. It should be noted, however, that about 60% of study patients and controls were males and that the study was conducted from a single study site. These 2 factors could have influenced the results. This study is nevertheless important in being the first to refute the association between WLI and FM.

Motor vehicle accidents are prevalent and frequent. Almost any impacting injury sustained in an MVA is associated with vigorous head movement relative to the torso. At one extreme, forceful neck movement may result in objective tissue injury to the spinal cord or bony structures, but more commonly, no such changes are identified. In the absence of objective measurable tissue injury, the concept of neck trauma resulting in regional pain, which may be prolonged, falls into the category of WLI[5]. The overall health related consequences of WLI remain controversial. It is almost 10 years since the editorial pages of this journal presented a lively debate regarding the very existence of this disorder[6]. Even today, our understanding of the pathophysiology of WLI is surprisingly limited. Excluding changes in the zygapophyseal joints, no other neck structures have been clearly identified as contributing to the pathological process underlining the symptoms of WLI[7]. In addition, the importance of psychological and psychosocial factors has been recognized in the progression to chronic WLI syndrome. Public awareness of the entity WLI may also be an important factor in perpetuating both the concept of injury as well as the continuation of symptoms.

Similar to whiplash injury, the challenge of FM is compounded by a limited understanding of pathogenesis and causation. Sixteen years after the publication of diagnostic criteria, FM remains a clinical entity requiring the practice of the art of medicine. Altered nervous system nociceptive mechanisms, rather than abnormalities in peripheral musculoskeletal structures, are currently believed to play a role in FM. Candidate mechanisms to explain the pathogenesis of FM include hypersensitivity to nociceptive input, defective inhibitory mechanisms, and hypervigilance, which may be modulated by psychogenic factors[8-11]. Familial predisposition to pain hypersensitivity has also been proposed[12]. Objective abnormalities have been demonstrated in patients with FM in multiple neurophysiological domains, adding credibility to the neurologically focused hypothesis. These include exaggerated stress ACTH release, elevated levels of

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substance P in the cerebrospinal fluid, and increased neural activity in pain-related brain areas associated with experimental pain[13-15]. It is therefore likely that multiple mechanisms operate in an individual patient, accounting for variable symptom presentation.

Continued chronic pain is likely related to neuroplastic changes occurring within the central nervous system. Animal studies have demonstrated neuronal hyperexcitability resulting in an exaggerated pain response following peripheral nerve injuries[16]. Pain may also be persistent in the absence of ongoing nociceptive stimuli[16]. Similarities in neurophysiological mechanisms may be used to explain ongoing pain in both FM and WLI. Neuronal hyperexcitability has been demonstrated by the presence of abnormal wind-up in FM and exaggerated muscular hyperalgesia in WLI[8,17]. Objective documentation of spinal cord hypersensitivity using the nociceptive withdrawal reflex provides compelling evidence of neurophysiologic similarity between these 2 conditions[18]. Other mechanistic similarities between both conditions include sympathetic hyperactivity and elevation of inflammatory cytokines. These findings support the hypothesis of neuroplastic changes as a factor in perpetuation of pain and add credence to the concept of neuronal excitability causing an exaggerated pain response in the absence of ongoing measurable tissue damage.

We are now left in a quandary. Science is progressively unravelling the mechanisms of pain and there is increasing evidence that trauma may lead to persistent pain in some situations. Trauma as an initiating factor in FM has been supported by subjective information and seems plausible. How then can the negative findings of the current study be explained? First, all evidence to date linking WLI and FM is based on retrospective information. The weakness of retrospective study for a condition characterized by subjective complaint is reliance upon patient recall. Second, it is a characteristic of human nature to attempt to explain causation in illness. Patients have an awareness of causative factors in other illnesses such as diabetes mellitus, heart disease, and cancers. Third, if various chronic pain syndromes shared a common mechanism, then it could be expected that individual pain complaints might lose their location specificity and evolve over time. This hypothesis was not upheld, however, over a 25-year followup study of patients followed in general practice. Distinct patterns of tracking of previous regional pain occurred, with neck pain associating with previous headaches and widespread pain associating with mental disorder[19]. The conclusions of this extensive study are that regional pain syndromes tend to remain distinct, rather than merging into other pain disorders. Finally, the pain mechanisms mentioned above are not specific to either FM or WLI, and have been described in other chronic pain conditions. For example, the sympathetic system plays a major role in complex regional pain syndrome, and central hypersensitivity has been described in other chronic pain conditions such as phantom pain and migraine headache.

Injury in the absence of identifiable structural change is known to occur. Concussion with subsequent cognitive change, but without structural brain damage, is a fully accepted entity. Therefore, the concept of "spinal cord concussion," neurophysiologically understood as neuronal hyperexcitability, would provide an attractive model to explain chronic pain after neck injury in some patients. Taking all these factors into account, it is important to recognize the need to shift from a disease-based to a mechanism-based approach in patients with chronic pain. Different clinical conditions may harbor similar pathophysiological mechanisms and vice versa[20]. Therefore, although patients with FM and WLI could present similar clinical symptoms that are indicative of common mechanisms (e.g., allodynia), these symptoms could differ in etiology and initiating pathophysiology.

In this setting of delicate nervous system balance, a triggering factor would be an attractive hypothesis to explain onset of illness. With regard to a traumatic causation in FM, pathophysiological explanations are plausible, and retrospective evidence has suggested a link between a precipitating event and persistent widespread pain. However, evidence-based medicine requires more definitive proof. Physiologic similarities and retrospective studies should not be used as cause and effect, but should rather complement prospective study. We now have a single, but large and well designed prospective study with a surprising conclusion. Taking into account all the above factors, Tishler's conclusion should be upheld[4]. WLI should not be considered a clinically important risk factor for the development of FM at the present time.

The results of this study have significant clinical, social, and medicolegal implications. The debate is, however, not completely settled for an association of a triggering event and the onset of FM, but requires further study in order to reach a final conclusion. Any definitive study will have to be large and prospective, and match the high standard set by Tishler and colleagues.

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