Whiplash and fibromyalgia: an ever-widening gap.

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*The Journal of Rheumatology* is a monthly international serial edited by Earl D. Silverman featuring research articles on clinical subjects from scientists working in rheumatology and related fields.
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 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...
in WLI8,17. Objective documentation of spinal cord hyper-
mal wind-up in FM and exaggerated muscular hyperalgesia
has been demonstrated by the presence of abnor-
going pain in both FM and WLI. Neuronal hyperex-
citability has been demonstrated by the presence of abnor-
mal wind-up in FM and exaggerated muscular hyperalgesia
in WLI8,17. Objective documentation of spinal cord hyper-
sensitivity using the nociceptive withdrawal reflex provides
compelling evidence of neurophysiologic similarity
between these 2 conditions18. Other mechanistic simili-
rtries between both conditions include sympathetic hyperac-
tivity and elevation of inflammatory cytokines. These find-
ings support the hypothesis of neuroplastic changes as a
factor in perpetuation of pain and add credence to the con-
cept of neuronal excitability causing an exaggerated pain
response in the absence of ongoing measurable tissue dam-
age.

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 sit-
uations. Trauma as an initiating factor in FM has been sup-
ported 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 retro-
spective 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 causa-
tion in illness. Patients have an awareness of causative fac-
tors in other illnesses such as diabetes mellitus, heart dis-
ease, 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 speci-
ficity 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 pre-
vious headaches and widespread pain associating with men-
tal disorder19. 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 con-
ditions. For example, the sympathetic system plays a major
role in complex regional pain syndrome, and central hyper-
sensitivity has been described in other chronic pain condi-
tions 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 con-
cussion,” 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 rec-
ognize the need to shift from a disease-based to a mecha-
nism-based approach in patients with chronic pain. Different
clinical conditions may harbor similar pathophysiological
mechanisms and vice versa20. 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 patho-
physiology.

In this setting of delicate nervous system balance, a trig-
kening factor would be an attractive hypothesis to explain
onset of illness. With regard to a traumatic causation in FM,
pathophysiologic explanations are plausible, and retro-
spective evidence has suggested a link between a precipitat-
ing event and persistent widespread pain. However, evi-
dence-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 conclu-
sion should be upheld4. 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.
REFERENCES


