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# Sex Differences in Musculoskeletal Pain

*Gary B. Rollman, Ph.D., and †Stefan Lautenbacher, Ph.D.

**Department of Psychology, University of Western Ontario, London, ON N6A 5C2, Canada; †Department of Psychiatry and Psychotherapy, University of Marburg, Marburg, Germany, and Department of Physiological Psychology, University of Bamberg, Bamberg, Germany*

**Abstract:**
Epidemiologic, clinical, and experimental evidence points to sex differences in musculoskeletal pain. Adult women more often have musculoskeletal problems than do men. Discrepant findings regarding the presence of such differences during childhood and adolescence continue. Biologic and psychosocial factors might account for these differences. The authors review evidence showing that mechanically induced pressure is more likely to show sex differences than other noxious stimuli and to discriminate between individuals suffering from musculoskeletal pain and matched controls. The authors suggest that a state of increased pain sensitivity, with a peripheral or central origin, predisposes individuals to chronic muscle pain conditions, and that there are sex differences in the operation of these mechanisms; women are vulnerable to the development and maintenance of musculoskeletal pain conditions.
**Key Words:** Musculoskeletal pain—Pain thresholds—Pressure—Risk factors—Sex differences

The title of this article really deals with two issues: (1) Is there a sex difference in the presentation of musculoskeletal pain and, (2) if so, how might we account for it? The answer to the first question is easier to find than the answer to the second question. Stated simply, the evidence suggests that a sex difference exists. In general, women report musculoskeletal pain more often than do men.

For example, Ruiz Moral et al.[1] examined patients younger than 50 years of age who attended a family medicine clinic in Cordoba, Spain. They identified two groups, one of which had widespread chronic musculoskeletal pain in three or more body sites for a duration of at least 2 years and a second group that also met the criteria of fatigue, stiffness, and 11 or more tender points, the presence of which is necessary to be diagnosed with fibromyalgia.[2] One hundred percent of the members in the first group were women, and 92% of the members in the second group were women.

Address correspondence to Dr. Gary B. Rollman, Department of Psychology, University of Western Ontario, London, ON N6A 5C2, Canada.

Consistent epidemiologic reports indicate that musculoskeletal pain is a major medical and economic problem. Pain and the associated disability is linked with a significant loss of productivity and substantial healthcare expenditures for women. With regard to the loss of productivity, Leijon et al.[3] observed that approximately 30% of all sick-leave days in Sweden were a result of neck/shoulder and low back pain and that absence because of sickness, and, in particular, musculoskeletal pain, is appreciably higher for women than for men. With regard to healthcare expenditures, Rekola et al.[4] found that nearly 40% of women in the 55–64-year-old age group seek medical attention for musculoskeletal problems, particularly neck and shoulder problems.

Reports of higher levels of pain in women are not limited to work settings. Unruh[5] noted that "women are more likely than men to experience a variety of recurrent pains, women report more severe levels of pain, more frequent pain and pain of longer duration than do men." Berkley[6] stated that, "for endogenous pains, women report more multiple pains in more body regions than men. With no obvious underlying rationale, some painful diseases are more prevalent among females, others among males and, for many diseases, symptoms differ between females and males." Von Korff et al.[7] found that women report a higher prevalence of acute pain and persistent pain than do men. These differences are particularly noteworthy for numerous forms of musculoskeletal pain, including fibromyalgia, temporomandibular disorders (TMD), and myofascial pain, even into old age.[8]

A random community sample of nearly 3,400 Canadians was screened for fibromyalgia.[9] Participants who met preliminary criteria were examined by a rheumatologist. One hundred patients with confirmed fibromyalgia were identified, 86 of whom were women. Correcting for sample characteristics, the authors estimated that fibromyalgia affects approximately 5% of adult women and 1.6% of adult men. Wolfe et al.[10] estimated a somewhat lower prevalence, but their ratio of female to male fibromyalgia patients (3.4% and 0.5%, respectively) was even greater. In fact, the incidence of fibromyalgia among men is so low that two recent articles[11,12] solely discussed the study of this uncommon syndrome. The findings suggest that musculoskeletal pain reports are markedly more common among women than among men.

There is debate regarding how early such sex differences appear. Guinsburg et al.[13] lanced the heels of neonates and observed facial expressions, cries, and bodily postures, and they found that female neonates expressed more facial features of pain during the puncture and 1 minute after the puncture than did their male counterparts, but male and female neonates did not differ for the other measures. The authors concluded that because differences in pain reactivity in neonates cannot be ascribed to sociocultural factors, female infants perceive the acute nociceptive stimulus as being more painful than male infants do or newborn girls show more facial expressivity.

Others have reported sex differences during childhood and adolescence. In a study involving 338 schoolchildren between the ages of 9 and 15 years, Buskila et al.[14] measured dolorimeter threshold for pressure tenderness at nine fibromyalgia tender points and four control points. Pain thresholds were significantly lower for the girls at the two types of sites. Nearly 9% of the girls met the criteria for having fibromyalgia in comparison with 4% of the boys.

Nevertheless, as Rollman et al.[15] noted, the data are contradictory. Meier et al.,[16] in an examination of children ranging in age from 6 to 17 years, observed no sex differences in heat or cold pain sensitivity, whereas others reported no differences in responses to venipuncture or heel prick. Similarly, Hogeweg et al.,[17] using a variable pressure dolorimeter at various body sites in a group of girls and boys between the ages of 6 to 17 years, found no sex difference for pressure pain thresholds. Pothmann[18] also did not find sex differences for a similar group that received pressure against the tip of the index finger. There are many interesting questions regarding the contributions of biologic and psychosocial factors to pain responsiveness in developing children.

**Physical and psychosocial stress as crucial factors for the understanding of sex differences in musculoskeletal pain**

Do physical risk factors account for all or part of these gender effects? A number of possible explanations have been offered,[19] including differential exposure to risks in the work environment, differences in muscle strength, work environments designed to male norms, or differences in the way in which injuries in men and women are evaluated, treated, or referred for rehabilitative services. Similarly, Fredriksson et al.[20] noted that neck, shoulder, and lower limb disorders are associated with heavy lifting, monotonous work tasks, static work postures, vibrations, repetitive jobs, and a high pace of work, and that women may be at greater risk for all these disorders. However, Fredriksson et al.[20] also pointed to psychosocial risk factors, such as low work content, low social support, high perceived workload, time pressure, low job control, perceived stress, and high psychological job demands.

In a 24-year longitudinal study performed by Nordander et al.,[21] psychosocial factors, such as monotony and high mental load at work, were associated with increased risk for neck and upper limb disorders in women (who had a prevalence rate approximately twice that of men), whereas more physical factors related to work were related to risk in men. The authors evaluated the physical and psychosocial factors in a large group of Swedish workers in a fish processing plant, and found that women with upper body musculoskeletal problems at nearly 3 times the rate as men, typically had jobs that involved repetition and awkward working postures. However, women reported a much poorer psychosocial work environment. They stated that "these two aspects of the work environment are so tightly entangled that it is not possible to estimate their separate impact on musculoskeletal disorders in this kind of work."[21]

Therefore, it is apparent that understanding the basis for these epidemiologic findings is much more difficult than showing their existence. Men and women differ in regard to body size and functional capacity and, perhaps, in factors such as mix of fast- and slow-twitch muscle fibers, cardiovascular endurance, and other physiologic variables.[22] Endocrine influences, including menstruation, oral contraceptive use, pregnancy, and hysterectomy, may increase the risk of musculoskeletal disorders.[23] The link between musculoskeletal pain and menstruation deserves more study[24]; certainly, the literature on temporomandibular disorders shows that the use of estrogen by postmenopausal women significantly increases their odds of having orofacial pain.[25–27]

Psychosocially, women may experience greater stress than men, both at and outside of the job setting, less control over the work process, fewer opportunities for advancement, and different implications for reporting musculoskeletal pain and seeking or accepting compensation. Hormonal events also have powerful psychologic consequences. One study of the relation between pain reports and menopause[28] found that one third of postmenopausal woman who required medical help presented with musculoskeletal pains, which the authors attributed to ineffective coping strategies. Waxman and Zatzkis,[29] observing that fibromyalgia patients had a significantly earlier menopause than did nonpatients, suggested that estrogen deficits may affect sleep and mood, causing emotional responses that are expressed as pain.

### Pressure pain as a test for sex differences in pain and for understanding the pathophysiology of musculoskeletal pain

Women have greater pain sensitivity than men in laboratory settings, but the effects are particularly striking when pressure pain is applied.[15,30] Because reviews of these sex differences are found elsewhere,[6,31–33] we will concentrate on demonstrating that the experimental use of noxious pressure is an especially sensitive test for analysis of the pathology of musculoskeletal pain and its underlying mechanisms.

There is abundant evidence that mechanical pressure is the most likely form of noxious input to show altered pain thresholds in musculoskeletal pain conditions. For example, responsiveness to experimental pain, which often is markedly increased in patients with fibromyalgia, is particularly noteworthy when pressure pain is used as the physical stressor.[34–36] Lautenbacher et al.[35] found that the effect sizes for differences between patients with fibromyalgia and pain-free volunteers were 1.53 for a tender point and 1.57 for a control point when pressure pain was applied. Effect sizes decreased to 0.65 and 0.84, respectively, for heat pain and to 0.22 and 0.91, respectively, for electrocutaneous pain. Although some of the differences between patients and controls for heat and electrocutaneous pain were significant, none reached the effect size obtained for pressure pain.

Similarly, patients with myofascial pain and temporomandibular disorder are exceptionally sensitive to pain when pressure pain is used for diagnostic purposes, especially within the region in which clinical pain is experienced most strongly.[37]

Consequently, the use of pressure pain seems to detect processes strongly linked to musculoskeletal pain more readily than the use of other methods of pain induction. This assumption is corroborated by the observation of Lautenbacher et al.[35] that a sizeable negative relation was found between the magnitude of concurrent pain in patients with fibromyalgia and the pain threshold for pressure, but not the threshold for heat or electrical current.

The question arises whether musculoskeletal pain reduces the pain threshold or whether a reduced pain threshold—because of a state of increased pain sensitivity of peripheral or central origin—leads to musculoskeletal pain. We are inclined to support the latter position. Musculoskeletal pain does not necessarily lead to a decrease in pressure pain threshold. Babenko et al.[38] induced muscle pain using various chemical agents without changing the local pressure pain thresholds. Similarly, Graven-Nielsen et al.[39,40] failed to decrease the local pressure pain thresholds reliably by inducing muscle pain via infusion of hypertonic saline. Rather, in that study, induced muscle pain increased the remote pressure pain thresholds, probably reflecting the phenomenon of "diffuse noxious inhibitory controls."[41] Accordingly, decreased pressure pain thresholds might indicate a generalized state of increased pain sensitivity that predisposes the individual to later symptoms of musculoskeletal pain.

Why does this state of increased pain sensitivity result in musculoskeletal pain and not in other forms of spontaneous pain? Perhaps this increased sensitivity is restricted to pain that originates from the stimulation of deep tissue. It is well-known that the pressure pain threshold reflects nociceptive sensitivity in superficial and deep tissue.[42,43] Thermal and electrical stimuli engage only more superficial nociceptors. This means that a diminished pressure pain threshold, in conjunction with relatively normal thresholds for heat and electrical current, might be particularly indicative of a state of increased risk of clinical deep tissue pain.

What might be the reasons for such a state of increased sensitivity for deep tissue pain? We can only speculate. Mense[44,45] suggested that the descending antinociceptive systems exert a more powerful influence on the input from muscle nociceptors than on that from skin nociceptors. Accordingly, a weakening of these antinociceptive systems should result in a lowering of pain thresholds for stimulation of muscles and in an increased likelihood of spontaneous muscle pain. Lautenbacher and Rollman[46] and Kosek and Hansson[47] found deficiencies in the pain inhibitory systems of fibromyalgia patients. Kosek and Hansson[47] showed a larger deficit of normal inhibition when they used pressure pain than when their phasic stimulus was heat pain.

This then leads to the question of whether there are sex differences in the operation of the central inhibitory mechanisms. Evidence is sparse. France and Suchowiecki[48] studied diffuse noxious inhibitory controls in male and female volunteers by measuring the $R_{III}$ nociception flexion reflex before, during, and after forearm ischemia. They found that women had lower thresholds for the reflex and reported greater pain during the ischemia but that no sex difference in the attenuation of the $R_{III}$ reflex by the tonic ischemia existed. Likewise, Lautenbacher, Prager, and Rollman (unpublished data), found that tonic heat to the thigh caused suppression of the pain evoked by phasic electrical current to the forearm, but no differences were found between men and women in this respect. It would be informative to conduct studies regarding diffuse noxious inhibitory controls involving phasic pressure stimuli to see whether there are sex-selective differences in the action of central modulatory systems that depend on the nature of the noxious stimulus.

In summary, pressure pain thresholds have been found to be diminished reliably in women (in comparison with men) and in individuals with musculoskeletal pain (in comparison with pain-free controls). We suggest that these decreases of pressure pain threshold are indicative of a sex-dependent state of increased sensitivity for deep tissue pain that may be the cause of musculoskeletal pain and make many women vulnerable to the development and maintenance of such pain conditions.

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