

## Fibromyalgia In Men

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### **Buskila D**

Genetics of chronic pain states. *Best Pract Res Clin Rheumatol* (2007 Jun) 21(3):535-47

Chronic pain states are common in the general population. Genetic factors can explain a significant amount of the variability in the perception of pain. Fibromyalgia syndrome (FMS) and related conditions are syndromes characterized by generalized pain sensitivity as well as a constellation of other symptoms. Family studies show a strong familial aggregation of FMS and related conditions, suggesting the importance of genetic factors in the development of these conditions. Recent evidence suggests a role for polymorphisms of genes in the serotonergic, dopaminergic and catecholaminergic systems in the pathogenesis of FMS and related conditions. Environmental factors may trigger the development of these disorders in genetically predisposed individuals. Future large well-designed studies are needed to further clarify the role of genetic factors in FMS and related conditions. The knowledge of these gene polymorphisms may help with better subgrouping of FMS patients and in designing a more specific pharmacologic treatment approach.

### **Buskila D, Neumann L**

Genetics of fibromyalgia. *Curr Pain Headache Rep* (2005 Oct) 9(5):313-5

The pathogenesis of fibromyalgia (FM) and related conditions is not entirely understood. Recent evidence suggests that these syndromes may share heritable pathophysiologic features. Familial studies suggest that genetic and familial factors may play a role in the etiopathogenesis of these conditions. There is evidence that polymorphisms of genes in the serotonergic and catecholaminergic systems are linked to the pathophysiology of FM and related conditions and are associated with personality traits. The precise role of genetic factors in the etiopathology of FM remains unknown, but it is likely that several genes are operating together to initiate this syndrome. Larger longitudinal studies are needed to better clarify the role of genetics in the development of FM.

**Buskila D, Neumann L, Alhoashle A, Abu-Shakra M**

Fibromyalgia syndrome in men. *Semin Arthritis Rheum* (2000 Aug) 30(1):47-51

**OBJECTIVE:** Fibromyalgia syndrome (FMS) is uncommon in men and data on its characteristics and severity are limited. The current study was undertaken to determine whether the clinical characteristics and the spectrum of this disorder are similar in men and women. **METHODS:** Forty men with FMS were matched with 40 women by age and educational level. All subjects were asked about the presence and severity (assessed by visual analog scale) of FMS symptoms; a count of 18 tender points was conducted by thumb palpation, and tenderness thresholds were measured by dolorimetry. Psychological status was assessed by the anxiety and depression subscales of the revised Arthritis Impact Measurement Scales. Quality of life was evaluated by two scales, QOL-16 and SF-36, and physical function was measured by the Fibromyalgia Impact Questionnaire. **RESULTS:** Men with FMS reported more severe symptoms than women, decreased physical function, and lower quality of life. Women had lower tender thresholds than men; however their mean point counts were similar. **CONCLUSION:** Although FMS is uncommon in men, its health outcome in our study population was worse than in women. Further studies in larger samples and in diverse ethnicultural populations are needed to confirm this observation.

**Chial HJ, Camilleri M**

Gender differences in irritable bowel syndrome. *J Genet Specif Med* (2002 May-Jun) 5(3):37-45

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder characterized by abdominal discomfort or pain associated with changes in stool frequency and/or stool form. It is the most common gastrointestinal disorder in both primary care and gastroenterology clinics. IBS is associated with high health care costs, disability, work absenteeism, and significant morbidity. In this article, we review the gender differences in epidemiology, diagnostic criteria, physiology, psychological features, and responses to therapy of IBS.

**Cohen H, Neumann L, Alhosshle A, Kotler M, Abu-Shakra M, Buskila D**

Abnormal sympathovagal balance in men with fibromyalgia. *J Rheumatol* (2001 Mar) 28(3):581-9

**OBJECTIVE:** It is possible that there are differences in clinical manifestations between men and women with fibromyalgia syndrome (FM), especially in autonomic dysfunction; we assessed the interaction between the sympathetic and parasympathetic systems in postural change in men with FM using power spectral analysis (PSA) of heart rate variability (HRV), and investigated the pathogenesis of the

orthostatic intolerance. **METHODS:** We studied 19 men with FM and 19 controls matched for age and sex. A high resolution electrocardiogram was obtained in supine and standing postures during complete rest. Spectral analysis of R-R intervals was done by the fast Fourier transform algorithm. **RESULTS:** PSA of HRV revealed that men with FM at rest are characterized by sympathetic hyperactivity and concomitantly reduced parasympathetic activity. During postural changes, male patients demonstrated an abnormal sympathovagal response. These results provide the physiological basis for the orthostatic intolerance in men with FM. **CONCLUSION:** This report of autonomic dysfunction in men with FM revealed an abnormal autonomic response to orthostatic stress. This abnormality may have implications regarding the symptoms of FM.

**Dannecker EA, Knoll V, Robinson ME**

Sex differences in muscle pain: self-care behaviors and effects on daily activities. *J Pain* (2008 Mar) 9(3):200-9

Women have a higher prevalence of fibromyalgia and myofascial pain than men, but sex differences in muscle pain are inconsistently detected. We examined sex differences in ratings and effects of recalled and experimentally-induced muscle pain. In study 1 (n = 188), participants completed a questionnaire about recalled muscle pain. In study 2 (n = 55), participants described muscle pain from an exercise stimulus across 3 days by telephone. Muscle pain ratings, self-care behaviors for muscle pain, and effects of muscle pain on activities were measured. No significant sex differences were found except that women tended to view exercise as more effective for decreasing muscle pain than men ( $F(1, 187) = 5.43, P = .02, \eta^2(2) = .03$ ), fewer women performed exercise for induced muscle pain than men, and women's activity interference was significantly higher than men's at the third day after exercise ( $F(2, 42) = 6.54, P = .01, \eta^2(2) = .14$ ). These findings support the absence of meaningful sex differences in muscle pain ratings. However, additional investigations are needed that consider the daily activities completed by people and the prevalence and incidence of performing a wide range of self-care behaviors for pain. **PERSPECTIVE:** These studies support that sex differences are not present in recalled and experimentally-induced muscle pain ratings. Therefore, we must be cautious about generalizing the musculoskeletal pain literature to muscle pain. Additional research is needed to interpret potential sex differences in self-care behaviors for muscle pain and activity interference from muscle pain.

**Garofalo JP, Lawler C, Robinson R, Morgan M, Kenworthy-Heinige T**

The role of mood states underlying sex differences in the perception and tolerance of pain. *Pain Pract* (2006 Sep) 6(3):186-96

While sex differences in pain reporting are frequently observed, the

reasons underlying these differences remain unclear. The present study examined sex differences in self-report and physiological measures of pain threshold and tolerance following the administration of two laboratory pain-induction tasks. The primary study aim centered on determining whether repeated exposure to such tasks would yield sex differences in terms of pain threshold and tolerance. In addition, it was hypothesized that if such differences did exist, negative mood states might account for changes in pain ratings, threshold, and/or tolerance in subsequent exposure to noxious stimuli. Recruited from a convenience sample, 66 participants (44 female and 22 male) were exposed to both thermal and cold noxious stimuli at three separate times, while psychophysiological and self-report data were collected. Because women outnumbered men 2:1, Fisher z transformations were performed to determine whether the observed associations between mood states and pain ratings differed. We found stronger associations between fatigue and thermal-heat pain ratings for men at their first and third exposure to the pain task compared to women ( $z = 2.11, P < 0.05$ ;  $z = 3.14, P < 0.001$ , respectively). Results indicated that women evidenced greater pain tolerance than men on both a behavioral and physiological level; however, they reported greater pain severity than men. Fatigue was also found to be particularly important to reports of pain severity in men and pain tolerance in response to noxious stimuli for women. Possible pathways in which mood states influenced these endpoints are discussed. [Comment in: *Pain Pract.* 2006 Sep;6(3):151-2]

**Green CR, Ndao-Brumblay SK, Nagrant AM, Baker TA, Rothman E**  
Race, age, and gender influences among clusters of African American and white patients with chronic pain. *J Pain* (2004 Apr) 5(3):171-82

Racial and ethnic minorities, older people, and women are differentially affected by chronic pain. This study aimed to identify the experiences of adult African Americans and whites with chronic pain while identifying patient clusters on the basis of clinical characteristics as well as race, age, and gender influences within and between clusters. Three clusters of patients with chronic pain were identified within race, age, and gender categories: chronic pain syndrome, good pain control, and disability with mild syndrome. African American and younger patients experiencing chronic pain were more likely to present with chronic pain syndrome. African American patients presenting with chronic pain syndrome or disability with mild pain syndrome reported a higher disability than their counterparts. Older patients and women within the good pain control cluster reported a lower level of (1) pain and depression and (2) depression, respectively. Older patients presenting with a disability with mild syndrome also reported lower pain and depression. Despite similar physical, emotional, and pain characteristics, this study confirmed that the chronic pain experience differs across racial and age groups. Further study is necessary to evaluate how these factors influence pain services among an ethnically diverse population across

the age continuum. PERSPECTIVE: This study found important racial and age-related variability in the symptom severity of patients with chronic pain presenting with similar physical, emotional, and pain characteristics to a tertiary care pain center. These findings have important clinical implications on chronic pain assessment and management. [Erratum in: *J Pain*. 2005 Oct;6(10):707-9]

**Greenspan JD, Craft RM, LeResche L, Arendt-Nielsen L, Berkley KJ, Fillingim RB, Gold MS, Holdcroft A, Lautenbacher S, Mayer EA, Mogil JS, Murphy AZ, Traub RJ**

Studying sex and gender differences in pain and analgesia: a consensus report. *Pain* (2007 Nov) 132 Suppl 1:S26-45

In September 2006, members of the Sex, Gender and Pain Special Interest Group of the International Association for the Study of Pain met to discuss the following: (1) what is known about sex and gender differences in pain and analgesia; (2) what are the “best practice” guidelines for pain research with respect to sex and gender; and (3) what are the crucial questions to address in the near future? The resulting consensus presented herein includes input from basic science, clinical and psychosocial pain researchers, as well as from recognized experts in sexual differentiation and reproductive endocrinology. We intend this document to serve as a utilitarian and thought-provoking guide for future research on sex and gender differences in pain and analgesia, both for those currently working in this field as well as those still wondering, “Do I really need to study females?”

**Hirsh AT, Waxenberg LB, Atchison JW, Gremillion HA, Robinson ME,**

Evidence for sex differences in the relationships of pain, mood, and disability. *J Pain* (2006 Aug) 7(8):592-601

Disability demonstrates strong univariate associations with pain and negative mood. These relationships are more complex at the multivariate level and might be further complicated by sex differences. We investigated sex differences in the relationships of pain and negative mood to overall disability and to disability in specific functional domains. One hundred ninety-seven consecutive patients with low back, myofascial, neck, arthritis, and fibromyalgia pain were recruited from university pain clinics and completed measures of disability and negative mood. Overall disability and disability in voluntary activities were significantly associated with pain and negative mood (factor score) for both sexes. Significant sex differences emerged in the strength of the disability-mood relationship, with women evincing a stronger relationship. Disability in obligatory activities was also significantly related to pain and negative mood for both sexes; however, there were no sex differences in the strength of these relationships. Mediation analyses indicated that, in men, negative mood partially mediated the relationship

between pain and both overall disability and disability in voluntary activities; mediation was not supported for disability in obligatory activities. In women, negative mood fully mediated the relationship between pain and all 3 types of disability. These data suggest that disability is more directly related to pain in men. In women, the effect of pain on disability appears to operate through negative mood. PERSPECTIVE: Results of this study demonstrate that sex differences exist in the relationships of pain, mood, and disability. Men and women might thus benefit from treatment interventions that differentially target these variables.

**Hooten WM, Townsend CO, Decker PA**

Gender differences among patients with fibromyalgia undergoing multidisciplinary pain rehabilitation. *Pain Med* (2007 Nov-Dec) 8(8):624-32

OBJECTIVE: This study was conducted to test the hypothesis that gender differences in physical and emotional functioning are present among patients with fibromyalgia undergoing multidisciplinary pain rehabilitation. DESIGN: Retrospective case-matched series. Setting. Multidisciplinary pain rehabilitation center at a tertiary referral medical center. PATIENTS: Thirty-three consecutive men with fibromyalgia admitted from January 2002 through June 2005 were matched to 33 women with fibromyalgia for age, treatment dates, and program completion status. Interventions. A 3-week outpatient multidisciplinary pain rehabilitation program based on a cognitive-behavioral model that incorporates analgesic medication withdrawal. OUTCOME MEASURES: Multidimensional Pain Inventory (MPI), Short Form-36 Health Status Questionnaire (SF-36), Coping Strategies Questionnaire-Catastrophizing subscale (CSQ-C), and the Center for Epidemiologic Studies-Depression scale (CES-D) were administered before and after treatment. The numbers of patients using opioids, nonsteroidal anti-inflammatory drugs (NSAIDs), and benzodiazepines before and after treatment were compared. RESULTS: Pretreatment MPI and SF-36 scores revealed men had lower health perception ( $P = 0.017$ ) and more physical limitations ( $P = 0.004$ ) while women had greater life interference due to pain ( $P = 0.005$ ). Mean differences in all pre- and post-treatment outcome measures demonstrated a statistically significant treatment response. However, men had lower post-treatment scores on the SF-36 health perception ( $P = 0.023$ ), role limitations-physical ( $P = 0.021$ ), and social functioning ( $P = 0.033$ ) subscales. Significant within-gender reductions in opioid analgesic, NSAID, and benzodiazepine use were observed but no significant between-gender differences were identified. CONCLUSIONS: These results support the hypothesis that pretreatment gender differences are present among fibromyalgia patients undergoing multidisciplinary pain rehabilitation and post-treatment gender differences persist despite improvements in physical and emotional functioning.

**Keogh E, Herdenfeldt M**

Gender, coping and the perception of pain. *Pain* (2002 Jun) 97(3):195-201

Research consistently indicates that gender differences exist in pain perception, with females typically reporting more negative responses to pain than males. It also seems as if males and females use and benefit from different coping strategies when under stress; females seem to prefer emotion-focused coping, whereas males prefer sensory-focused coping. Unfortunately, experimental research that examines such differences in the context of pain has not yet been adequately investigated. The aim of the current study was, therefore, to determine whether gender differences would be found in the effect that sensory-focused and emotion-focused coping instructions have on cold pressor pain experiences. Participants consisted of 24 male and 26 female healthy adults, all of whom reported no current pain. A consistent pattern of effects was found, over both behavioural and self-report measures of pain. Compared to females, males exhibited less negative pain responses when focusing on the sensory component of pain (i.e. increased threshold, tolerance and lower sensory pain). Furthermore, compared to sensory focusing, emotional focusing was found to increase the affective pain experience of females. Together these results confirm that important differences exist between men and women in the effects pain coping instructions have on the experience of pain. The implications of such findings for research and practice are discussed.

**Leveille SG, Zhang Y, McMullen W, Kelly-Hayes M, Felson DT**

Sex differences in musculoskeletal pain in older adults. *Pain* (2005 Aug) 116(3):332-8

Little is known about sex differences in musculoskeletal pain in older persons. There were 682 women and 380 men aged 72 years and older who participated in the 22nd biennial exam of the Framingham Study (1992-1993). Participants were asked to identify pain locations on a homunculus showing all regions of the body. Pain was categorized according to number of regions, with the most disseminated pain classified as widespread pain (back pain and upper and lower extremity pain with bilaterality). Among the women, 63% reported pain in one or more regions, compared to 52% of men. Widespread pain was more prevalent among women than men (15 versus 5%, respectively). In both men and women, pain was associated with fair or poor self-rated health, history of back pain before age 65, and disability. Factors associated with pain only in women included body mass index, systolic blood pressure, and depressive symptoms. In men but not women, pain was associated with polyarticular radiographic osteoarthritis. In conclusion, musculoskeletal pain was more prevalent and more widespread in older women than older men. Men and women differ in the factors associated with musculoskeletal pain in older ages. Further research is needed to understand sex differences in musculoskeletal pain the older population.

**Lynch AM, Kashikar-Zuck S, Goldschneider KR, Jones BA**

Sex and age differences in coping styles among children with chronic pain. *J Pain Symptom Manage* (2007 Feb) 33(2):208-16

The purpose of this study was to examine sex and age differences in coping strategies among pediatric patients with chronic pain. Sex differences are reported in the adult pain and coping literatures, but little attention has been given to possible distinctions in coping styles in the pediatric chronic pain population. Investigating pain coping skills at an early age may provide clinicians with a better understanding of the evolution of characteristic coping styles and identify areas for intervention. Pain intensity (Visual Analog Scale), pain coping strategies (Pain Coping Questionnaire), and coping efficacy were assessed in children (ages 8-12 years) and adolescents (ages 13-18 years), presenting to a pediatric chronic pain clinic (n=272). Significant sex differences in coping strategies were found. After controlling for pain intensity, girls used social support seeking more than boys, while boys used more behavioral distraction techniques. Adolescents engaged in more positive self-statements (a cognitive strategy) than children. Both boys and girls showed a trend toward pain coping efficacy being negatively correlated with average pain intensity. For girls, pain coping efficacy was also significantly negatively correlated with internalizing/catastrophizing. However, no sex or age differences in coping efficacy were found. This study demonstrates the early emergence of sex- and aged-based preferences in coping strategies among children and adolescents with chronic pain. The findings establish a basis for further research on early social influences in the development of pain coping styles in males and females. Implications for further clinical research in this area are discussed.

**Paulson M, Norberg A, Soderberg S**

Living in the shadow of fibromyalgic pain: the meaning of female partners' experiences. *J Clin Nurs* (2003 Mar) 12(2):235-43

The aim of this study was to elucidate the meaning of being a female partner living with a man with fibromyalgic pain. Fourteen partners were interviewed about the meaning of their experiences, using a narrative approach. A phenomenological hermeneutic method, inspired by the French philosopher Ricoeur, was used to interpret the interview text. The structural analysis is presented in three major themes: struggling to give support and comfort, struggling to keep going on, and experiencing lack of understanding and support. The findings elucidate that the meaning of living with a man with fibromyalgic pain meant living a life strongly influenced by the man's illness and in the shadow of the man's pain. Taking daily life for granted was interrupted and restricted family and social life.

Prominent in this study was the frustration partners felt as a result of men's reluctance to communicate. This led to feelings of being excluded from men's emotions. The responsibility day in and day out meant that women's own caring and tenderness were replaced, which brought about an almost constant sense of fatigue. Women became drained by the long duration of men's illness. This gave them a feeling of being alone, although they were a couple. Gaining comfort outside the family helped partners to reach a new insight and appreciation for life, which was viewed from a renewed perspective. This involved feelings of both togetherness and separateness in the relationship. The findings also consider the lack of support from the health care system for female partners living with men with fibromyalgic pain.

**Paulson M, Norberg A, Danielson E**

Men living with fibromyalgia-type pain: experiences as patients in the Swedish health care system. *J Adv Nurs* (2002 Oct) 40(1):87-95

**BACKGROUND:** Individuals with fibromyalgia (FM) frequently use health care services and experience only short-term improvements. They often feel that health care staff do not take them seriously. This increases the burden of living with the illness. **AIM:** To describe how men living with fibromyalgia-type pain experienced being patients in the Swedish health care system. **METHOD:** Narrative interviews with 14 men who fulfilled the American College of Rheumatology criteria for classification of fibromyalgia. Content analysis was used when analysing the data. **RESULTS:** The results are described using five themes. Theme 1 'Feeling afraid of being looked upon as being a whiner' highlights how the men endured a lot of pain before they sought health care, and how difficult it was to find a receptive listener. Theme 2 'Feeling like a guinea pig' shows that the men's feelings were twofold; they wanted examinations, even if these made them feel that they were being exposed to numerous treatments without any cure. Theme 3 'Feeling hopeful' describes the hope for a cure after having been referred to a specialist clinic. Theme 4 'Feeling neglected' illustrates being looked upon as an uninteresting patient and theme 5 'Feeling no recovery' illustrates the pain relief they gained, but not the actual cure. **CONCLUSION:** Men with FM type pain experienced a long wait before treatment at a specialist clinic as well as no continuity and follow-ups in primary care and general hospitals. Encounters with engaged and skilful staff promoted the men's well-being despite the fact that no cure was available. Not being respected led to a feeling of being neglected despite the care received. Thus, the men had to accept the fact that they would never recover.

**Paulson M, Danielson E, Soderberg S**

Struggling for a tolerable existence: the meaning of men's lived experiences of living with pain of fibromyalgia type. *Qual Health Res* (2002 Feb) 12(2):238-49

Chronic pain is a major health problem in Sweden because of its consequences in daily life. Fourteen men with fibromyalgia-type pain were interviewed regarding their experiences. A phenomenological hermeneutic method was used to interpret the transcribed interviews. Three major themes emerged: experiencing the body as an obstruction, being a different man, and striving to endure. Overall, the meaning of men's lived experience of chronic pain was experienced as change in the body, self, and relationships. Striving to live life required achieving balance during both calm and difficult phases of the illness--struggling for a tolerable existence. Information from this study could provide guidelines for health care staff members to give empathic and supportive care to men living with a long-term illness.

**Rhudy JL, Williams AE**

Gender differences in pain: do emotions play a role? *Gend Med* (2005 Dec) 2(4):208-26

**BACKGROUND:** Research suggests that the influence of gender on the processing and experience of pain is a result of several mechanisms. One mediating variable is emotion, which may modulate pain through an interaction of valence (pleasant-unpleasant) and arousal (calm-excited). **OBJECTIVE:** This review examines whether gender differences in the experience and processing of emotion contribute to differences in the modulation and perception of pain. **METHODS:** An English-language search of MEDLINE and PsycINFO was conducted from 1887 to May 2005. Additional literature was obtained from reference lists of articles retained in the initial search. **RESULTS:** Emotion appears to influence pain through a valence-by-arousal interaction. Specifically, negatively valenced emotions with low to moderate arousal (eg, anxiety) enhance pain, whereas negatively valenced emotions with high arousal (eg, fear) reduce pain. In contrast, positively valenced emotions always reduce pain, as long as minimal arousal is achieved. Some evidence suggests that women are more sensitive than men to threat-related stimuli and thus experience more negative affect than men. This would generally lead to enhanced pain perception in women. It is also possible that women are more likely than men to experience negative affect with high arousal (intense fear) and thus pain inhibition. However, the relatively lower base rate of intense negative emotions is not likely to contribute much to gender differences in pain. Evidence also suggests that men may be more sensitive to positive events, particularly sexual/erotic stimuli, which may lead to more positive emotion-induced pain reduction in men, relative to women. **CONCLUSIONS:** This review suggests that gender differences in the experience of pain may arise from differences in the experience and processing of emotion that, in

turn, differentially alter pain processing. Specifically, the system associated with negative affect may be more attuned to threatening stimuli in women, and the system associated with positive affect may be more attuned to pleasurable stimuli in men. However, there is a paucity of research directly addressing this issue; much of the research on this topic has failed to test a comprehensive model of emotion, failed to use adequate manipulation checks, or failed to use within-subject experimental designs that control for intra- and interindividual differences. Therefore, it is concluded that additional research is warranted.

**Robinson ME, Wise EA**

Gender bias in the observation of experimental pain. *Pain* (2003 Jul) 104 (1-2):259-64

The aim of this study was to examine how men and women observe experimentally induced pain in male and female participants and to specifically determine the accuracy of observed pain ratings, the possible interactions between the sex of the viewer and the sex of the individual being observed, and the influence of gender role expectations on observed pain ratings. The sample comprised 29 participants (15 females). They each completed a battery of psychological questionnaires and viewed a presentation of 10 randomly ordered video clips. Each presentation consisted of 10 video clips, lasting 30s, of a participant (five males and five females) in the cold pressor task. The participants viewing the videos were asked to provide several ratings, including observed pain intensity and gender role related characteristics of the individual in the video. In terms of sex of the video participant, results indicated that viewers rated male videos as having less pain than female videos although the effect was small. Regarding sex of the viewer, results indicated that for both male and female videos, female viewers rated observed pain intensity significantly higher than did male viewers. In terms of accuracy, results indicated that on average, female video participants' pain was underestimated by 14 points, while male videos participants' pain was underestimated by 22 points (on a 0-100-point scale). Pain intensity ratings and pain tolerance from the participants in the videos did not differ significantly with respect to sex, though women had shorter tolerance times and higher pain ratings than men. Hierarchical regression analyses indicated that expectations of gender related 'endurance of pain' significantly predicted ratings of both male and female videos. When endurance expectations were controlled, sex of the viewer no longer significantly predicted observed pain ratings. The 'willingness to report pain' variable was not a significant predictor of observed pain ratings. Our results show that women are perceived to have more pain than men, that there was a tendency by both sexes to underestimate pain in others, but men showed even greater underestimation, and that gender role expectations of pain endurance

given by the video observers accounted for substantial variance in their ratings of pain in the videos.

**Robinson ME, Wise EA, Gagnon C, Fillingim RB, Price DD**

Influences of gender role and anxiety on sex differences in temporal summation of pain. *J Pain* (2004 Mar) 5(2):77-82

Previous research has consistently shown moderate to large differences between pain reports of men and women undergoing experimental pain testing. These differences have been shown for a variety of types of stimulation. However, only recently have sex differences been demonstrated for temporal summation of second pain. This study examined sex differences in response to temporal summation of second pain elicited by thermal stimulation of the skin. The relative influences of state anxiety and gender role expectations on temporal summation were investigated. Asymptomatic undergraduates (37 women and 30 men) underwent thermal testing of the thenar surface of the hand in a temporal summation protocol. Our results replicated those of Fillingim et al indicating that women showed increased temporal summation compared to men. We extended those findings to demonstrate that temporal summation is influenced by anxiety and gender role stereotypes about pain responding. When anxiety and gender role stereotypes are taken into account, sex is no longer a significant predictor of temporal summation. These findings highlight the contribution of social learning factors in the differences between sexes' pain perception. PERSPECTIVE: Results of this study demonstrate that psychosocial variables influence pain mechanisms. Temporal summation was related to gender role expectations of pain and anxiety. These variables explain a significant portion of the differences between men and women's pain processing, and may be related to differences in clinical presentation.

**Robinson ME, Gagnon CM, Riley JL, Price DD**

Altering gender role expectations: effects on pain tolerance, pain threshold, and pain ratings. *J Pain* (2003 Jun) 4(5):284-8

The literature demonstrating sex differences in pain is sizable. Most explanations for these differences have focused on biologic mechanisms, and only a few studies have examined social learning. The purpose of this study was to examine the contribution of gender-role stereotypes to sex differences in pain. This study used experimental manipulation of gender-role expectations for men and women. One hundred twenty students participated in the cold pressor task. Before the pain task, participants were given 1 of 3 instructional sets: no expectation, 30-second performance expectation, or a 90-second performance expectation. Pain ratings, threshold, and tolerance were recorded. Significant sex differences in the "no expectation" condition for pain tolerance ( $t = 2.32$ ,  $df = 38$ ,  $P < .05$ ) and post-cold pressor pain ratings ( $t = 2.6$ ,  $df = 37$ ,  $P < .05$ ) were found.

Women had briefer tolerance times and higher post-cold pressor ratings than men. When given gender-specific tolerance expectations, men and women did not differ in their pain tolerance, pain threshold, or pain ratings. This is the first empirical study to show that manipulation of expectations alters sex differences in laboratory pain.

**Robinson ME, Riley JL, Myers CD, Papas RK, Wise EA, Waxenberg LB, Fillingim RB**

Gender role expectations of pain: relationship to sex differences in pain. *J Pain* (2001 Oct) 2(5):251-7

Empirical research supports the existence of sex differences in pain; yet these differences are poorly understood. Although biological mechanisms have been posited to explain variability, results of pain modeling manipulations suggest social learning may be a stronger influence on pain response. In this report we use the term sex to refer to the biological category of male or female. We use the term gender to refer to the socially acquired aspects of being male or female sometimes referred to as femininity and masculinity. This study investigated a new measure, the Gender Role Expectations of Pain questionnaire (GREP), which was designed to measure sex-related stereotypic attributions of pain sensitivity, endurance, and willingness to report pain. Subjects were 156 male and 235 female undergraduates at a southeastern university. Psychometric investigation of the questionnaire revealed a 5-factor solution that closely mirrored the theoretical construction of the items. Test-retest reliability was also shown for individual items on a separate sample of 28 subjects. Results supported hypotheses about gender role: both men and women rated men as less willing to report pain than women ( $F(1,389) = 336, P < .001$ ); both men and women rated women more sensitive ( $F(1,389) = 9.5, P < .05$ ) and less enduring of pain ( $F(1,389) = 65.7, P < .001$ ) than men; and men rated their own endurance as higher than the typical man ( $F(1,389) = 65.7, P < .001$ ). Sex accounted for 46% of the variance in willingness to report pain. Results suggest that the GREP distinguished between the socially learned reactions to pain for men and women. It is recommended that the influence of gender-related expectations for pain be assessed in all studies investigating human sex differences in pain.

**Roth RS, Geisser ME, Theisen-Goodvich M, Dixon PJ**

Cognitive complaints are associated with depression, fatigue, female sex, and pain catastrophizing in patients with chronic pain. *Arch Phys Med Rehabil* (2005 Jun) 86(6):1147-54

**OBJECTIVE:** To examine the relation between demographic, pain-related, psychosocial, affective, and treatment factors and complaints of cognitive dysfunction among patients with chronic pain. **DESIGN:** Cross-sectional survey. **SETTING:** A university hospital outpatient

multidisciplinary chronic pain program. **PARTICIPANTS:** Chronic pain patients (N=222; 135 women, 87 men) completed a battery of psychometric questionnaires as part of an initial evaluation on referral to the program. **INTERVENTIONS:** Not applicable. **MAIN OUTCOME MEASURES:** Cognitive impairment was assessed with items from the Brief Symptom Inventory; measures of depressive symptoms, pain intensity, posttraumatic stress disorder (PTSD), and pain catastrophizing were obtained from the Beck Depression Inventory (negative affect, negative self, somatic/physical function), McGill Pain Questionnaire, Modified Posttraumatic Chronic Pain Test, and Coping Strategies Questionnaire, respectively; and measures of subjective sleep disturbance, fatigue, opiate use, compensation/litigation status, pain location, and relevant demographic data were obtained from an open-ended questionnaire. **RESULTS:** Correlational analysis indicated that female sex, pain intensity, PTSD symptoms, depressive symptoms, catastrophizing, pain location (neck), and fatigue were all positively related to cognitive complaints. Simultaneous regression analysis showed that all factors combined accounted for 52% of the variance in self-report of cognitive difficulties and that 6 variables had a significant unique contribution to the report of cognitive complaints in the following order of importance: depression-negative affect (beta=.28,  $P < .05$ ), fatigue (beta=.17,  $P < .05$ ), depression-somatic/physical function (beta=.16,  $P < .05$ ), depression-negative self (beta=.14,  $P = .05$ ), pain catastrophizing (beta=.12,  $P = .08$ ), and female sex (beta=.12,  $P < .05$ ). **CONCLUSIONS:** Complaints of cognitive impairment among chronic pain patients appear to be associated with multiple factors, with particular attention to depressive symptoms, fatigue, and catastrophizing. Our results also suggest that women with chronic pain are particularly vulnerable to cognitive dysfunction.

**Staud R, Robinson ME, Vierck CJ, Price DD**

Diffuse noxious inhibitory controls (DNIC) attenuate temporal summation of second pain in normal males but not in normal females or fibromyalgia patients. *Pain* (2003 Jan) 101(1-2):167-74

Diffuse noxious inhibitory control (DNIC) is part of a central pain modulatory system that relies on spinal and supraspinal mechanisms. Previous studies have shown that fibromyalgia (FMS) patients are lacking DNIC effects on experimental pain, compared to normal control (NC) subjects. Because DNIC has a greater effect on second pain than on first pain, we hypothesized that wind-up (WU) of second pain should be attenuated by a strong conditioning stimulus. Thus, we compared DNIC's effect on WU in three groups of subjects: 11 NC males, 22 NC females, and 11 FMS females. To separately assess the contributions of distraction related mechanisms to inhibition of second pain, we designed the experiment in such a way that directed the subjects' attention to either the test or conditioning stimulus. Repeated heat taps to the thenar surface of the right hand were used as test stimuli to generate WU of second pain. Immersion of the left

hand into a hot water bath was the conditioning stimulus. As previous experiments have shown, DNIC requires a strong conditioning stimulus for pain attenuation, which may be at least partly dependent on a distraction effect. DNIC significantly inhibited thermal WU pain in normal male subjects, but adding distraction to the DNIC effect did not increase the extent of this inhibition. In contrast, neither DNIC nor DNIC plus distraction attenuated thermal WU pain in female NCs. DNIC plus distraction but not DNIC alone produced significant inhibition of thermal WU pain in female FMS patients. Our results indicate that DNIC effects on experimental WU of second pain are gender specific, with women generally lacking this pain-inhibitory mechanism.

**Visuri T, Lindholm H, Lindqvist A, Dahlstrom S, Viljanen A**

Cardiovascular functional disorder in primary fibromyalgia: a noninvasive study in 17 young men. *Arthritis Care Res* (1992 Dec) 5(4):210-5

Cardiovascular functional stability was studied in 17 young men (20-year-old conscripts) with the symptoms of primary fibromyalgia (PF). They were compared to 20 medical students of the same age. The subjects underwent an orthostatic test, deep breathing test, Valsalva maneuver, and a handgrip test. They were evaluated by an autoanamnesic questionnaire on vegetative symptoms and laboratory tests on blood chemistry. The heart rate of the PF group after 8 min of active standing was 32 +/- 15 beats/min greater than at supine rest. The corresponding figure for the controls was 23 +/- 7 beats/min ( $p = 0.001$ ). Twelve conscripts with PF (71%) presented sympathetic cardiovascular reaction on the orthostatic test ( $p < 0.001$ ). Four of these sympathetic conscripts and two other conscripts (total 35%) had an abnormal high index of dystonic symptoms ( $p = 0.01$ ). The results suggest that young men with symptoms of PF have not only cardiovascular dystonic symptoms but also increased sympathetic nervous reactivity of the cardiovascular system.

**Wahner-Roedler DL, Olson EJ, Narayanan S, Sood R, Hanson AC, Loehrer LL, Sood A**

Gender-specific differences in a patient population with obstructive sleep apnea-hypopnea syndrome. *Gen Med* (2007 Dec) 4(4):329-38

**BACKGROUND:** Sleep-related breathing disorders are increasingly recognized as an important cause of morbidity and mortality. Women with obstructive sleep apnea-hypopnea syndrome (OSA) are less likely to be assessed or to receive a diagnosis, and they may have poorer survival rates. **OBJECTIVE:** This study assessed gender-specific differences in patients with OSA. **METHODS:** Data were collected with a prospective, point-of-care, anonymous 25-question survey about basic medical information and therapies for patients undergoing polysomnography at the sleep center of a US tertiary care center from

January 1 through March 31, 2005. **RESULTS:** Of the 646 consecutive patients who received the survey, 522 (80.8%) patients completed it, and 406 subsequently received a diagnosis of OSA. Of those 406 patients, 267 (65.8%) were men. Overall mean age was 57 years (56.4 years for men; 56.7 years for women). Alcohol use was more common in men (132 [49.4%]) than in women (43 [30.90,6]) ( $P < 0.001$ ). Women were more likely to have the following associated comorbidities: obesity (body mass index  $\geq 30$ ) ( $P = 0.047$ ), fibromyalgia ( $P < 0.001$ ), migraine ( $P < 0.001$ ), depression ( $P = 0.01$ ), and irritable bowel syndrome ( $P = 0.01$ ). The 4 most frequently reported sleep-related symptoms in both sexes were snoring (279 [68.7%]), lack of energy (235 [57.9%]), difficulty staying asleep (206 [50.7%]), and daytime sleepiness (204 [50.2%]). Lack of energy ( $P = 0.01$ ), difficulty falling asleep ( $P = 0.02$ ), and night sweats ( $P = 0.01$ ) were observed more frequently in women than in men. There was no significant gender difference in the recalled duration of sleep-related symptoms. The mean (SD) apnea-hypopnea index (AHI) was 26.6 (26.6) for men and 22.1 (26.5) for women ( $P = 0.02$ ). Conventional medications (including prescription and over-the-counter medications) for sleep-related problems were used more by women (35 [25.2%]) than by men (29 [10.9%]) ( $P < 0.001$ ). **CONCLUSIONS:** The majority of patients who received a diagnosis of OSA were men (male-female ratio, 2:1), and the mean AHI was higher in men than in women. However, women presented with more nonspecific symptoms than did men, although there was no significant gender-specific difference in the recalled duration of symptoms. In addition, women reported more comorbidities and used significantly more conventional medications for sleep-related problems.

**Weisse CS. Sorum PC. Sanders KN. Syat BL**

Do gender and race affect decisions about pain management? *J Gen Intern Med* (2001 Apr) 16(4):211-7

**OBJECTIVE:** To determine if patient gender and race affect decisions about pain management. **DESIGN, SETTING, AND PARTICIPANTS:** Experimental design using medical vignettes to evaluate treatment decisions. A convenience sample of 111 primary care physicians (61 men, 50 women) in the Northeast was asked to treat 3 hypothetical patients with pain (kidney stone, back pain) or a control condition (sinusitis). Symptom presentation and severity were held constant, but patient gender and race were varied. **MEASUREMENTS AND MAIN RESULTS:** The maximum permitted doses of narcotic analgesics (hydrocodone) prescribed at initial and return visits were calculated by multiplying mg per pill x number of pills per day x number of days x number of refills. No overall differences with respect to patient gender or race were found in decisions to treat or in the maximum permitted doses. However, for renal colic, male physicians prescribed higher doses of hydrocodone to white patients versus black patients (426 mg vs 238 mg), while female physicians prescribed higher doses to blacks (335 mg vs 161 mg,  $F_{1,85} = 9.65$ ,  $P = .003$ ). This pattern was repeated for persistent kidney stone pain. For persistent back pain,

male physicians prescribed higher doses of hydrocodone to males than to females (406 mg vs 201 mg), but female physicians prescribed higher doses to females (327 mg v. 163 mg,  $F_{1,28} = 5.50$ ,  $P = .03$ ).  
**CONCLUSION:** When treating pain, gender and racial differences were evident only when the role of physician gender was examined, suggesting that male and female physicians may react differently to gender and/or racial cues.

**Wijnhoven HA, de Vet HC, Picavet HS**

Explaining sex differences in chronic musculoskeletal pain in a general population. *Pain* (2006 Sep) 124(1-2):158-66

Many studies report a female predominance in the prevalence of chronic musculoskeletal pain (CMP) but the mechanisms explaining these sex differences are poorly understood. Data from a random postal questionnaire survey in the Dutch general population were used to examine whether sex differences in the prevalences of CMP are due to sex differences in the distribution of known potential risk factors for CMP (exposure model) and/or to the different importance of risk factors for CMP (i.e. show different strength of association) in men and women (vulnerability model). In the present analyses, 909 men and 1178 women aged 25-65 were included. CMP was defined as pain lasting longer than 3 months and was assessed for 10 anatomical locations (neck, shoulder, higher back, elbow, wrist/hand, lower back, hip, knee, ankle, foot). Sex differences in CMP could not be explained by a different distribution of age, educational level, smoking status, overweight, physical activity, and pain catastrophizing. Having no paid job was associated with CMP, explaining part of the sex differences, but its role seems complex. Risk factors with a sex-specific association were: overweight (all pain locations) and older age (lower extremities)--both having only an effect among women--and pain catastrophizing (upper extremities), which was stronger associated with CMP among men than among women. In conclusion, sex differences in prevalence of CMP may partly be explained by sex differences in vulnerability to risk factors for CMP. Future research towards sex-specific identification of risk factors for CMP is warranted. Eventually this may lead to sex-specific prevention and management of CMP.

**Wise EA, Price DD, Myers CD, Heft MW, Robinson ME**

Gender role expectations of pain: relationship to experimental pain perception. *Pain* (2002 Apr) 96(3):335-42

The primary purpose of this study was to investigate the influence of an individual's Gender Role Expectations of Pain (GREP) on experimental pain report. One hundred and forty-eight subjects (87 females and 61 males) subjects underwent thermal testing and were asked to report pain threshold, pain tolerance, VAS ratings of pain intensity and unpleasantness, and a computerized visual analogue

scales (VAS) rating of pain intensity during the procedure. Subjects completed the GREP questionnaire to assess sex-related stereotypic attributions of pain sensitivity, pain endurance, and willingness to report pain. Consistent with previous research, significant sex differences emerged for measures of pain threshold, pain tolerance, and pain unpleasantness. After statistically controlling for age, GREP scores were significant predictors of threshold, tolerance, and pain unpleasantness, accounting for an additional 7, 11, and 21% of the variance, respectively. Sex remained a significant predictor of pain tolerance in hierarchical regression analyses after controlling for GREP scores. Results provide support for two competing but not mutually exclusive hypotheses related to the sex differences in experimental pain. Both psychosocial factors and first-order, biological sex differences remain as viable explanations for differences in experimental pain report between the sexes. It appears that GREP do play a part in determining an individual's pain report and may be contributing to the sex differences in the laboratory setting.

**Yunus MB**

The role of gender in fibromyalgia syndrome. *Curr Rheumatol Rep* (2001 Apr) 3(2):128-34

Fibromyalgia syndrome (FMS), characterized by widespread pain and tenderness on palpation (tender points), is much more common in women than in men in a proportion of 9:1. Two recent studies have shown important gender differences in various clinical characteristics of FMS. In a community and a clinic sample, women experienced significantly more common fatigue, morning fatigue, hurt all over, total number of symptoms, and irritable bowel syndrome. Women had significantly more tender points. Pain severity, global severity and physical functioning were not significantly different between the sexes, nor were psychologic factors, eg, anxiety, stress, and depression. Gender differences have also been observed in other related syndromes, eg, chronic fatigue syndrome, irritable bowel syndrome, and headaches. The mechanisms of gender differences in these illnesses are not fully understood, but are likely to involve an interaction between biology, psychology, and sociocultural factors.

**Yunus MB, Inanici F, Aldag JC, Mangold RF**

Fibromyalgia in men: comparison of clinical features with women. *J Rheumatol* (2000 Feb) 27(2):485-90

**OBJECTIVE:** To describe possible differences between male and female patients with fibromyalgia syndrome (FM) in their clinical manifestations. **METHODS:** Five hundred thirty-six consecutive patients with FM (469 women, 67 men) seen in a university rheumatology clinic and 36 healthy men without significant pain seen in the same clinic

were included in the study. Data on demographic and clinical features were gathered by a standard protocol. Tender point examination was performed by the same physician. Level of significance was set at  $p < \text{or} = 0.01$ . RESULTS: Several features were significantly ( $p < \text{or} = 0.01$ ) milder or less common among men than women, including number of tender points (TP), TP score, "hurt all over," fatigue, morning fatigue, and irritable bowel syndrome (IBS). The total number of symptoms was also fewer among men and approached significance ( $p = 0.02$ ) by parametric test, but reached significance ( $p = 0.001$ ) by nonparametric analysis. All clinical and psychological symptoms as well as TP were significantly ( $p < 0.01$ ) more common or greater in male patients with FM than healthy male controls, with the exception of IBS ( $p = 0.03$ ). Patient assessed global severity of illness, Health Assessment Questionnaire disability score, and pain severity were similar in both sexes. CONCLUSION: Male patients with FM had fewer symptoms and fewer TP, and less common "hurt all over," fatigue, morning fatigue, and IBS, compared with female patients. Stepwise logistic regression showed significant differences between men and women in number of TP ( $p < 0.001$ ).

**Yunus MB, Khan MA, Rawlings KK, Green JR, Olson JM, Shah S**  
Genetic linkage analysis of multicase families with fibromyalgia syndrome. *J Rheumatol* (1999 Feb) 26(2):408-12

OBJECTIVE: Based on the reports of familial aggregation of fibromyalgia (FM) syndrome, we investigated its possible genetic linkage to HLA by studying multicase families. METHODS: Forty Caucasian multicase families with a diagnosis of FM (American College of Rheumatology criteria) in 2 or more first degree relatives were investigated. Eighty-five affected and 21 unaffected members of 41 sibships were studied. Depression symptomology was assessed by Zung Self-rating Depression Scale (SDS). HLA typing was performed for A, B, and DRB 1 alleles, and haplotypes were determined with no knowledge of the subject's diagnosis. We investigated genetic linkage to the HLA region by evaluating sibships in multicase families. RESULTS: Sibship analysis showed significant genetic linkage of FM to the HLA region ( $p = 0.028$ ). Subgroup analysis was also performed for 17 families where the proband was also noted to have depression (with an SDS index value  $> \text{or} = 60$ ). We found that the presence of depression did not influence the observed results ( $p = 0.22$ ). CONCLUSION: Our study of 40 multicase families confirms existence of a possible gene for FM that is linked with the HLA region. Our results should be regarded as preliminary and their independent confirmation by other studies is warranted.