

## **FIBROMYALGIA: ABSTRACTS 2012 FROM ARTICLES IN MEDICAL JOURNALS**

The abstracts in this collection are intended to provide doctors and other health professionals with a convenient overview of trends in research on fibromyalgia published in medical journals during the year 2012. The studies were selected from the extensive literature on fibromyalgia so as to cover a wide range of subjects in limited space.

Abstracts for 2013 will be posted at intervals during the year. Similar collections of abstracts produced annually from 1999 on can be found on the website of the National Fibromyalgia Partnership: [www.fmpartnership.org](http://www.fmpartnership.org).

The abstracts are arranged in alphabetical order by lead author.

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Abbi B, Natelson BH

### **Is chronic fatigue syndrome the same illness as fibromyalgia: evaluating the ‘single syndrome’ hypothesis**

Chronic fatigue syndrome (CFS) and fibromyalgia (FM) are medically unexplained syndromes that can and often do co-occur. For this reason, some have posited that the two are part of the same somatic syndrome—examples of symptom amplification. This hypothesis would suggest that few differences exist between the two syndromes. To evaluate this interpretation, we have searched the literature for articles comparing CFS to FM, reviewing only those articles which report differences between the two. **This review presents data showing differences across a number of parameters—implying that the underlying pathophysiology in CFS may differ from that of FM.** We hope that our review encourages other groups to look for additional differences between CFS and FM. By continuing to preserve the unique illness definitions of the two syndromes, clinicians will be able to better identify, understand and provide treatment for these individuals.

*QJM*. 2012 Aug 26. [Epub ahead of print]

Ambrose KR, Gracely RH, Glass JM

### **Fibromyalgia dyscognition: concepts and issues**

Fibromyalgia is characterized by widespread pain and tenderness; however, comorbid cognitive difficulties are a common complaint among patients. Known as fibro fog or dyscognition, this symptom comprises difficulties with complex cognitive processes including memory, executive function, concentration and attention. While the mechanisms that initiate and maintain these cognitive deficits

are still largely unknown, recent research has increased the understanding of subjective symptoms and objectively-determined deficits in cognitive performance. Treatments have also improved to include complementary cognitive and physical strategies. **This review focuses on issues of dyscognition in fibromyalgia.** Details of objective testing methods are not within the scope of this paper.

*Reumatismo.* 2012 Sep 28; 64(4):206–15

Ang DC, Kaleth AS, Bigatti S, Mazzuca SA, Jensen MP, Hilligoss J, Slaven J, Saha C

**Research to encourage exercise for fibromyalgia (REEF): use of motivational interviewing, outcomes from a randomized-controlled trial**

**OBJECTIVES:** Regular exercise is associated with important benefits in patients with fibromyalgia (FM). Unfortunately, long-term maintenance of exercise after a structured program is rare. The present study tested the efficacy of Motivational Interviewing (MI) to promote exercise and improve symptoms in patients with FM. **METHODS:** A total of 216 patients with FM were randomized to 6 MI sessions (n=107) or an equal number of FM self-management lessons (education control/EC, n=109). Co-primary endpoints were an increase of 30 minutes in moderate-vigorous physical activity and improvement in the Fibromyalgia Impact Questionnaire (FIQ)-Physical Impairment score, assessed at pretreatment, posttreatment, and 3-month and 6-month follow-up. Secondary outcomes included clinically meaningful improvements in FIQ score, pain severity ratings, and a 6-minute walk test. **RESULTS:** There were no significant treatment group differences in either co-primary endpoint at 6-month follow-up. However, more MI participants than controls exhibited meaningful improvements in FIQ score at 6-month follow-up (62.9% vs. 49.5%, P=0.06). Compared with EC participants, MI participants also displayed a larger increment in their 6-minute walk test (43.9 vs. 24.8 m, P=0.03). In addition, **MI was superior to EC in increasing the number of hours of physical activity immediately postintervention and in reducing pain severity both immediately after the intervention and at 3-month follow-up.** **CONCLUSIONS:** Despite a lack of benefits on long-term outcome, MI seems to have short-term benefits with respect to self-report physical activity and clinical outcomes. This is the first study in FM that explicitly addresses exercise maintenance as a primary aim. **CLINICAL TRIAL REGISTRATION:** NCT00573612.

*Clin J Pain.* 2012 Oct 5. [Epub ahead of print]

Bachasson D, Guinot M, Wuyam B, Favre-Juvin A, Millet GY, Levy P, Verges S

**Neuromuscular fatigue and exercise capacity in fibromyalgia syndrome**

**OBJECTIVE:** To assess quadriceps strength and fatigability by using femoral nerve magnetic stimulation (FNMS) and its relationship with exercise capacity in patients with fibromyalgia syndrome (FMS) and healthy controls. **METHODS:** 22 women (11 FMS, 11 controls) performed a maximal incremental cycling test and a quadriceps fatigue test on two separated visits. For quadriceps assessment, we used FNMS during and after maximum voluntary contraction (MVC) to evaluate central and peripheral factors of neuromuscular fatigue. Subjects performed sets of 10 intermittent (5-s on/5-s off) isometric contractions starting at 10% MVC, with 10% MVC increment from one set to another until exhaustion. Neuro-muscular fatigue was assessed with FNMS after each set. **RESULTS:** FMS had reduced initial MVC compared to controls (102±18 versus 120±24 Nm, respectively; P<0.05) without significant impairment of voluntary activation (93.5±3.0 versus 93.1±3.4%; P<0.05). During the fatiguing task, FMS exhibited greater fall in evoked muscular responses (e.g. -26±6 versus -16±8% at set 50% MVC; P<0.05) but not in MVC (e.g. -24±7% versus -19±4% at set 50% MVC; P=0.12). During the cycling test, FMS had lowered maximal exercise capacity and enhanced rate of perceived exertion (RPE) compared to controls. Percentage reduction in evoked muscular responses during the quadriceps fatigue test correlated with maximal oxygen consumption (r=0.56; P<0.05) and RPE at submaximal intensity (r=0.84; P<0.05) during cycling. **CONCLUSION:** Larger impairment in muscle contractility is associated with enhanced perception of exertion and reduced maximal exercise capacity in FMS patients. **Neuromuscular impairments should be considered as an important factor underlying functional limitations in FMS patients.** Copyright © 2012 by the American College of Rheumatology

*Arthritis Care Res* (Hoboken). 2012 Sep 10. [Epub ahead of print]

Baker NA, Rubinstein EN, Rogers JC

### **Problems and accommodation strategies reported by computer users with rheumatoid arthritis or fibromyalgia**

**INTRODUCTION:** Little is known about the problems experienced by and the accommodation strategies used by computer users with rheumatoid arthritis (RA) or fibromyalgia (FM). This study (1) describes specific problems and accommodation strategies used by people with RA and FM during computer use; and (2) examines if there were significant differences in the problems and accommodation strategies between the different equipment items for each diagnosis. **METHODS:** Subjects were recruited from the Arthritis Network Disease Registry. Respondents completed a self-report survey, the Computer Problems Survey. Data were analyzed descriptively (percentages; 95% confidence intervals). Differences in the number of problems and accommodation strategies were calculated using nonparametric tests (Friedman's test and Wilcoxon Signed Rank Test). **Results:** Eighty-four percent of respondents reported at least one problem with at least one equipment item (RA = 81.5%; FM = 88.9%), with most respondents reporting problems with their chairs. Respondents most commonly

used timing accommodation strategies to cope with mouse and keyboard problems, personal accommodation strategies to cope with chair problems and environmental accommodation strategies to cope with monitor problems. CONCLUSIONS: The number of problems during computer use was substantial in our sample, and our respondents with RA and FM may not implement the most effective strategies to deal with their chair, keyboard, or mouse problems. **This study suggests that workers with RA and FM might potentially benefit from education and interventions to assist with the development of accommodation strategies to reduce problems related to computer use.**

*J Occup Rehabil.* 2012 Jan 24. [Epub ahead of print]

Berstad A, Undseth R, Lind R, Valeur J

### **Functional bowel symptoms, fibromyalgia and fatigue: A food-induced triad?**

OBJECTIVE: Patients with perceived food hypersensitivity typically present with multiple health complaints. We aimed to assess the severity of their intestinal and extra-intestinal symptoms. MATERIALS AND METHODS: In a prospective study, 84 patients referred to our outpatient clinic for investigation of perceived food hypersensitivity were enrolled consecutively. Irritable bowel syndrome (IBS) was diagnosed according to the Rome III criteria. Severity and impact of bowel symptoms, fatigue and musculoskeletal pain were evaluated by using the following questionnaires: the IBS Severity Scoring System (IBS–SSS), the Fatigue Impact Scale (FIS), the FibroFatigue Scale (FFS), and visual analogue scales (VAS) for scoring of musculoskeletal pain. RESULTS: All but one patient were diagnosed with IBS, 58% with severe symptoms. Extra-intestinal symptoms suggestive of chronic fatigue and fibromyalgia were demonstrated in 85% and 71%, respectively. Neither IgE-mediated food allergy nor organic pathology could explain the patients' symptoms. Nevertheless, malabsorption of fat was demonstrated in 10 of 38 subjects. CONCLUSIONS: **Perceived food hypersensitivity may be associated with severe, debilitating illness.** The comorbid triad of IBS, chronic fatigue, and musculoskeletal pain is striking and may point to a common underlying cause.

*Scand J Gastroenterol.* 2012 May 18. [Epub ahead of print]

Buskila D, Ablin J

### **Pediatric fibromyalgia**

Fibromyalgia (FM) is currently defined as chronic widespread pain (CWP) with allodynia or hyperalgesia to pressure pain. It is classified as one of the large group of soft-tissue pain syndromes. Pain is the cardinal symptom of FM; however, most patients also experience additional symptoms such as debilitating fatigue, disrupted or non-restorative sleep, functional bowel disturbances, and a variety of

neuropsychiatric problems, including cognitive dysfunction, anxiety and depressive symptoms. Its pathogenesis is not entirely understood, although it is currently believed to be the result of a central nervous system (CNS) malfunction that increases pain transmission and perception. FMS usually involves females, and in these patients it often makes its first appearance during menopause. But it is often diagnosed both in young as well as elderly individuals. Pediatric FMS is a frustrating condition affecting children and adolescents at a crucial stage of their physical and emotional development. Pediatric FMS is an important differential diagnosis to be considered in the evaluation of children suffering from widespread musculoskeletal pain, and must be differentiated from a spectrum of inflammatory joint disorders such as juvenile idiopathic arthritis (JIA), juvenile ankylosing spondylitis, etc. **The management of pediatric FMS is centered on the issues of education, behavioral and cognitive change (with a strong emphasis on physical exercise), and a relatively minor role for pharmacological treatment with medications such as muscle relaxants, analgesics and tricyclic agents.**

*Reumatismo*. 2012 Sep 28; 64(4):230–7

Dell’Osso L, Carmassi C, Consoli G, Conversano C, Ramacciotti CE, Musetti L, Massimetti E, Pergentini I, Corsi M, Ciapparelli A, Bazzichi L

### **Lifetime post-traumatic stress symptoms are related to the health-related quality of life and severity of pain/fatigue in patients with fibromyalgia**

**OBJECTIVES:** The aim of the present study was to investigate the impact of lifetime potentially traumatic events, including losses, and of post-traumatic stress symptoms on the severity of illness and health-related quality of life in patients with fibromyalgia (FM). **METHODS:** Seventy patients with FM, diagnosed according to the American College of Rheumatology criteria, were consecutively enrolled at the Unit of Rheumatology of the University of Pisa, Italy. Assessments included: SCID-I/P; the Fibromyalgia Impact Questionnaire (FIQ) and the Medical Outcomes Study Short Form-36 Health Survey (MOS SF-36), for the severity of pain; the Health-Related Quality of Life (HRQoL); the Trauma and Loss Spectrum Self-Report (TALS-SR) life-time version. **RESULTS:** The FIQ total score was related to the number of loss events (Domain I) and to symptoms of grief reactions (Domain II) and re-experiencing (Domain V) of the TALS-SR. The ‘VAS fatigue’ scores (FIQ) were significantly related to the TALS-SR symptoms of grief reactions (Domain II) and re-experiencing (Domain V). The Mental Component Summary and Bodily Pain scores of the MOS SF-36 were significantly related to all TALS-SR domains, the latter with the exception of the VIII (Arousal). **CONCLUSIONS:** **Our results corroborate the presence of a relationship between the lifetime exposure to potentially traumatic events, in particular loss events, and lifetime post-traumatic stress symptoms and the severity of illness and HRQoL in patients with FM.**

*Clin Exp Rheumatol*. 2011 Nov–Dec; 29(6 Suppl 69):S73–8. Epub 2012 Jan 3

Friedberg F, Williams DA, Collinge W

## **Lifestyle-oriented non-pharmacological treatments for fibromyalgia: a clinical overview and applications with home-based technologies**

Fibromyalgia (FM) is a persistent and disabling widespread pain condition often accompanied by chronic fatigue, cognitive problems, sleep disturbance, depression, anxiety, and headache. To date, the most thoroughly studied non-pharmacological approaches to managing FM are those with a focus on changing patient activities and beliefs that affect the illness. These interventions are intended to facilitate enduring improvement in pain and functional status. **Lifestyle-oriented treatments include patient education, aerobic or other physical exercise, and cognitive-behavioral therapy (CBT).** These interventions in FM can be delivered in medical or behavioral health care settings by trained professionals, through patient-oriented treatment manuals, or via remote-access technologies. Non-pharmacological treatments, in particular exercise and CBT, have yielded effect sizes and cost-benefit ratios comparable to medications. This paper describes lifestyle-oriented non-pharmacological treatments for FM and highlights selected literature reviews of these interventions. **In addition, behavioral and practical issues are addressed that may affect these non-pharmacological treatments, including patient expectations, participant burden, and treatment availability.** Recommendations are made to facilitate these interventions and potentially improve outcomes. In particular, the increasing availability of convenient home-based mobile technologies to deliver these non-pharmacological treatments is described.

*J Pain Res.* 2012; 5:425–35. Epub 2012 Oct 25

Ghazan-Shahi S, Towheed T, Hopman W

## **Should rheumatologists retain ownership of fibromyalgia? A survey of Ontario rheumatologists**

Fibromyalgia is a controversial widespread chronic pain disorder that includes a wide constellation of somatic and emotional symptoms. This study surveyed the opinion of Ontario rheumatologists with respect to their beliefs about the nature and management of fibromyalgia. A key objective was to ascertain if rheumatologists should continue to be the main care providers for these patients. A survey comprising 13 questions was sent electronically to all 150 Ontario rheumatologists. The questionnaire was designed to obtain demographic data as well as opinions regarding different aspects of fibromyalgia. Data were analysed descriptively, and comparisons were made using chi-square tests. A total of 80 respondents completed our survey for a completion rate of 53%. The majority had completed their training in Canada (85%) and had been practising for more than 15 years (50%). Key findings were: (1) 71% believe that rheumatologists should not retain ownership of fibromyalgia, (2) **55% believe that fibromyalgia is**

**primarily a psychosomatic illness as opposed to a physical illness**, (3) 89% believe that the family physician should be the main care provider for these patients, and (4) rheumatologists who consider fibromyalgia to be a physical illness were also significantly more likely to believe that rheumatologists should retain ownership of this disease ( $p = 0.023$ ) and were more likely to continue managing these patients in their practice ( $p = 0.011$ ). The majority of Ontario rheumatologists do not wish to retain ownership of fibromyalgia. However, most of them continue to manage these patients, even though they believe that the family physician should be the main care provider for patients with fibromyalgia. **Rheumatologists may be providing care to these patients primarily because this care is not available to them from their primary care physicians.**

*Clin Rheumatol.* 2012 May 2. [Epub ahead of print]

Góes SM, Leite N, Shay BL, Homann D, Stefanello JM, Rodacki AL

### **Functional capacity, muscle strength and falls in women with fibromyalgia**

BACKGROUND: Patients with fibromyalgia have difficulty with activities of daily living: they exhibit reduced muscle strength and high incidence of reported falls. The objective of this study was to evaluate the functional performance and lower limb muscle strength in women with fibromyalgia and determine the relationship between muscle strength and falls. METHODS: Sixteen females with fibromyalgia and 16 healthy women participated in the study. Pain intensity, fibromyalgia impact on quality of life, physical activity level and fall prevalence were assessed. The peak torque and the rate of torque development were determined in maximal voluntary isometric contraction (hip, knee and ankle joints) using a load cell. The 30s chair stand, 8ft up and go, sit and reach, and functional reach tests were used to characterize functional performance. FINDINGS: Women with fibromyalgia showed deficits in lower limb muscle strength, balance and agility and exhibited decreased knee extension peak torque and rate of torque development. In addition, they showed lower hip adduction and extension peak torque in comparison to the control group ( $P > 0.05$ ). Hip extension rate of torque development, duration of fibromyalgia symptoms, overall pain, knee pain, and fibromyalgia impact were strong predictors of the number of falls in patients with fibromyalgia ( $R^2 = 0.86$ ;  $P < 0.05$ ), when considered collectively. INTERPRETATION: Women with fibromyalgia showed reduced functional performance and lower limb muscle strength, mostly explained by pain. **There was a high prevalence of falls in this population, as explained by hip extensors rate of torque development, duration of fibromyalgia symptoms and pain.** Copyright © 2011 Elsevier Ltd. All rights reserved.

*Clin Biomech* (Bristol, Avon). 2012 Jan 7 [Epub ahead of print]

Gracely RH, Ceko M, Bushnell MC

### **Fibromyalgia and depression**

Fibromyalgia and depression might represent two manifestations of affective spectrum disorder. They share similar pathophysiology and are largely targeted by the same drugs with dual action on serotonergic and noradrenergic systems. Here, we review evidence for genetic and environmental factors that predispose, precipitate, and perpetuate fibromyalgia and depression and include laboratory findings on the role of depression in fibromyalgia. Further, we comment on several aspects of fibromyalgia which support the development of reactive depression, substantially more so than in other chronic pain syndromes. However, while sharing many features with depression, fibromyalgia is associated with somatic comorbidities and absolutely defined by fluctuating spontaneous widespread pain. **Fibromyalgia may, therefore, be more appropriately grouped together with other functional pain disorders, while psychologically distressed subgroups could be grouped additionally or solely with affective spectrum disorders.**

*Pain Res Treat.* 2012; 2012:486590. Epub 2011 Nov 19

Hassett AL, Epel E, Clauw DJ, Harris RE, Harte SE, Kairys A, Buyske S, Williams DA

### **Pain is associated with short leukocyte telomere length in women with fibromyalgia**

Telomere length, considered a measure of biological aging, is linked to morbidity and mortality. Psychosocial factors associated with shortened telomeres are also common in chronic pain; yet, little is known about telomere length in pain populations. Leukocyte telomere length was evaluated in 66 women with fibromyalgia and 22 healthy female controls. Participants completed questionnaires and a subgroup of fibromyalgia patients underwent quantitative sensory testing (QST; n = 12) and neuroimaging (n = 12). Telomere length was measured using the quantitative polymerase chain reaction method. Although patients had shorter telomere length than controls, the difference was not statistically significant. However, higher levels of pain within fibromyalgia were associated with shorter telomere length (P = .039). When pain and depression were combined, patients categorized as high-pain/high-depression had an age-adjusted telomere length 265 base pairs shorter than those with low-pain/low-depression (P = .043), a difference consistent with approximately 6 years of chronological aging. In the subset tested, telomere length was also related to pain threshold and pain sensitivity, as well as gray matter volume, such that patients with shorter telomeres were more sensitive to evoked pain and had less gray matter in brain regions associated with pain processing (e.g., primary somatosensory cortex). These preliminary data support a relationship between pain and telomere length. **PERSPECTIVE: Our findings support a link between premature cellular aging and chronic pain. These preliminary data imply that chronic pain is a more**

**serious condition than has typically been recognized in terms of bodily aging.**  
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*J Pain.* 2012 Oct; 13(10):959–69

Häuser W, Wolfe F

### **Diagnosis and diagnostic tests for fibromyalgia (syndrome)**

**OBJECTIVES:** To present diagnostic criteria for the clinical diagnosis of fibromyalgia syndrome (FMS) and to offer a scheme for diagnostic work-up in clinical practice. **METHODS:** Narrative review of the literature, consensus documents by the American College of Rheumatology (ACR), evidence-based interdisciplinary German guidelines on the diagnosis and management of FMS. **RESULTS:** The ACR 1990 classification criteria emphasized tender points and widespread pain as the key features of FMS. In 2010, the ACR proposed preliminary diagnostic criteria for fibromyalgia that abandoned the tender point count and placed increased emphasis of patient symptoms. A later modification of the ACR 2010 criteria for use in surveys employed a self-report questionnaire (Fibromyalgia Survey Questionnaire, FSQ) to assess patient symptoms. The FSQ can be used to assist physicians' diagnosis of FMS. We recommend a stepwise diagnostic work-up of patients with chronic widespread pain (CWP) in primary care: Complete medical history including medication, complete medical examination, basic laboratory tests to screen for inflammatory or endocrinology diseases, referral to specialists only in case of suspected somatic diseases, assessment of limitations of daily functioning, screening for other functional somatic symptoms and mental disorders, and referring to mental health specialists in case of mental disorder. **CONCLUSIONS: The diagnosis of FMS is easy in most patients with CWP and does not ordinarily require a rheumatologist. A rheumatologist's expertise might be needed to exclude difficult to diagnose or concomitant inflammatory rheumatic diseases. In the presence of mental illness, referral to a mental health specialist for evaluation is recommended.**

*Reumatismo.* 2012 Sep 28; 64(4):194–205

Häuser W, Wolfe F, Tölle T, Uçeyler N, Sommer C

### **The role of antidepressants in the management of fibromyalgia syndrome: a systematic review and meta-analysis**

**BACKGROUND:** The role of antidepressants in the management of fibromyalgia syndrome (FMS) still needs to be determined. **OBJECTIVE:** The objective of this study was to provide a quantitative analysis (meta-analysis) of the efficacy and harms of antidepressants in the management of adult FMS patients. **DATA SOURCES:** The data sources used were the databases MEDLINE, SCOPUS and the Cochrane Central Register of Controlled Trials (until December 30, 2010), the reference lists of included articles, and the websites of the US National Institutes

of Health (NIH) and the Pharmaceutical Research and Manufacturers of America (PhRMA). **STUDY SELECTION:** Studies with a randomized controlled trial (RCT) design comparing any types of antidepressants with pharmacological placebo or head-to-head comparisons of different types of antidepressants in FMS patients were included. RCTs in which antidepressants were combined with any other defined treatment or antidepressants were tested against anything but drug placebo were excluded. Patients diagnosed with FMS according to predefined criteria of any age were included. To be included, studies had to assess at least one key domain of FMS (pain, sleep, fatigue, health-related quality of life [HRQOL]) as outcomes of efficacy and report total treatment discontinuation rates and/or dropout rates due to adverse events as outcomes for harms. **DATA EXTRACTION:** Data were extracted according to protocols of previous systematic reviews on antidepressants in FMS. Methodology quality was assessed by the van Tulder score. **DATA SYNTHESIS:** Standardized mean differences (SMD) were calculated for continuous outcomes by means and standard deviations and relative risks (RR) for 30% pain reduction and total dropout rate for comparisons of antidepressants with placebo. Examination of the combined results was performed by a random effects model. We used Cohen's categories to evaluate the magnitude of the effect size, calculated by SMD. Heterogeneity was tested by the I<sup>2</sup> statistic. Thirty-five studies were included in the meta-analysis. The SMDs of serotonin noradrenaline (norepinephrine) reuptake inhibitors (SNRIs) on pain, sleep, fatigue, depression and HRQOL were significant. Based on Cohen's categories, the effect size on pain was small and the ones on sleep, fatigue, depression and HRQOL were not substantial. 1481/3528 (42.0%) patients with SNRIs and 737/2304 (32.0%) patients with placebo reported a 30% pain reduction (number needed to treat [NNT] 10.0; 95% CI 8.00, 13.4; 12 = 4%). The RR of dropouts due to adverse events was 1.83 (95% CI 1.53, 2.18; 12 = 33%). The SMDs of selective serotonin reuptake inhibitors (SSRIs) on pain, sleep, depression and HRQOL were significant. Based on Cohen's categories, the effect sizes on pain, depression and HRQOL were small and the one on sleep not substantial. 72/198 (36.4%) patients with SSRIs and 40/194 (20.6%) patients with placebo reported a 30% pain reduction (NNT 6.3; 95% CI 4.1, 14.1). The RR of dropouts due to adverse events was 1.60 (95% CI 0.84, 3.04; 12 = 0%). The SMDs of tricyclic antidepressants (TCAs) on pain, sleep, fatigue and HRQOL were significant. Based on Cohen's categories, the effect sizes on pain and sleep were moderate and the ones on fatigue and HRQOL were small. 140/290 (48.3%) patients with TCAs and 70/252 (27.8%) patients with placebo reported a 30% pain reduction (NNT 4.9; 95% CI 3.5, 8.0). The RR of dropouts due to adverse events was 0.84 (95% CI 0.46, 1.52; 12 = 0%). **CONCLUSIONS:** The TCA amitriptyline and the SNRIs duloxetine and milnacipran are first-line options for the treatment of FMS patients. **Physicians and patients should be realistic about the potential benefits of antidepressants in FMS. A small number of patients experience a substantial symptom relief with no or minor adverse effects. However, a remarkable number of patients drop out of therapy because of intolerable adverse effects or experience only a small relief of symptoms, which does not outweigh the adverse effects.**

CNS Drugs. 2012 Apr 1; 26(4):297–307

Jensen KB, Loitole R, Kosek E, Petzke F, Carville S, Fransson P, Marcus H, Williams SC, Choy E, Mainguy Y, Vitton O, Gracely RH, Gollub R, Ingvar M, Kong J

### **Patients with fibromyalgia display less functional connectivity in the brain's pain inhibitory network**

**BACKGROUND:** There is evidence for augmented processing of pain and impaired endogenous pain inhibition in fibromyalgia syndrome (FM). In order to fully understand the mechanisms involved in FM pathology, there is a need for closer investigation of endogenous pain modulation. In the present study, we compared the functional connectivity of the descending pain inhibitory network in age-matched FM patients and healthy controls (HC). We performed functional magnetic resonance imaging (fMRI) in 42 subjects; 14 healthy and 28 age-matched FM patients (2 patients per HC), during randomly presented, subjectively calibrated pressure pain stimuli. A seed-based functional connectivity analysis of brain activity was performed. The seed coordinates were based on the findings from our previous study, comparing the fMRI signal during calibrated pressure pain in FM and HC: the rostral anterior cingulate cortex (rACC) and thalamus. **RESULTS:** FM patients required significantly less pressure (kPa) to reach calibrated pain at 50 mm on a 0–100 visual analogue scale ( $p < .001$ , two-tailed). During fMRI scanning, the rACC displayed significantly higher connectivity to the amygdala, hippocampus, and brainstem in healthy controls, compared to FM patients. There were no regions where FM patients showed higher rACC connectivity. Thalamus showed significantly higher connectivity to the orbito-frontal cortex in healthy controls but no regions showed higher thalamic connectivity in FM patients. **CONCLUSION:** Patients with FM displayed less connectivity within the brain's pain inhibitory network during calibrated pressure pain, compared to healthy controls. **The present study provides brain-imaging evidence on how brain regions involved in homeostatic control of pain are less connected in FM patients. It is possible that the dysfunction of the descending pain modulatory network plays an important role in maintenance of FM pain** and our results may translate into clinical implications by using the functional connectivity of the pain modulatory network as an objective measure of pain dysregulation.

*Mol Pain.* 2012 Apr 26; 8(1):32. [Epub ahead of print]

Kadetoff D, Lampa J, Westman M, Andersson M, Kosek E

### **Evidence of central inflammation in fibromyalgia: increased cerebrospinal fluid interleukin-8 levels**

Activation of glia cells resulting in intrathecal elevation of cytokines and chemokines has been hypothesized in chronic pain syndromes such as fibromyalgia. To our knowledge, this is the first study assessing intrathecal concentrations of pro-inflammatory substances in fibromyalgia. We report elevated cerebrospinal fluid and serum concentrations of interleukin-8, but not interleukin-1beta, in FM

patients. **This profile is in accordance with FM symptoms being mediated by sympathetic activity rather than dependent on prostaglandin associated mechanisms and supports the hypothesis of glia cell activation in response to pain mechanisms.** Copyright © 2011 Elsevier B.V. All rights reserved.

*J Neuroimmunol.* 2012 Jan 18; 42(1–2):33–8. Epub 2011 Nov 2

Klaver-Król EG, Rasker JJ, Henriquez NR, Verheijen WG, Zwarts MJ

### **Muscle fiber velocity and electromyographic signs of fatigue in fibromyalgia**

INTRODUCTION: Fibromyalgia (FM) is a disorder of widespread muscular pain. We investigated possible differences in surface electromyography (sEMG) in clinically unaffected muscle between patients with FM and controls. METHODS: sEMG was performed on the biceps brachii muscle of 13 women with FM and 14 matched healthy controls during prolonged dynamic exercises, unloaded, and loaded up to 20% of maximum voluntary contraction. The sEMG parameters were: muscle fiber conduction velocity (CV); skewness of motor unit potential (peak) velocities; peak frequency (PF) (number of peaks per second); and average rectified voltage (ARV). RESULTS: There was significantly higher CV in the FM group. Although the FM group performed the tests equally well, their electromyographic fatigue was significantly less expressed compared with controls (in CV, PF, and ARV). CONCLUSION: **In the patients with FM, we clearly showed functional abnormalities of the muscle membrane, which led to high conduction velocity and resistance to fatigue in electromyography.** Copyright © 2012 Wiley Periodicals, Inc.

*Muscle Nerve.* 2012 Nov; 46(5):738–45

Klein CJ, Lennon VA, Aston PA, McKeon A, Pittock SJ

### **Chronic pain as a manifestation of potassium channel-complex autoimmunity**

OBJECTIVE: Autoantibodies targeting voltage-gated potassium channel (VGKC) complexes cause a spectrum of neuronal hyperexcitability disorders. We investigated pain as a manifestation of VGKC-complex autoimmunity. METHODS: We reviewed the prevalence and characteristics of pain in VGKC-complex-immunoglobulin G (IgG)-seropositive patients in 25 months of comprehensive service testing for neural autoantibodies, subtyped positive sera for LGI1-IgG and CASPR2-IgG specificities, and reviewed pain prevalence in autoimmune control patients. RESULTS: VGKC-complex-IgG was identified in 1,992 patients of 54,853 tested (4%). Of 316 evaluated neurologically at Mayo Clinic, 159 (50%) had pain, in isolation (28%) or with accompanying neurologic manifestations (72%), and not attributable to alternative cause. Pain was subacute in onset, chronic in course, neuropathic, nociceptive, regional, or diffuse and sometimes

attributed to fibromyalgia (6%) or psychogenic cause (13%). Most patients had normal peripheral nervous system function, measured by neuropathy impairment scores and nerve conduction. Evidence of neuronal hyperexcitability, quantitative heat-pain hyperalgesia, or electromyographic excitability was 25-fold more common in pain patients. Pain management required multiple medications in 70% (narcotics, 30%); 13 of 16 patients reported pain relief with immunotherapy. Pain was significantly associated with CASPR2-IgG-positivity (16% positive with pain, 7% without pain;  $p = 0.014$ ) but not with LGI1-IgG. Less than 10% of 167 patients with neural autoantibodies other than VGKC-complex-IgG reported pain. **CONCLUSIONS: Chronic idiopathic pain is a syndromic manifestation of VGKC-complex autoimmunity.** Hyperexcitability of nociceptive pathways is implicated. CASPR2-IgG significantly associates with pain, but in most patients the antigenic VGKC-complex molecule remains to be determined. **VGKC-complex autoimmunity represents an important new direction for pain research and therapy.**

*Neurology.* 2012 Sep 11; 79(11):1136–44. Epub 2012 Aug 15

Low LA, Schweinhardt P

### **Early life adversity as a risk factor for fibromyalgia in later life**

The impact of early life events is increasingly becoming apparent, as studies investigate how early childhood can shape long-term physiology and behaviour. Fibromyalgia (FM), which is characterised by increased pain sensitivity and a number of affective co-morbidities, has an unclear etiology. **This paper discusses risk factors from early life that may increase the occurrence or severity of FM in later life:** pain experience during neonatal life causes long-lasting changes in nociceptive circuitry and increases pain sensitivity in the older organism; premature birth and related stressor exposure cause lasting changes in stress responsiveness; maternal deprivation affects anxiety-like behaviours that may be partially mediated by epigenetic modulation of the genome—all these adult phenotypes are strikingly similar to symptoms displayed by FM sufferers. In addition, childhood trauma and exposure to substances of abuse may cause lasting changes in developing neurotransmitter and endocrine circuits that are linked to anxiety and stress responses.

*Pain Res Treat.* 2012; 2012:140832. Epub 2011 Oct 12

Martinez-Lavin M

### **Fibromyalgia: when distress becomes (un)sympathetic pain**

Fibromyalgia is a painful stress-related disorder. A key issue in fibromyalgia research is to investigate how distress could be converted into pain. The sympathetic nervous system is the main element of the stress response system. In animal models, physical trauma, infection, or distressing noise can induce abnormal connections between the sympathetic nervous system and the noci-

ceptive system. Dorsal root ganglia sodium channels facilitate this type of sympathetic pain. Similar mechanisms may operate in fibromyalgia. Signs of sympathetic hyperactivity have been described in this condition. Genetic factors and/or distressful lifestyle may lead to this state of sympathetic hyperactivity. Trauma and infection are recognized fibromyalgia triggers. Women who suffer from fibromyalgia have catecholamine-evoked pain. Sympathetic dysfunction may also explain nonpain-related fibromyalgia symptoms. In conclusion, **in fibromyalgia, distress could be converted into pain through forced hyperactivity of the sympathetic component of the stress response system.**

*Pain Res Treat.* 2012; 2012:981565. Epub 2011 Sep 19

McBeth J, Prescott G, Scotland G, Lovell K, Keeley P, Hannaford P, McNamee P, Symmons DP, Woby S, Gkazinou C, Beasley M, Macfarlane GJ

### **Cognitive behavior therapy, exercise, or both for treating chronic widespread pain**

BACKGROUND: The clinical impact of telephone-delivered cognitive behavioral therapy (TCBT), exercise, or a combined intervention in primary care patients with chronic widespread pain (CWP) is unclear. METHODS: A total of 442 patients with CWP (meeting the American College of Rheumatology criteria) were randomized to receive 6 months of TCBT, graded exercise, combined intervention, or treatment as usual (TAU). The primary outcome, using a 7-point patient global assessment scale of change in health since trial enrollment (range: very much worse to very much better), was assessed at baseline and 6 months (intervention end) and 9 months after randomization. A positive outcome was defined as “much better” or “very much better.” Data were analyzed using logistic regression according to the intention-to-treat principle. RESULTS: The percentages reporting a positive outcome at 6 and 9 months, respectively, were TAU group, 8% and 8%; TCBT group, 30% and 33%; exercise group, 35% and 24%; and combined intervention group, 37% and 37% ( $P < .001$ ). After adjustment for age, sex, center, and baseline predictors of outcome, active interventions improved outcome compared with TAU: TCBT (6 months: odds ratio [OR], 5.0 [95% CI, 2.0-12.5]; 9 months: OR, 5.4 [95% CI, 2.3-12.8]), exercise (6 months: OR, 6.1 [95% CI, 2.5-15.1]; 9 months: OR, 3.6 [95% CI, 1.5-8.5]), and combined intervention (6 months: OR, 7.1 [95% CI, 2.9-17.2]; 9 months: OR, 6.2 [95% CI, 2.7-14.4]). **At 6 and 9 months, combined intervention was associated with improvements in the 36-Item Short Form Health Questionnaire physical component score and a reduction in passive coping strategies.** Conclusions on cost-effectiveness were sensitive to missing data. CONCLUSION: TCBT was associated with substantial, statistically significant, and sustained improvements in patient global assessment.

*Arch Intern Med.* 2012 Jan 9; 172(1):48–57. Epub 2011 Nov 14

McCarberg BH

### **Clinical overview of fibromyalgia**

Fibromyalgia (FM) is a complex disorder that affects up to 5% of the general population worldwide, more frequently in women than in men. In addition to chronic widespread pain, patients with FM usually experience other characteristic symptoms, including fatigue, disturbed sleep, stiffness, reduced functioning, dyscognition, and depressed mood. Many patients also have comorbid conditions such as depression, irritable bowel syndrome, temporomandibular disorder, or migraine. Although the etiology of FM remains unclear, evidence suggests that biologic, genetic, and environmental factors are involved. The variability of symptoms and the frequency of comorbidities among patients with FM make this a difficult disorder to diagnose. Diagnosis may be further complicated by the stigmatization of this disorder among treatment providers, the health insurance industry, and the general population. Treating chronic pain disorders such as FM can be time consuming and costly, and other issues such as polypharmacy, treatment adherence, and access to treatment often need to be addressed. The aim of this article is to provide physicians with a general overview of FM, including a brief review of the pathophysiology that explains the biologic and genetic bases of this disorder. Also **included is a synopsis of new diagnostic criteria and other useful diagnostic tools and a discussion of various treatment challenges and strategies.**

*Am J Ther.* 2012 Sep;19(5):357–68

Napadow V, Kim J, Clauw DJ, Harris RE

### **Decreased intrinsic brain connectivity is associated with reduced clinical pain in fibromyalgia**

**OBJECTIVE:** A major impediment to the development of novel treatment strategies for fibromyalgia (FM) is the lack of an objective marker that reflects spontaneously reported clinical pain in patients with FM. Studies of resting-state intrinsic brain connectivity in FM have demonstrated increased insular connectivity to the default mode network (DMN), a network whose activity is increased during nontask states. Moreover, increased insular connectivity to the DMN was associated with increased spontaneous pain levels. However, as these analyses were cross-sectional in nature, they provided no insight into dynamic changes in connectivity or their relationship to variations in self-reported clinical pain. The purpose of this study was to evaluate longitudinal changes in the intrinsic brain connectivity of FM patients treated with nonpharmacologic interventions known to modulate pain levels in this patient population, and to test the hypothesis that the reduction of DMN-insula connectivity following therapy would correlate with diminished pain. **METHODS:** Seventeen FM patients underwent resting-state functional magnetic resonance imaging at baseline and following 4 weeks of a nonpharmacologic intervention to diminish pain. Intrinsic DMN connectivity was evaluated using probabilistic independent components analysis. Longitudinal

changes in intrinsic DMN connectivity were evaluated by paired analysis, and correlations between longitudinal changes in clinical pain and changes in intrinsic DMN connectivity were investigated by multiple linear regression analysis. Changes in clinical pain were assessed with the short form of the McGill Pain Questionnaire (SF-MPQ). RESULTS: Clinical pain as assessed using the sensory scale of the SF-MPQ was reduced following therapy (P=0.02). Intrinsic DMN connectivity to the insula was reduced, and this reduction correlated with reductions in pain (corrected P<0.05). CONCLUSION: **Our findings suggest that intrinsic brain connectivity can be used as a candidate objective marker that reflects changes in spontaneous chronic pain within individual FM patients.** We propose that intrinsic connectivity measures could potentially be used in either research or clinical settings as a complementary, more objective outcome measure for use in FM. Copyright © 2012 by the American College of Rheumatology

*Arthritis Rheum.* 2012 Jul; 64(7):2398–403

Reed C, Birnbaum HG, Ivanova JI, Schiller M, Waldman T, Mullen RE, Swindle R

### **Real-world role of tricyclic antidepressants in the treatment of fibromyalgia**

OBJECTIVE: To examine the real-world role of tricyclic antidepressants (TCAs) in fibromyalgia (FM) treatment. METHODS: Using privately insured U.S. administrative claims data, this study examined TCA use for newly diagnosed FM patients. Patients ages 18 to 64 years with  $\geq 2$  FM diagnoses (ICD-9-CM: 729.1) during Q1:2007 to Q1:2009, no previous FM diagnosis, and continuous eligibility for insurance during the year before and after the first FM diagnosis (“study period”) were identified as newly diagnosed (N = 10,129). Treatment with TCAs was examined over the first treatment episode (allowing up to a 45-day gap between refills). A sensitivity analysis was performed excluding patients with depression/anxiety diagnoses during the study period. RESULTS: During the study period, 8.9% of patients with FM used TCAs at any time, 5.0% used TCAs during the year before FM diagnosis, and 7.2% used TCAs during the year after. The mean (median) duration of the first treatment episode was 150 (58) days. During this episode, 84.0% used other medications concomitantly, with 60.3% using analgesics and 39.6% using other antidepressants. Additionally, 60.8% augmented TCA use with other drugs, 61.8% switched to another drug at the end of their TCA episode, and 22.8% discontinued TCAs without switching. Similar patterns were observed for the subset of patients with no depression or anxiety (N = 7,655). DISCUSSION: Research covering 1999 to 2005 using the same methods found that 15.9% of patients with FM used TCAs during the year before FM diagnosis and 20.7% used TCAs during the year after. These findings suggest that **TCA use among the patients with FM is uncommon and may be declining in real-world practice.** © 2012 The Authors. Pain Practice © 2012 World Institute of Pain

*Pain Pract.* 2012 Sep;12(7):533–40. Epub 2012 Jan 9

Riva R, Mork PJ, Westgaard RH, Lundberg U

### **Comparison of the cortisol awakening response in women with shoulder and neck pain and women with fibromyalgia**

Shoulder and neck pain (SNP) and fibromyalgia syndrome (FMS), two musculoskeletal conditions of unknown pathogenesis, share some common features in terms of altered neuroendocrine responses, pain and stress perception. However, the pain distribution in SNP is localized, whereas in FMS is more widespread. Because regional musculoskeletal pain may represent an intermediate stage along a continuum towards widespread musculoskeletal pain we compared the cortisol awakening response (CAR) in women with SNP with the CAR in FMS patients and healthy controls (HC) in a controlled hospital-hotel setting. The aim of the study was to investigate whether SNP is related to a deviant regulation of the hypothalamic-pituitary-adrenal (HPA) axis. Eighteen women with SNP, 29 female FMS patients, and 27 female HC participated in the study. Cortisol samples were collected upon awakening, [then] 30 and 60 min later. Questionnaires measuring pain levels, sleeping problems, perceived stress, and psychological characteristics were administered to the participants. Compared with HC, women with SNP had a tendency towards higher cortisol levels, whereas FMS had lower cortisol levels. Adjustment for potential confounders did not influence the results. Women with SNP and FMS patients reported more health complaints, pain, and perceived stress than the HC, but women with SNP were less affected than the FMS patients. Women with SNP showed a tendency towards an elevated HPA axis activity compared with HC. **The current findings may indicate that the hypercortisolism in regional musculoskeletal pain represent an intermediate stage towards the development of a hypocortisolism in widespread musculoskeletal pain.**

*Psychoneuroendocrinology*. 2012 Feb; 37(2):299–306. Epub 2011 Jul 18

Robinson RL, Kroenke K, Mease P, Williams DA, Chen Y  
D'Souza D, Wohlreich M, McCarberg B

### **Burden of illness and treatment patterns for patients with fibromyalgia**

**OBJECTIVE.** This study was designed to describe burden of illness and treatment patterns, and to examine the patient, physician, and care factors associated with the treatment choices of individuals receiving new prescriptions for fibromyalgia (FM). **DESIGN.** This is a baseline assessment of the Real-World Examination of Fibromyalgia: Longitudinal Evaluation of Costs and Treatments (REFLECTIONS), a prospective observational study. Baseline data (including a physician survey, a patient visit form, and computer-assisted telephone interviews) were collected from July 2008 through May 2010 in 58 care settings in the United States, including Puerto Rico. **RESULTS.** Patients (N = 1,700) were mostly female (94.6%) and white (82.9%). Mean age was 50.4 years and mean duration of illness was 5.6 years. Mean Fibromyalgia Impact Questionnaire total

score was 54.4 (range 0-80), and Brief Pain Inventory average pain severity level was 5.5 (range 0-10). Patients reported high annual health care use and numerous work limitations related to FM. Patients were taking 182 unique types of medications prescribed for FM, including duloxetine (26.8%), nonsteroidal anti-inflammatory drugs (26.6%), pregabalin (24.5%), opioids (24.2%), tramadol (15.3%), benzodiazepines (15.2%), cyclobenzaprine (12.9%), milnacipran (8.9%), and others. Most patients took more than one medication concurrently (77.8%). Type of current medications used was most strongly associated with medication history and physician specialty. **CONCLUSIONS. Burden of illness was high for patients with FM, and treatment patterns were highly variable. Importantly, the treatments with the most evidence to support their use were not always the most frequently chosen.** Wiley Periodicals, Inc.

*Pain Med.* 2012 Sep 7 [Epub ahead of print]

Shang Y, Gurley K, Symons B, Long D, Srikuea R,  
Crofford LJ, Peterson CA, Yu G

### **Noninvasive optical characterization of muscle blood flow, oxygenation, and metabolism in women with fibromyalgia**

**INTRODUCTION:** Women with fibromyalgia (FM) have symptoms of increased muscular fatigue and reduced exercise tolerance, which may be associated with alterations in muscle microcirculation and oxygen metabolism. This study used near-infrared diffuse optical spectroscopies to noninvasively evaluate muscle blood flow, blood oxygenation and oxygen metabolism during leg fatiguing exercise and during arm arterial cuff occlusion in post-menopausal women with and without FM. **METHODS:** Fourteen women with FM and twenty-three well-matched healthy controls participated in this study. For the fatiguing exercise protocol, the subject was instructed to perform 6 sets of 12 isometric contractions of knee extensor muscles with intensity steadily increasing from 20 to 70% maximal voluntary isometric contraction (MVIC). For the cuff occlusion protocol, forearm arterial blood flow was occluded via a tourniquet on the upper arm for 3 minutes. Leg or arm muscle hemodynamics, including relative blood flow (rBF), oxy- and deoxy-hemoglobin concentration ([HbO<sub>2</sub>] and [Hb]), total hemoglobin concentration (THC) and blood oxygen saturation (StO<sub>2</sub>), were continuously monitored throughout protocols using a custom-built hybrid diffuse optical instrument that combined a commercial near-infrared oximeter for tissue oxygenation measurements and a custom-designed diffuse correlation spectroscopy (DCS) flowmeter for tissue blood flow measurements. Relative oxygen extraction fraction (rOEF) and oxygen consumption rate (rVO<sub>2</sub>) were calculated from the measured blood flow and oxygenation data. Post-manipulation (fatiguing exercise or cuff occlusion) recovery in muscle hemodynamics was characterized by the recovery half-time, a time interval from the end of manipulation to the time that tissue hemodynamics reached a half-maximal value. **RESULTS:** Subjects with FM had similar hemodynamic and metabolic response/recovery patterns as healthy controls during exercise and during arterial occlusion. However, tissue

rOEF during exercise in subjects with FM was significantly lower than in healthy controls, and the half-times of oxygenation recovery ( $\Delta[\text{HbO}_2]$  and  $\Delta[\text{Hb}]$ ) were significantly longer following fatiguing exercise and cuff occlusion. **CONCLUSIONS: Our results suggest an alteration of muscle oxygen utilization in the FM population.** This study demonstrates the potential of using combined diffuse optical spectroscopies (i.e., NIRS/DCS) to comprehensively evaluate tissue oxygen and flow kinetics in skeletal muscle.

*Arthritis Res Ther.* 2012 Nov 1; 14(6):R236. [Epub ahead of print]

Srikuea R, Symons TB, Long DE, Lee JD, Shang Y, Chomentowski PJ, Yu G, Crofford LJ, Peterson CA

### **Fibromyalgia is associated with altered skeletal muscle characteristics which may contribute to post-exertional fatigue in post-menopausal women**

**OBJECTIVE:** To identify muscle physiological properties that may contribute to post-exertional fatigue and malaise in women with fibromyalgia (FM). **METHODS:** Healthy postmenopausal women with (n=11) and without (n=11) fibromyalgia, age 51-70 years, participated in this study. Physical characteristics along with self-reported questionnaires were evaluated. Strength loss and tissue oxygenation in response to a fatiguing exercise protocol were used to quantify fatigability and the local muscle hemodynamic profile. Muscle biopsies were obtained to assess between-group differences in baseline muscle properties using histochemical, immunohistochemical and electron microscopic analyses. **RESULTS:** No significant difference in muscle fatigue in response to exercise was apparent between healthy controls and subjects with FM. However, self-reported fatigue and pain were correlated to prolonged loss of strength following 12-min of recovery in subjects with FM. Although there was no difference in percent SDH positive (type I) and SDH negative (type II) fibers or in mean fiber cross-sectional area between groups, subjects with FM showed greater size variability and altered fiber size distribution. Only in healthy controls, fatigue-resistance was strongly correlated with the size of SDH positive fibers and hemoglobin oxygenation. By contrast, subjects with FM with the highest percentage of SDH positive fibers recovered strength most effectively, which was correlated to capillary density. However, overall, capillary density was lower in subjects with FM. **CONCLUSION: Peripheral mechanisms, i.e., altered muscle fiber size distribution and decreased capillary density, may contribute to post-exertional fatigue in subjects with FM.** Understanding these defects in fibromyalgic muscle may provide valuable insight for treatment.

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Staud R

### **Abnormal endogenous pain modulation is a shared characteristic of many chronic pain conditions**

The intensity of acute and chronic pain depends on interactions between peripheral impulse input and CNS pain mechanisms, including facilitation and inhibition. Whereas tonic pain inhibition is a characteristic of most pain-free individuals, pain facilitation can be detected in many chronic pain patients. The capability to inhibit pain is normally distributed along a wide continuum in the general population and can be used to predict chronic pain. Accumulating evidence suggests that endogenous pain inhibition depends on activation of the prefrontal cortex, periaqueductal gray and rostral ventral medulla. Quantitative sensory test paradigms have been designed to acquire detailed information regarding each individual's endogenous pain inhibition and facilitation. Such tests include: temporal summation of pain, which is mostly used to assess facilitatory pain modulation by measuring the change in pain perception during a series of identical nociceptive stimuli; and conditioned pain modulation, which tests pain inhibition by utilizing two simultaneously applied painful stimuli (the 'pain inhibits pain' paradigm). **Considerable indirect evidence seems to indicate that not only increased pain facilitation but also ineffective pain inhibition represents a predisposition for chronic pain.** This view is supported by the fact that many chronic pain syndromes (e.g., fibromyalgia, temporomandibular joint disorder, irritable bowel syndrome, headache and chronic fatigue syndrome) are associated with hypersensitivity to painful stimuli and reduced endogenous pain inhibition. However, future prospective studies will be necessary to provide definitive evidence for this relationship. Such research would not only provide important information about mechanisms relevant to chronic pain but would also permit identification of individuals at high risk for future chronic pain.

*Expert Rev Neurother.* 2012 May;12(5):577–85

Staud R

### **Brain imaging in fibromyalgia syndrome**

Fibromyalgia (FM) is a chronic musculoskeletal pain syndrome which is characterised by clinical pain as well as widespread hyperalgesia/allodynia to mechanical, thermal, electrical, and chemical stimuli. Lack of consistent tissue abnormalities in FM patients has more and more shifted the focus away from peripheral factors and towards central nervous system abnormalities including central sensitisation as well as aberrant pain facilitation and inhibition. Besides quantitative sensory testing, functional brain imaging has been increasingly utilised to characterise the abnormal pain processing of FM patients. Whereas initial work in FM patients identified abnormally increased pain-related brain activity within the thalamus, insula, anterior cingulate, S1, and prefrontal cortex (so-called 'pain matrix'), more recent research focused on altered 'connectivity' between multiple interconnected brain networks in these patients. Additionally,

magnetic resonance spectroscopy studies demonstrated high concentration of the excitatory neurotransmitter glutamate in FM patients in pain-related brain areas which correlated not only with experimental but also with clinical pain ratings. **Overall, functional brain imaging studies have provided compelling evidence for abnormal pain processing in FM, including brain activity that correlated with patients' augmented pain sensitivity (hyperalgesia/allodynia), temporal summation of pain, and prolonged pain aftersensations.** Future imaging work needs to focus on identifying the neural correlates of FM patients' abnormal endogenous pain modulation which will likely not only shed more light on this important pain regulatory mechanism but may also provide useful information for future treatments of FM symptoms.

*Clin Exp Rheumatol.* 2011 Nov–Dec; 29(6 Suppl 69):S109–17. Epub 2012 Jan 3

van Wilgen CP, Vuijk PJ, van Ittersum MW, Nijs J

### **Not throwing out the baby with the bathwater: lessons from the Fibromyalgia Impact Questionnaire**

The Fibromyalgia Impact Questionnaire (FIQ) is the most frequently used questionnaire in patients with fibromyalgia in the last 20 years. Recently, a revised version of the FIQ has been published. In this study, we examined the factor structure of the original version using explorative and confirmative factor analyses in a representative group of about 500 Dutch and Belgian patients with fibromyalgia, in which the work-related item was excluded. The FIQ consists of a three-factor structure with a functional domain (ten items), physical symptom domain (six items), and mental symptom domain (two items), which is the most accurate. **From the data presented, it is concluded that the [original] FIQ is a solid, worldwide-used questionnaire with a history of 20 years consisting of three domains.** When constructing a revised FIQ, the results of this study can be incorporated.

*Clin Rheumatol.* 2012 Nov 30. [Epub ahead of print]

Veldhuijzen DS, Sondaal SF, Oosterman JM

### **Intact cognitive inhibition in patients with fibromyalgia but evidence of declined processing speed**

Patients with fibromyalgia frequently report cognitive complaints. In this study we examined performance on 2 cognitive inhibition tests, the Stroop Color-Word Test (SCWT) and the Multi-Source Interference Test (MSIT), in 35 female patients with fibromyalgia and 35 age-matched healthy female controls. Experimental pressure pain thresholds (PPT) were determined, and fibromyalgia patients rated their current pain on a visual analog scale and completed the pain and fatigue subscales of the Fibromyalgia Impact Questionnaire. Further, all subjects completed questionnaires assessing symptoms of pain catastrophizing, depression, and

anxiety. Significant group differences were found for SCWT and MSIT performance in both the neutral (N) and interference (I) conditions with slower reaction times in patients versus controls. However, no significant group differences were found for the difference (I-N) or proportion (I/N) scores, or on the number of errors made. For patients, pain experienced during PPT correlated significantly to several indices of cognition. Psychosocial variables were not related to cognitive test performance. Fibromyalgia patients performed worse on both tests but to a similar extent for the neutral condition and the interference condition, indicating that there is no specific problem in cognitive inhibition. Evidence of decreased mental processing and/or psychomotor speed was found in patients with fibromyalgia. PERSPECTIVE: Fibromyalgia patients performed worse on interference tests, but no specific problem in cognitive inhibition was found. **Decreased reaction time performance may instead point to an underlying problem of psychomotor or mental processing speed in fibromyalgia.** Future studies should examine potential deficits in psychomotor function in fibromyalgia patients in more detail.

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Wilson B, Spencer H, Kortebein P

### **Exercise recommendations in patients with newly diagnosed fibromyalgia**

OBJECTIVE: To evaluate exercise recommendations in patients newly diagnosed with fibromyalgia. DESIGN: A retrospective chart review. SETTING: A public university rheumatology clinic. PATIENTS: Patients newly diagnosed with fibromyalgia (N = 122). MAIN OUTCOME MEASUREMENTS: Frequency and type of exercise recommendations. RESULTS: The mean (standard deviation) age of these patients with fibromyalgia was 45 ±12 years; 91% were women. Exercise was recommended as part of the documented treatment plan in 47% of these patients (57/122); only 3 patients had a documented contraindication for exercise. Aquatic exercise was most frequently recommended (56% [32/57]), followed by combined aquatic-aerobic exercise (26% [15/57]), and, infrequently, aerobic exercise only (5% [3/57]); only 7% of these patients (4/57) were referred for physical therapy. The primary method of communication was verbal discussion (94% [54/57]). CONCLUSIONS: **Although there is well-documented evidence that exercise is beneficial for patients with fibromyalgia, we found that less than half of patients with newly diagnosed fibromyalgia in our study were provided recommendations to initiate an exercise program as part of their treatment plan.** Further investigation of these findings are warranted, including evaluation of other university and community rheumatology practices as well as that of other physicians caring for patients with fibromyalgia. However, **our findings indicate that there appears to be an opportunity to provide more specific and practical education regarding the implementation of an exercise regimen for patients with newly diagnosed fibromyalgia.** Psychiatrists may be particularly

well suited to manage the exercise component of patients with fibromyalgia because of their specialized training in exercise prescription.

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