

Oral Presentation
Free Presentations 12: Best Selected Abstracts

Abstract: 150

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S52

A COMPARISON OF THE US-AMERICAN AND GERMAN GUIDELINE WITH EULAR RECOMMENDATIONS FOR THE MANAGEMENT OF FIBROMYALGIA

W. Häuser^{1,4}, **K. Thieme**², T. Denis³

¹ *Klinikum Saarbrücken, Saarbrücken, Germany*

² *Department of Clinical and Cognitive Neuroscience, University of Heidelberg, Central Institute of Mental Health, Mannheim, Germany*

³ *Department of Anesthesiology, University of Washington, Seattle, United States*

⁴ *Interdisciplinary center of pain therapy, Saarbrücken, Germany*

Objective: To compare evidence-based guidelines for the management of fibromyalgia syndrome (FMS).

Methods: Systematic searches up to April 2008 of the US-American National Guideline Clearing House, the Scottish Intercollegiate Guidelines Network, the Association of the Scientific Medical Societies in Germany (AWMF) and Medline were conducted. Three evidence-based guidelines for the management of FMS published by professional organizations were identified: The American Pain Society (APS) (2005), the European League Against Rheumatism (EULAR) (2007), and the AWMF (2008). The composition of panels, search strategies, categorization of evidence and recommendations, methods for developing recommendations and the recommendations of the 3 guidelines were compared and contrasted.

Results: The steering committees and panels of APS and AWMF were comprised of multiple disciplines engaged in the management of FMS and included patients, whereas the task force of EULAR only consisted of physicians, predominately rheumatologists. APS and AWMF ascribed the highest level of evidence to systematic reviews and meta-analyses, whereas EULAR credited the highest level of evidence to randomised controlled studies. Both APS and AWMF assigned the highest level of recommendation to aerobic exercise, cognitive-behavioral therapy, amitriptyline, and multicomponent treatment. In contrast, EULAR assigned the highest level of recommendation to a set of to pharmacological treatment.

Conclusion: The APS and AWMF guidelines assigned higher ratings to CBT and multicomponent treatments. The inconsistencies across guidelines are likely attributable to the criteria used for study inclusion, weighting systems, and composition of the panels.

W. Häuser received honoraria by Elli Lilly, Janssen-Cilag, Mundipharma and Pfizer for educational lectures

Abstract: 517

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S153

A COMPARISON OF TWO MULTIDISCIPLINARY INPATIENT REHABILITATION PROGRAMMES FOR FIBROMYALGIA: A REGISTER LINKAGE STUDY ON WORK DISABILITY

H. Suovriö¹, T. Oksanen², K. Hinkka³, J. Pentti², M. Kivimäki⁴, T. Klaukka³, J. Vahtera²

¹ *The Hospital District of South Ostrobothnia, Seinäjoki, Finland*

² *Finnish Institute of Occupational Health, Turku, Finland*

³ *Research Department, Social Insurance Institution of Finland, Turku, Finland*

⁴ *Department of Epidemiology and Public Health, University College London, London, United Kingdom*

Background: Patients with fibromyalgia have a high risk of temporary and permanent work disability. Little is known about the effects of fibromyalgia rehabilitation on work disability.

Aims: To determine whether a specific fibromyalgia rehabilitation programme is superior to a non-specific musculoskeletal rehabilitation of patients with fibromyalgia in terms of work disability.

Methods: A prospective observational study of 215 local government employees with a 6-year post-intervention follow-up to monitor the occurrence of long sick-leave and disability pensions among the participants of two different fibromyalgia rehabilitation programmes.

Results: Specific fibromyalgia rehabilitation was not superior to a non-specific musculoskeletal rehabilitation, with the corresponding hazard ratios (95% confidence intervals) after adjustments being 1.02 (0.75-1.40) for long sick-leave, 1.18 (0.75-1.87) for very long sick-leave, and 1.07 (0.63-1.83) for disability pension.

Conclusion: The results suggest that in reducing work disability among patients with fibromyalgia a specific multidisciplinary fibromyalgia rehabilitation programme practised in Finland provides no benefit compared with non-specific multidisciplinary musculoskeletal rehabilitation. Further research is needed to develop an optimal programme (or several different programmes) to control the burden of work disability related to fibromyalgia.

Abstract: 515

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S152

A CROSS SECTIONAL COHORT SURVEY IN 1434 PATIENTS WITH FIBROMYALGIA: DEMOGRAPHIC DATA, CO-MORBIDITIES AND SENSORY SYMPTOMS

S. Rehm¹, J. Koroschetz¹, U. Gockel², M. Brosz³, R. Baron¹

¹ *Division of Neurological Pain Research and Therapy, Kiel, Germany*

² *Pfizer Pharma GmbH, Berlin, Germany*

³ *StatConsult GmbH, Magdeburg, Germany*

Background: Patients with fibromyalgia are heterogeneous. They present a variety of sensory abnormalities, pain qualities and co-morbidities. These data are important to optimise trial design and to tailor individual therapies.

Methods: This investigation uses epidemiological and clinical data on the symptomatology of 1434 fibromyalgia patients from a cross-sectional survey (painDETECT) to 1) describe characteristic epidemiological and age/gender related differences, to 2) analyse typical patterns of pain quality, sensory pain symptoms and co-morbidities and to 3) determine whether questionnaires capture these data.

Results: Clinically relevant sensory abnormalities (strongly, very strongly present) included pressure pain (58%), prickling (33%), burning (30%) and thermal hypersensitivity (26%). Frequent pain attacks were complained by 40% of patients. Moderate to severe co-morbid depression occurred in 66%. Half of the patients suffered from sleep disturbances. The 153 male patients of this cohort were on average younger and more depressive. A hierarchical cluster analysis revealed four distinct subgroups of patients showing a characteristic sensory profile, i.e. a typical constellation and combination of symptoms. All subgroups occurred in relevant numbers. Significant but not clinically relevant differences in co-morbidities (depression, sleep disturbance) were found between subgroups.

Conclusions: Since different pain symptoms and co-morbidities are likely associated with distinct pain-generating mechanisms, enrichment for potential treatment responders might be possible in clinical trials by assessing the individual phenotype. Patient-Reported Outcomes can be used to assess the individual impact of pain symptoms on quality of life and the individual constellation of co-morbidities. This research was supported by a grant from Pfizer Germany. U.G. is an employee of Pfizer Germany. R.B. has received research support, consulting, or speaking fees from Grünenthal, Lilly/Boehringer, Mundipharma, Pfizer, Schwarz Pharma, Allergan, Genzyme.

Oral Presentation

Free Presentations 03: Treatment approaches (psychosocial and cognitive)

Abstract: 84

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S33

ACTIVE AVOIDANCE BUT NOT ACTIVITY PACING IS ASSOCIATED WITH DISABILITY IN FIBROMYALGIA

P.A. Karsdorp¹, J.W.S. Vlaeyen²

¹ *Maastricht University, Maastricht, Netherlands*

² *University of Leuven, Leuven, Belgium*

Background and Aims: Activity pacing has been suggested as a behavioural strategy that may protect patients with fibromyalgia (FM) against activity dysregulation and disability. The aim of the present study was to examine whether the construct of activity pacing is distinct from other behavioural strategies assessed with the Chronic Pain Coping Inventory (CPCI), such as guarding, resting, asking for assistance, relaxation, task persistence exercise, seeking social support, and coping self-statements. The second objective was to test whether pacing was associated with physical disability when controlling for pain catastrophizing, pain severity and the other behavioural strategies.

Methods: A random sample of patients with FM (N = 409) completed the CPCI, the Pain Catastrophizing Scale (PCS), the Physical Index of the Fibromyalgia Impact Questionnaire (FIQ-PH) and the Pain Disability Index (PDI).

Results: The results demonstrated that the Dutch version of the CPCI including the pacing subscale has adequate internal consistency and construct validity. Moreover, guarding and asking for assistance, but not pacing strategies, were associated with disability.

Conclusion: These findings are in line with fear-avoidance models and suggest that specifically active avoidance behaviours are detrimental in FM. The authors recommend developing cognitive-behavioural and exposure-based interventions and challenge the idea that pacing as an intervention is essential in pain self-management programs.

Abstract: 512

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S151

ALTERATION OF CORTICAL EXCITABILITY IN PATIENTS OF FIBROMYALGIA

A. Mhalla¹, S. Baudic¹, D. Ciampi de Andrade¹, M. Gautron¹, S. Perrot², N. Attal¹, D. Bouhassira¹

¹ INSERM U 792 Laboratoire de Physiopathologie et Pharmacologie, Clinique de la Douleur. Hôpital Ambroise Paré, Boulogne Billancourt, France

² Service de Médecine Interne et Consultation de la Douleur, AP-HP, Hôtel Dieu, Université Descartes, Paris, France

Aim of Investigation: To evaluate the pattern of cortical excitability (CE) in patients of fibromyalgia (FM) with transcranial magnetic stimulation (TMS).

Methods: 46 FM patients were compared to 21 normal subjects of similar age and gender. The following CE parameters were measured bilaterally in the first interosseous muscle by transcranial magnetic stimulation (TMS): The motor cortex rest motor threshold (RMT), the amplitude ratio of motor evoked potentials (MEP) at 140% and 120% of RMT (MEP 140%/120%), intra-cortical facilitation (ICF) and inhibition (ICI) by double-pulse technique at 10, 15 and 2, 4 ms inter-stimulus interval (ISI), respectively. Values were expressed as the average of four measures for each ISI divided by the average MEP at 120%.

Results: No right-left asymmetry was presented for any of the parameters. RMT was higher in FM ($p < 0.001$). MEP140%/120% was lower in FM ($p = 0.01$). ICI (ISI of 4 ms) and ICF (ISI of 10 ms) were less marked in FM ($p = 0.009$; $p = 0.003$) respectively. All of these parameters were independent of use of psychotropic agents or mood disorders.

Conclusions: Cortical excitability measured by TMS is low in FM patients, irrespectively of possible medication side effects or mood disorders.

Abstract: 152

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S53

AN EVIDENCE-BASED MODEL OF CHRONIC WIDESPREAD PAIN IN CHRONIC FATIGUE SYNDROME

J. Nijs^{1,2}, J. Van Oosterwijk¹, M. Meeus^{1,2}

¹ *Vrije Universiteit Brussel Department of Human Physiology, Brussels, Belgium*

² *Artesis University College Antwerp, Division of Musculoskeletal Physiotherapy, Antwerp (Merksem), Belgium*

Background and Aims: Although fatigue is the primary characteristic of chronic fatigue syndrome (CFS), the majority of CFS patients experience chronic widespread pain. Pain appears to be equally debilitating as fatigue to patients with CFS. Until recently, there was a dearth of knowledge on chronic widespread pain in CFS. Contrary to the multiple studies on pain in fibromyalgia, a disease considerably overlapping with CFS, studies in CFS were scarce. At present, a series of studies have provided more insight into the nature of chronic widespread pain in CFS. The present study aimed at critically assessing the existing knowledge on chronic widespread pain in CFS.

Methods: Systematic literature review.

Results: First, various studies have provided evidence indicating that a number of psychological factors like pain catastrophizing, depressive symptoms and coping strategies influence chronic widespread pain in those with CFS. These factors may contribute to pain facilitation. Second, impairments in pain inhibitory mechanisms at rest and during physical activity have been observed. Impaired pain inhibition accounts in part for post-exertional malaise as typically seen in CFS. Third, exercise-mediated increases in oxidative stress contribute to pain in patients with CFS. Finally, cognitive therapies like cognitive behaviour therapy and pain neurophysiology education re able to improve chronic widespread pain in those with CFS.

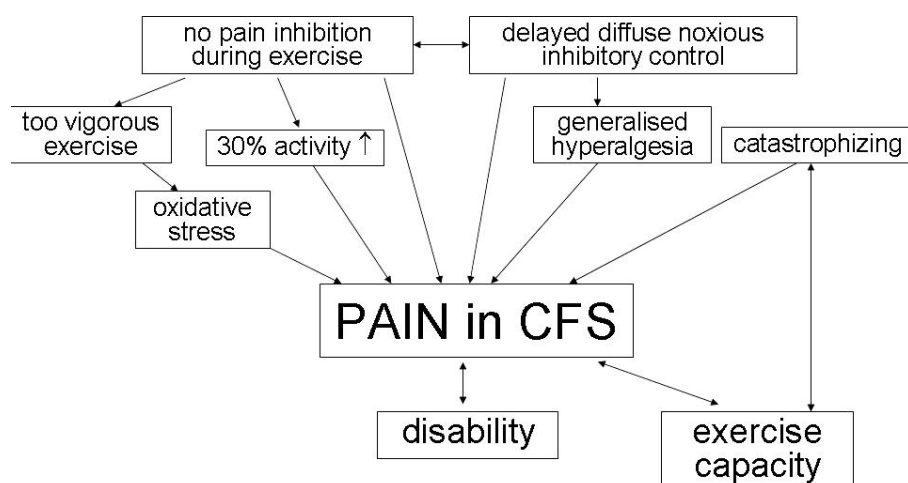


Figure 1. Model for chronic widespread pain in chronic fatigue syndrome.

Conclusions: Based on the available evidence, a model of chronic widespread pain in CFS was constructed (figure 1). This pain model for CFS n be used to steer treatment.

Abstract: 510

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S151

ANAESTHESIA AND FIBROMYALGIA SYNDROME: A RETROSPECTIVE SURVEY

B. le Polain de Waroux¹, A. Berquin², E. Masquelier³

¹ *Cliniques Universitaires Saint-Luc, Anaesthesiology Department, Brussels, Belgium*

² *Cliniques Universitaires Saint-Luc, Department of Rehabilitation Medicine, Brussels, Belgium*

³ *Cliniques Universitaires Saint-Luc, Department of Rehabilitation Medicine, Brussels, Belgium*

Background and Aims: Literature about anaesthesia in patients with chronic pain due to fibromyalgia syndrome (FMS) is scarce. The aim of this retrospective survey was to ask FMS patients about interference of FMS with surgery and anaesthesia, fear of anaesthesia and post operative pain.

Methods: A questionnaire was sent to FMS patients via a patients association. Questions assess perioperative widespread or localized pain, memory loss and fatigue after surgery, fear of anaesthesia or procedure. Other open questions were related to the attitude of the nursing or medical staff or other comments.

Results: We received 30 answers. All the patients were women, mean age of 51 years old (34/62) and usual FMS symptoms: classical FMS points (n = 28), fatigue (n = 30), sleep disturbance (n = 29), attention disturbance (n = 27), irritable bowel syndrome (n = 23), anxiety/depression (n = 15). After 48 procedures, all together, pain at the surgery site was described as severe or very severe after 24 procedures (50%) despite classical management, widespread pain was increased in 31 (65%), severe to very severe fatigue was observed in 29 (60%), and memory loss in 28 (59)%. Fear not to be understood by the medical staff, fear not to receive sufficient amount of analgesics, fear to have to stay in the same position during long procedures were often reported. Many patients ask a compassionate attitude and empathy.

Conclusion: This retrospective survey shows that pain and other FMS symptoms may increase during the post operative period. Special attention and management by the medical staff is necessary.

Oral Presentation
Refresher Course

Abstract: 3

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S2

ANTIDEPRESSANTS AND PAIN

J.A. Mico

Department of Neuroscience, Pharmacology & Psychiatry. CIBER of Mental Health, CIBERSAM, School of Medicine, University of Cádiz, Cadiz, Spain

Antidepressants drugs are commonly used in the treatment of anxiety and depression. In addition, antidepressants are widely used in the treatment of chronic pain, as an adjuvant or alone. Several meta-analyses have confirmed this efficacy. Tricyclic antidepressants (e.g., amitriptyline, nortriptyline, desipramine) and certain novel antidepressants (i.e., venlafaxine, duloxetine, milnacipran) are effective in the treatment of neuropathic pain, but non-tricyclic antidepressants show variable degrees of effectiveness. Antidepressants with mixed-receptor or noradrenergic activity appear to have the greatest analgesic effect in patients with neuropathic pain. Predominantly serotonergic drugs, such as selective serotonin reuptake inhibitors, often are ineffective in treating chronic pain. Amitriptyline and its metabolite nortriptyline have the best documented efficacy in the treatment of neuropathic and non-neuropathic pain syndromes. The novel antidepressants venlafaxine, duloxetine and milnacipran also have proved effective in patients with chronic pain. These drugs modulate pain transmission by interacting with specific neurotransmitters, mainly noradrenaline and serotonin. Transmission of painful stimuli through the spinal column and CNS is modulated by excitatory and inhibitory neurotransmitters, as well as actions at sodium channels. Norepinephrine and serotonin may be excitatory or inhibitory, but they are functionally inhibitory on pain transmission; thus, it is suggested that the mechanism of action of antidepressants as analgesics is related with the modulation of these two neurotransmitters. Moreover, the analgesic mechanism of action of amitriptyline has been associated with sodium channels or some adenosine and NMDA receptors, and with the opioid system. The clinical effects of antidepressants take several weeks to manifest, suggesting that these drugs induce adaptive changes in brain structures affected by anxiety and depression, but this delay is shorter in neuropathic and other pain states, also suggesting that other different mechanisms might be implicated. It is important to understand how antidepressants bring about their beneficial effects on pain. Recent reports suggest that antidepressants can induce neurogenesis in the adult brain, although the mechanisms involved are not clearly understood. Curiously, there are some reports suggesting that chronic pain of different etiologies can reduce neurogenesis. Finally, new research technologies as blood oxygen level dependent (BOLD) contrast functional magnetic resonance imaging (fMRI) has been used to identify whether there are region specific effects of antidepressants in experimental neuropathic pain. It has been demonstrated that modulation of BOLD signal intensity, a surrogate marker of brain activity, discrete brain areas is associated with the analgesic effects of antidepressant treatment in neuropathic pain. The development of new technologies and newer classes of antidepressants drugs has created unprecedented opportunities for the treatment of chronic pain, but more research is necessary in order to establish clearly their mechanism of action and to know specific pain pathologies susceptible to be treated with the old and these new agents. For example, the efficacy of different antidepressants has been documented in a large variety of non-neuropathic pain syndromes such as fibromyalgia or low back pain, but the experience is insufficient in these pathologies.

Acknowledgments: Fondo de Investigación Sanitaria (PI070687) and Plan Andaluz de Investigación (CTS-510 and CTS-4303).

Abstract: 603

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S175

ANXIETY AND DEPRESSION IN FIBROMYALGIA IS RELATED TO LOW HEALTH ESTEEM BUT NOT TO PAIN-SENSITIVITY OR CEREBRAL PROCESSING OF PAIN

K. Jensen, F. Petzke, S. Carville, P. Fransson, H. Marcus, S.C.R. Williams, E. Choy, Y. Mainguy, R.H. Gracely, M. Ingvar, E. Kosek

Karolinska Institutet, Stockholm, Sweden

Background and Aims: This study assessed the differential impact of depression and anxiety on; a) the clinical aspects of fibromyalgia, i.e., pain intensity and subjective ratings of general health status; b) sensitivity to and cerebral processing of pressure pain.

Methods: Female fibromyalgia patients (n = 92), mean age 44.2 (SD = 8.2), fulfilling the ACR1990 classification criteria participated. Patients rated average weekly pain (VAS), general health status (SF-36), depression (BDI), anxiety (STAI) and catastrophizing (CSQ). Pressure was applied to the thumb nail by a computer-controlled stimulator. Functional magnetic resonance imaging (fMRI) was performed during individually calibrated pressures representing 50 mm on a 100 mm VAS and non-painful pressures. The onsets of the stimulations were randomly jittered over the scanning time preventing subjects from anticipating the onset time and event type.

Results: A correlation analysis (Pearson's) including all self-ratings showed that depression, anxiety and catastrophizing scores were significantly correlated ($p < 0.001$), but did not correlate with average weekly pain, nor with sensitivity to pressure pain. However, the subjective rating of general health was inversely correlated with ratings of depression ($p < 0.001$) and anxiety ($p < 0.001$). Results from the three imaging analyses where depression-, anxiety- or catastrophizing scores were used as co-variates showed no significant results, i.e. brain activity during pressure pain was not modulated by different levels of depression, anxiety, or catastrophizing.

Conclusion: This present study provides evidence for two segregated neurofunctional mechanisms involved in pain and depression in FMS.

This study was performed as part of a placebo controlled drug intervention study (EudraCT # 2004-004249-16) financed by Pierre Fabre

Abstract: 516

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S152

ANXIETY, DEPRESSION AND PERCEIVED SOCIAL SUPPORT IN FIBROMYALGIA SYNDROME PATIENTS

M. Salgueiro¹, I. Buesa¹, Z. Aira¹, J. Bilbao², L. Aguilera³, J.J. Azkue¹

¹ *Department of Neurosciences, School of Medicine and Dentistry, Basque Country University, Leioa, Spain*

² *Department of Preventive Medicine and Public Health, School of Medicine and Dentistry, Basque Country University, Leioa, Spain*

³ *Department of Surgery, Radiology and Physical Medicine, Basque Country University, Basurto Hospital, Bilbao, Spain*

Negative affective states such as depression and anxiety often accompany chronic pain. Psychosocial factors such as social support affect pain perception and may contribute to chronic pain patients' well-being.

In order to evaluate perceived social support and other psychosocial factors in Fibromyalgia Syndrome (FMS) patients, as well as to determine their relationship with depression and anxiety, data from 229 FMS patients was collected by means of a self-applied questionnaire.

The sample was composed largely of women (98%), aged 25-66 (42.69 ± 0.64). Pain was reported as the most disturbing aspect of the condition, followed by fatigue, sleep disturbances, alteration of mood, memory loss and focus deficiency problems. The average level of satisfactoriness with the received medical care was 3.76 ± 0.2 on a 10 points Lickert scale. Responders placed a high value on support from their life partners and family setting, but less so from their close social relationships.

High anxiety and depression indices were found in FMS patients ($m = 2.02 \pm 0.07$ and $m = 2.55 \pm 0.06$, respectively on a 0-4 scale), as assessed by means of a SCL90-R checklist. Depression was negatively correlated with perceived social support from partners, family setting, and close social relationships.

Anxiety scores were negatively correlated only with perceived support from the family setting and close social environment, but not with perceived support from partners or health care professionals.

We suggest that interventions improving perceived social support may contribute to pain alleviation in FMS patients by lowering anxiety and depression.

Abstract: 1015

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S284

ASSESSMENT OF NEGATIVE LIFE EVENTS AND OPIOID USE IN PATIENTS WITH FIBROMYALGIA

A. Coutinho¹, M. Barbosa², Ví. Rebelo², P. Barbosa², A. Gomes²

¹ Hospital S. Teotónio, EPE, Viseu, Portugal

² Chronic Pain Unit, Hospital São João, EPE, Porto, Portugal

Background and Aims: Fibromyalgia patients describe more negative life events (NLE). Conflicts with partner/parents, psychological/physical abuse and death of close friends/relatives are the most common events [1,2]. The aim of the study was to assess the relationship between the prevalence of NLE and opioid use in these patients.

Methods: Patients who fulfilled the criteria for fibromyalgia were included in a prospective study in the Chronic Pain Unit from January 1st, 2006 until July 31st, 2008. We applied the following questionnaires: Visual Analogic Scale (VAS), Hospital Anxiety and Depression Scale (HADS) and Medical Outcomes Study 36-item Short-Form Health Survey (SF-36). Statistical analysis: SPSS 17.0.

Results: Sixty consecutive patients were enrolled (Table 1). Of those considered NLE, 86.7% had at least one (Table 2). The average VAS score was 7.32±2.00 (Min = 2 & Max = 10). The number of NLE and the use of major (p = 0.724) or minor (p = 0.774) opioids were not statistically different (Table 3). Higher VAS scores were associated with the use of major opioids (p = 0.003), but not with the use of minor opioids (p = 0.058) (Table 4).

Conclusions: Patients with more NLE reports did not experience higher VAS scores and did not consume more opioids.

Reference: 1. Anderberg UM et al. The impact of life events in female patients with fibromyalgia and in female healthy controls. *Eur Psychiatry* 2000 Aug;15(5):295-301.

2. Castro I et al. Prevalence of abuse in fibromyalgia and other rheumatic disorders at a specialized clinic in rheumatic diseases in Guatemala City. *J Clin Rheumatol* 2005 Jun;11(3):140-5.

Table 1. Sociodemographic characteristics

		Frequency	Percent
Gender	Women	59	98.3
	Men	1	1.7
	Total	60	100
Age (yrs)	18-29	2	3.3
	30-49	37	61.7
	50-69	21	35.0
	Total	60	100
Ongoing relationship	Single	19	31.7
	Married	36	60.0
	Divorced	3	5.0
	Widower	2	3.3
	Total	60	100
Education level (yrs)	≤4	29	48.3
	5-9	19	31.7
	10-12	7	11.7
	>12	5	8.3
	Total	60	100
Occupation	Employed	17	28.3
	Absent for illness	17	28.3
	Retired	14	23.3
	Unemployed	12	20.0
	Total	60	100

Table 2. Life events

Life event(s)		Frequency	Percent
Presence	No	8	13.3
	Yes	52	86.7
	Total	60	100.0
Number	1	19	36.5
	2	24	46.2
	3	9	17.3
	Total	52	100.0
Type Physical abuse	No	31	59.6
	Yes	21	40.4
	Total	52	100.0
Family conflicts	No	26	50.0
	Yes	26	50.0
	Total	52	100.0
Family diseases	No	43	82.7
	Yes	9	17.3
	Total	52	100.0
Death of close friends/relatives	No	19	36.5
	Yes	33	63.5
	Total	52	100.0
Post-traumatic stress	No	47	90.4
	Yes	5	9.6
	Total	52	100.0

Table 3

		Number of Life Events			Total	Chi-square test
		1	2	3		
Minor opioids	No	6	10	3	19	Asymp. sig. (2-sided) 0.774
	Yes	13	14	6	33	
	Total	19	24	9	52	
Major opioids	No	15	19	6	40	Asymp. sig. (2-sided) 0.724
	Yes	4	5	3	12	
	Total	19	24	9	52	

Table 4

	Minor opioids	Number	Mann-Whitney U test	Major opioids	Number	Mann-Whitney U test
VAS	No	18	Asymp. sig. (2-tailed) 0.058	No	34	Asymp. sig. (2-tailed) 0.003
	Yes	28		Yes	12	
	Total	46		Total	46	

Abstract: 768

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S221

ASYMMETRIC BENEFITS AFFECT COST BENEFIT CALCULATIONS IN FIBROMYALGIA

S. Straube¹, C. Phillips², **A. Moore**³, S. Derry³, H. McQuay³

¹ *University of Göttingen, Göttingen, Germany*

² *University of Wales-Swansea,, Swansea, Wales*

³ *University of Oxford, Oxford, United Kingdom*

Background: Economic evaluations of therapies usually use average results from clinical trials. In pain, most patients have results either much better or worse than average; few patients have average.

Methods: Individual patient data from clinical trials of pregabalin in fibromyalgia (2757 patients) were used to evaluate concordance between level of pain relief and benefits in other efficacy variables including fatigue, sleep, function, anxiety, depression, and individual domains of SF-36, as well as individual questions relating to ability to work. Responder status from baseline used withdrawal, <0% pain relief (worse), 0-15% pain relief (trivial improvement), 15-<30% (minimal), 30-50% (moderate), and ≥ 50% (substantial), irrespective of treatment group. Economic analysis was performed for each group.

Results: Of 2757 patients, 899 (33%) were withdrawn, 288 (10%) were worse, 366 (13%) benefited trivially, 304 (11%) benefited minimally, 390 (14%) benefited moderately, and 510 (19%) benefited substantially. Patients with moderate or substantial pain benefit also benefited most in all other efficacy measures, while those with minimal or trivial pain benefit, or worse pain outcomes, had no benefit in other efficacy measures. Treatment was cost-effective in responders, but not non-responders.

Conclusions: The asymmetry in fibromyalgia clinical trial results was not limited to pain outcomes. The 35% of patients with moderate or substantial pain benefit gathered all the benefits for other outcomes also. For the lucky 35%, costs were moderate and quality of life approached normative values; cost effectiveness is proved. Health economic assessments using average results may substantially underestimate genuine cost effectiveness.

Abstract: 518

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S153

CLUSTER ANALYSIS OF DATA FROM FOUR DULOXETINE STUDIES IN FIBROMYALGIA

P. Van Wambeke¹, E.H. Choy², L.A. Bradley³, I.A. Lipkovich⁴, W. Deberdt⁵

¹ University Hospitals Leuven, Leuven, Belgium

² King's College London, London, United Kingdom

³ University of Alabama, Birmingham, United States

⁴ Eli Lilly and Company, Indianapolis, United States

⁵ S.A. Eli Lilly Benelux N.V., Brussels, Belgium

Aims: The aim was to identify distinct groups of subjects with fibromyalgia across multiple outcome measures and evaluate their predictors.

Methods: Measures from 631 duloxetine-treated females collected post-treatment (12 weeks) in 4 randomized placebo-controlled trials were used to identify distinct subject groups using cluster analysis (k-means method). Corresponding classification rules were constructed using a classification tree method. Baseline predictors for outcome clusters were evaluated with logistic regression.

Results: Five clusters were identified, ranging from "worst" with high pain levels and severe mental/physical impairment to "best" with low pain levels and nearly normal mental/physical function (Table 1).

Table 1. Cluster characteristics (selection) and classification rules

Cluster	N	Week 12 mean score					Classification rule
		BDI total	BPI		FIQ		
			Pain intensity	Pain interference (BPIAI)	Interference with work (FIQ14)	depression (FIQ20)	
1 (worst)	78	25.08	7.58	7.89	8.26	6.91	BPIAI ≥ 7.14
2	135	7.93	5.93	4.77	6.29	1.45	3.29 ≤ BPIAI < 7.14, FIQ20 < 5
3	104	15.81	4.12	4.21	4.82	5.09	3.29 ≤ BPIAI < 7.14, FIQ20 ≥ 5
4	185	5.99	3.55	2.23	3.16	1.12	BPIAI < 3.29, FIQ14 ≥ 2
5 (best)	129	3.46	1.43	0.60	0.77	0.57	BPIAI < 3.29, FIQ14 < 2

BDI = Beck Depression Inventory; BPI = Brief Pain Inventory; FIQ = Fibromyalgia Impact Questionnaire.

Classification rules mimicking the clusters were derived and used to classify duloxetine- and placebo-treated female subjects at Week 12 (N = 1160) and at baseline. Duloxetine subjects were significantly more likely to transition to better outcome categories at Week 12 than placebo subjects.

Conclusions: Outcomes were spread over a broad range. Baseline category and treatment were the most significant predictors.

P Van Wambeke: advisory board member for Eli Lilly (Belgium); E Choy: consultant and advisor for Eli Lilly; L Bradley: consultant and advisor for Eli Lilly, Forest Laboratories, Cypress BioScience, Pfizer; grants from National Institutes of Health; I

Abstract: 507

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S150

CNS INFLAMMATION IN FIBROMYALGIA - CEREBROSPINAL PRODUCTION OF TNF-ALPHA IS RELATED TO FATIGUE AND IL-8 TO FIBROMYALGIA IMPACT

D. Kadetoff¹, J. Lampa², M. Westman³, C. Gillis-Haegerstrand⁴, L. Walther-Jallow⁵, M. Andersson⁶, E. Kosek⁷

¹ *Karolinska Institute, Dept of Clinical Neuroscience, Stockholm, Sweden*

² *Karolinska Institute, Dept of Medicine, Stockholm, Sweden*

³ *Karolinska Institute, Dept of Medicine, Stockholm, Sweden*

⁴ *Karolinska Institute, Dept of Clinical Sciences, Danderyd, Stockholm, Sweden*

⁵ *Karolinska University Hospital, Centre for Infectious Disease, Stockholm, Sweden*

⁶ *Karolinska University Hospital, Dept of Neurology, Stockholm, Sweden*

⁷ *Karolinska Institute, Dept of Clinical Neuroscience, Stockholm, Sweden*

Background and Aims: This exploratory study addressed central nervous system (CNS) inflammation in fibromyalgia (FM). We hypothesized that elevated levels of TNF-alpha, IL-1 and IL-8 would be related to symptoms such as pain, fatigue and functional impairment.

Methods: Cerebrospinal fluid (CSF) samples were taken from 15 female FM patients and 12 age-matched women undergoing surgery for benign gynecological problems (before spinal anesthesia). Cytokine levels were analyzed by luminex assay and the amount of cytokine mRNA from CSF cells by quantitative RT-PCR. FM patients rated pain, fatigue (Multidimensional Fatigue Inventory) and FM impact (Fibromyalgia Impact Questionnaire, FIQ).

Results: FM patients had higher mRNA levels for TNF-alpha ($p < 0.02$), but lower mRNA levels for IL-1 ($p < 0.001$) and IL-8 ($p < 0.002$) than controls. We found a positive correlation between TNF-alpha mRNA and fatigue ($p < 0.05$) (Spearman one-tailed) and between IL-8 mRNA and FIQ ($p < 0.02$) (Spearman two-tailed) in the FM group. There were no group differences in CSF levels of IL-1, IL-6, IL-8 or IL-10, although FM patients had a tendency to lower levels of IL-1 ($p = 0.06$) and IL-8 ($p = 0.1$). CSF TNF-alpha levels were not detectable.

Conclusion: This is to our knowledge the first evidence of increased CNS inflammation in FM. Interestingly, TNF-alpha production was positively correlated to fatigue and IL-8 production to the impact of FM.

Oral Presentation
Free Presentations 09: Diseases

Abstract: 128

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S46

COMPARISON OF LEVEL OF AGREEMENT BETWEEN TWO NEUROPATHIC PAIN QUESTIONNAIRES IN TWO DIFFERENT PATIENT POPULATIONS

B. Tampin, K. Briffa, H. Slater

School of Physiotherapy, Curtin University of Technology, Perth, Australia

Neuropathic pain (NeP) questionnaires screen for the likelihood of a NeP component in chronic pain disorders. The painDETECT is a self reported tool, whereas the LANSS requires input from a clinician. The aim of this study was to investigate the agreement between these two questionnaires in two patient groups: (a) fibromyalgia (FM) patients in a research setting; (b) patients with neck/arm pain (NAP) referred to a neurosurgery department.

Method: 26 FM patients and 50 NAP patients completed both questionnaires. Responses were classified into two groups and scored (LANSS: <12 non neuropathic; ≥12 neuropathic; painDETECT <18 non neuropathic; ≥19 neuropathic).

Results: In the FM group, agreement between questionnaires for classification was demonstrated in 21 patients (12 non-neuropathic, 9 neuropathic; Kappa.62, CI:.32-.91). Of the remaining 5, the painDETECT scored 4 with a NeP component. In NAP patients, agreement occurred in 35 cases (30 non-neuropathic, 5 neuropathic; (Kappa.27 CI:.03-.50). Out of the 15 remaining cases, the LANSS scored 1 and the painDETECT 14 with a NeP. In 50% of these remaining 14 cases, NAP answered questions in the painDETECT as positive, resulting in the classification of a NeP component but answered negative in the LANSS. For both groups, the main discrepancies between questionnaire responses related to the presence/absence of (i) spontaneous pain; (ii) burning pain; and (iii) sensitivity to light touch.

Conclusion: Variance between painDetect and LANSS in scoring NeP in both FM and NAP patients does occur and may be important if influencing treatment decisions.

Acknowledgement: The study is supported by the National Health and Medical Research Council, Arthritis Australia, Physiotherapy Research Foundation. Thanks to Dr Roger Goucke at Sir Charles Gairdner Hospital/Perth

Abstract: 506

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S150

COMPARISON OF SLEEP QUALITY IN PATIENTS WITH FIBROMYALGIA SYNDROME AND MAJOR DEPRESSION

G. Güleç¹, S. Tufan Temiz², O. Armagan³, **S. Güleç**⁴

¹ *Eskisehir Osmangazi University School of Medicine, Psychiatry Department, Eskisehir, Turkey*

² *Yunusemre Hospital, Eskisehir, Turkey*

³ *Eskisehir Osmangazi University, Department of Physical Therapy and Rehabilitation, Eskisehir, Turkey*

⁴ *Eskisehir Osmangazi University, Department of Algoloji, Eskisehir, Turkey*

Objective: To clarify the relationship between Fibromyalgia Syndrome (FMS) and Major Depression according to subjective sleep quality in patients and to establish the clinical parameters associated with these sleep complaints by considering the suggestion that these two disorders share the similar pathophysiological mechanisms and can be accepted in the same spectrum.

Method: Study was conducted on 52 patients with FMS, 31 patients with Major Depression and 37 healthy controls. Subjects were evaluated by Socio-demographic Questionnaire, State-Trait Anxiety Inventory, Hospital Anxiety and Depression Scale, Pittsburgh Sleep Quality Index, Van Dream Anxiety Scale, Visual Analog Scale and Fibromyalgia Impact Questionnaire.

Results: While depression and anxiety scores were higher in Major Depression group, state anxiety scores were higher in fibromyalgia group compared to other groups; sleep quality scores in patients with FMS and Major Depression were similar and higher than those in the control group. Poor sleep quality was associated with depression and anxiety in patients with Major Depression, whereas it was associated with severity of pain, anxiety and dream anxiety in patients with Fibromyalgia Syndrome.

Conclusion: These results indicate that sleep quality decreases similarly in both patient groups with distinct causes, and also suggest that more detailed studies are required to explain the relationship between FMS, sleep disorder, pain, anxiety and depression, in which serotonin and noradrenalin are the commonly involved neurotransmitters.

Abstract: 505

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S149

CONTRIBUTION OF THE LOCAL AND REFERRED PAIN FROM ACTIVE MYOFASCIAL TRIGGER POINTS BILATERALLY IN THE UPPER TRAPEZIUS IN FIBROMYALGIA SYNDROME

H.Y. Ge¹, H. Nie¹, P. Madeleine¹, B. Danneskiold-Samsøe², T. Graven-Nielsen¹, [L. Arendt-Nielsen](#)¹

¹ *Aalborg University, Aalborg, Denmark*

² *The Parker Institute, Frederiksberg Hospital, Copenhagen, Denmark*

Background and Aims: The generalized hypersensitivity associated with fibromyalgia syndrome (FMS) can be produced by a peripheral source of pain. The aim of the study was to investigate whether active myofascial trigger points (MTrPs) contributes to the pain in FMS.

Methods: FMS patients and healthy controls (n = 22, each) were examined for the existence of latent and active MTrPs by manual palpation and pressure pain threshold (PPT) mapping bilaterally in the upper trapezius muscle. The upper trapezius muscle on each side was divided into 13 points of 1 cm in diameter. At 13 points on each side of the muscle, the local and referred pain area induced by manual palpation were recorded and PPT was measured.

Results: PPT levels at all measured points in FMS group were significantly lower than the controls. PPT distribution patterns revealed that the anterior- and the mid-parts had lower PPT levels than the posterior part of the upper trapezius muscle in both the patient group and the control group. Multiple active MTrPs were identified bilaterally in the muscle in FMS patients, but no active MTrPs were found in healthy controls. The local and referred pain pattern induced from active MTrPs bilaterally in the trapezius muscle were similar to the ongoing pain pattern in the neck and shoulder region in patients with FMS.

Conclusion: Active MTrPs bilaterally in the upper trapezius muscle contributes to the neck and shoulder pain pattern in FMS. Active MTrPs constitute one of the peripheral sources of pain in FMS. The study was supported by The American Fibromyalgia Syndrome Association, Inc.

Abstract: 368

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S111

CHRONIC CONTENTION STRESS INDUCES MECHANICAL AND COLD ALLODYNIA, AND ENHANCES INFLAMMATORY PAIN IN RAT: A POTENTIAL MODEL OF FIBROMYALGIA

L. Bardin, N. Malfetes, A. Newman-Tancredi, R. Depoortere

Centre de Recherche Pierre Fabre, Castres, France

Whereas acute stress often results in analgesia, chronic stress can trigger hyperalgesia/allodynia. This influence of long term stress on nociception is relevant to numerous painful pathologies, in particularly fibromyalgia, characterized by diffuse muscular pain (i.e. hyperalgesia) and/or tenderness (i.e. allodynia). Hence, there is a need for pre-clinical models integrating a chronic-stress dimension to the study of pain.

Here, we assessed the effects of long-term intermittent stress (contention in a cylinder, 1 h/day, 4 days/week over 5 weeks) on noxious or non-noxious behavioural pain tests in rats. This type of stress potentiated chemical hyperalgesia in the formalin model (160% and 76% increase of pain score above controls, during the early and late phases, respectively). It also produced thermal allodynia in response to cold (paw acetone test: 200% increase of allodynia) and heat (42°C tail immersion test: 15% decrease of withdrawal threshold). This stress also resulted in mechanical allodynia in the von Frey filaments (60% decrease in threshold). However, such a stress regimen had no influence in the Randall-Selitto test of mechanical hyperalgesia, and in the tail immersion models of cold (4°C) or hot (48°C) thermal hyperalgesia, as well as cold (15°C) allodynia.

This model of prolonged, intermittent restraint stress may be useful in investigating the mechanisms linking stress and pain, and provide an assay to assess the potential therapeutic efficacy of drugs targeted against painful pathologies with a strong stress component, such as fibromyalgia

Oral Presentation

Free Presentations 10: Diseases and treatment approaches (invasive)

Abstract: 134

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S48

DEFI (DETERMINATION OF EPIDEMIOLOGY OF FIBROMYALGIA): A FRENCH PREVALENCE STUDY OF FIBROMYALGIA

S. Perrot¹, E. Vicaut², D. Servant³, L. Pichot⁴, M. Kosa⁵, P. Ravaud⁶

¹ *Hôtel Dieu, Paris, France*

² *Hôpital Fernand Widal, Paris, France*

³ *Clinique Michel Fontan, Lille, France*

⁴ *Pfizer France, Paris, France*

⁵ *Pfizer France, Paris, France*

⁶ *Groupe hospitalier Bichat, Paris, France*

Background and aims: Fibromyalgia is a frequent chronic debilitating condition. Few studies have estimated its prevalence in Europe, based on screening tests without clinical examination. A prevalence study in french general population setting, with a clinical assessment performed by specialists may be of great interest.

Methods: This french cross-sectional survey in a general population setting consisted in 2 steps: First, a telephone screening among a randomly selected sample of 6,000 households using the French validated version of London Fibromyalgia Epidemiological Study Screening Questionnaire or LFES-SQ (1), then a clinical confirmation by a rheumatologist based on ACR criteria (2).

Results: Of 3081 polled subjects, 232 (7.5%) were screened positive; 96 subjects accepted the consultation (41.4%), 70.8% were females. Mean age was 58.2 CI95 [55.2; 61.2] years. Finally 20 subjects (20.8%) met the ACR criteria, 17 were females. Mean age was 56.9 CI95 [50.7; 63.1]. Thus FM prevalence is estimated to 1.5% CI95 [1.1; 2.0] based on the following algorithm: Prevalence (%) = $[N_{\text{diagnosis}} + (N_{\text{diagnosis}}/N_{\text{consultations}} \cdot N_{\text{refusals}})] \cdot 100 / N_{\text{screened patients}}$, where N_{refusals} : screened positive patients who refused to consult; $N_{\text{diagnosis}}$: confirmed FM patients.

Conclusions: This 1.5% FM prevalence is consistent with other studies but lower than estimated by screening tests like London Fibromyalgia Epidemiological Study figures (2.7%) [1]. Those discrepancies can be attributable to patients' easier access to specialists and a stricter physician's interpretation of ACR criteria.

This study was supported by Pfizer France. Martine Kosa and Laurence Pichot are employees of Pfizer France

Reference: 1. White KP; *J Rheumatol* 1999 26: 1570-1576
2. Wolfe W; *Arthritis & Rheumatism* 1990 33: 160-172

Abstract: 789

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S227

DEFINING THE BORDER BETWEEN MILD AND MODERATE PAIN

A. Moore¹, R. Mhuircheartaigh¹, S. Straube², S. Derry¹, H. McQuay¹

¹ *University of Oxford, Oxford, United Kingdom*

² *University of Göttingen, Göttingen, Germany*

Background: On a 100 mm VAS scale, 30-40 mm is usually taken as the border between mild and moderate pain, based on evidence from classic postoperative pain trials that used both VAS and categorical scales.

Methods: Paired categorical and VAS scale measurements were taken from individual-patient meta-analyses of randomised trials. One meta-analysis involved five trials (>900 patients) of epidural morphine, extended-release morphine, or placebo in major surgery, with pain assessed over 48 hours. Another meta-analysis involved four trials (2700 patients) of pregabalin in fibromyalgia with end of trial pain assessments.

Results: In acute pain, almost 28,000 paired observations were available in postsurgical patients, both at rest and on activity. Median and IQR for no pain and mild pain were below 30 mm VAS, while median and IQR for moderate and severe pain were above 30 mm. In fibromyalgia, patient global impression of change of minimally improved, no change, minimally worse, much worse and very much worse were associated with average weekly pain VAS scores above 30 mm. For very much improved almost all scores were below 30 mm. For much improved there was no clear division.

Conclusions: The assumption that 30 mm marks the border between mild and moderate pain held true in large evaluations in pain conditions as disparate as postoperative pain after major surgery and fibromyalgia. It is reasonable to ask whether pain scores of less than 30 mm might be a useful outcome in clinical trials, and a target for clinical practice.

Oral Presentation
Free Presentations 09: Diseases

Abstract: 127

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S46

DETECTION OF ALTERED SENSATION IN FIBROMYALGIA PATIENTS - DO RESPONSES TO THE PAINDETECT QUESTIONNAIRE MATCH WITH QUANTITATIVE SENSORY TESTING?

B. Tampin, K. Briffa, H. Slater

School of Physiotherapy, Curtin University of Technology, Perth, Australia

The painDETECT questionnaire is a self-reported screening tool used to determine the presence of a neuropathic pain (NeP) component in chronic pain disorders. This study investigated if the somatosensory profile of patients who, using painDETECT, responded as being sensitive to cold and heat, to slight pressure, light touch and feeling numbness in the area of pain, was confirmed by laborative quantitative sensory testing (QST).

Methods: 26 Fibromyalgia patients (FM) (22 females, 46±12 years) completed the painDETECT questionnaire. Standardized QST measures of cold and heat pain thresholds (CPT, HPT), pressure pain thresholds (PPT), dynamic allodynia (DA), mechanical detection thresholds (MDT) and vibration detection thresholds (VDT) were recorded from the maximal pain area (FM: upper trapezius muscle n = 14). In order to determine if these thresholds were abnormal, FM data were compared to those of 26 age matched healthy controls (HC; 13 females; upper trapezius muscle). Only those FM patients who responded positively to these questions were included in the analysis.

Results: Fifteen patients reported sensitivity to cold/heat, and their CPT and HPT were significantly decreased ($p < 0.001$) compared to HC. Twenty-five FM patients demonstrated significantly decreased PPT ($p < 0.001$) compared with HC. Fifteen FM patients indicated sensitivity to light touch, but only 3 demonstrated DA. In those FM patients reporting numbness (n = 16), no significant difference in MDT and VDT compared to HCs was demonstrated.

Conclusion: These preliminary data suggest that in FM patients, QST data may be more sensitive in detecting alterations of sensory processing compared with painDETECT.

Acknowledgement: The study is supported by the National Health and Medical Research Council, Arthritis Australia and the Physiotherapy Research Foundation.

Oral Presentation

Free Presentations 01: Organisation and anatomy

Abstract: 70

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S29

DEVELOPMENT AND VALIDATION OF THE FIBROMYALGIA RAPID SCREENING TOOL (FiRST)

S. Perrot¹, D. Bouhassira², J. Fermanian³

¹ *Hotel Dieu APHP, University Paris Descartes, Paris, France*

² *Inserm U792, Boulogne, France*

³ *Biostatistics Department, Hopital Necker, Paris, France*

Background and Aims: Development and validation of a new screening tool for fibromyalgia (FMS).

Methods: The French Pain In Rheumatology Group (CEDR) developed a self-questionnaire, named FiRST (Fibromyalgia Rapid Screening Tool), in a 3-steps protocol: (1) After literature review and expert consensus, an initial questionnaire was developed, consisting of 10 items investigating the main domains involved in FMS. (2) The tool was tested in a multicenter study, in 3 pain units and 3 rheumatology departments, to compare its properties in FMS patients (N = 92, 86 women/6 men, confirmed by ACR criteria), and in patients with painful non FMS rheumatological disorders: rheumatoid arthritis (N = 32), diffuse osteoarthritis (N = 13), and ankylosing spondylitis (N = 25). (3) The psychometric validation included: face validity, test-retest reliability, assessment of the internal consistency, factorial analysis, sensitivity and specificity of each item to discriminate fibromyalgia and other chronic rheumatologic syndromes.

Results: Analysis of the metrologic properties of the FiRST questionnaire allowed to exclude four items from the initial version and identified the 6 most discriminative items. We confirmed that the 6-item FiRST questionnaire has excellent properties to discriminate FMS.

Conclusion: FiRST is a new, simple and easy-to-use questionnaire with good sensitivity and specificity to detect patients with FMS. It may help physicians to detect FMS patients, for a better and earlier management both in clinical research and daily practice.

Oral Presentation

Free Presentations 02: Multidisciplinary and ethics

Abstract: 74

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S30

DIFFERENT PAIN THRESHOLDS IN PATIENTS WITH CHRONIC LOW BACK PAIN AND FIBROMYALGIA DURING WITHDRAW OF OPIOIDS

H. Wang, N. Weinsheimer, M. Schiltenswolf

Ruprecht-Karls-University of Heidelberg, Germany, Heidelberg, Germany

Background and aims: To understand the effect of opioids on pain perception, we measured cold, warm sensation and cold, warm thresholds using Quantitative sensory testing (QST) in patients with low back pain and Fibromyalgia before and after opioids withdraw treated with a multimodal pain therapy.

Methods: All patients who underwent an opioids withdraw were treated with multimodal pain therapy inclusive oral pain medication, intensive physiotherapy, physical therapy and adjuvant psychotherapy. QST was performed in area of the L4, L5 and S1 dermatomes at the admission of hospital stay and 3 weeks, 6 months later. A patient control group and a healthy control group were enrolled after age and sex matched, respectively.

Results: At the beginning of the therapy patients with opioids showed delayed reaction to cold and warm stimuli than patients without opioids. This difference disappeared at 3 weeks and 6 months after initiation of multidisciplinary pain therapy. Both patient groups showed lower cold and warm pain thresholds than healthy controls during the first 3 weeks meaning they were more sensitive to cold and warm than healthy subjects in back area. These significant changes disappeared 6 months after therapy in the patient group without opioids withdrawal but not in the withdrawal group.

Conclusion: We conclude that a peripheral pain sensitization do exist in patients with low back pain and fibromyalgia as the results by QST showed. Opioid intake delayed the pain perception in these patients. The multidisciplinary pain therapy may improve the pain perception during and after withdrawal of opioids.

Abstract: 508

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S150

EMOTIONAL MODULATION OF PAIN PERCEPTION IN PATIENTS WITH FIBROMYALGIA AND HEALTHY CONTROLS

S. Kamping¹, I.C. Bomba¹, E. Diesch², H. Flor²

¹ *Department of Cognitive and Clinical Neuroscience, Central Institute of Mental Health, Mannheim, Germany*

² *Department of Cognitive and Clinical Neuroscience, Central Institute of Mental Health, University of Heidelberg, Mannheim, Germany*

To investigate the effect of experimental mood induction on pain perception, we assessed 14 fibromyalgia patients (FMS) and 14 controls. An infrared Nd:YAP-laser was used to apply individually adapted painful stimuli to the dorsum of the hand. The emotional background of the painful stimuli was modulated by presenting them together with negative, neutral, and positive picture stimuli selected from the International Affective Picture System. During the five randomized laser-picture trials of each condition, subjects received 10 painful stimuli and were asked to rate the average painfulness and unpleasantness. MR-images were obtained on a 3T TRIO Siemens scanner using a T2* sensitive echo planar (EPI) sequence. Additionally, a high-resolution T1-weighted structural MRI was obtained. Images were evaluated with SPM2. Laser stimuli elicited a distinct pain sensation in all subjects. The FMS and the controls did not differ in objective laser output intensity or pain and unpleasantness ratings (all $p > 0.18$). In line with the literature (Kennner-Mabiala, R. & Pauli, P. *Psychophysiology* 2005;42:559-67), we found higher pain intensity ratings while the FMS group viewed negative pictures, but there was no significant difference in pain-related brain activation. We observed a significantly reduced activation in the anterior cingulate cortex (ACC) in the FMS compared to the controls while they viewed positive pictures during painful stimulation. Additional correlational and connectivity analyses will be reported. The higher pain ratings together with the reduced ACC activation suggest that FMS patients are less able to modulate pain with positive affect. Supported by the BMBF 01GW0531.

Abstract: 501

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S148

EVALUATION OF THE QUANTITATIVE AND QUALITATIVE ASPECTS OF THE PAIN IN THE FIBROMYALGIA

S. Saltarelli, D.F.A. Pedrosa¹, P. Hortense², **F. Faleiros Sousa**¹

¹ *University of São Paulo, Ribeirão Preto, Brazil*

² *University Federal of São Carlos, São Carlos, Brazil*

Objective: Evaluate the perception of pain in the fibromyalgia through the quantitative and qualitative methodological technique.

Method: A total of 30 clients were assessed through an interview analyzed by the thematic content and through the instrument Descriptors of Pain. Arithmetic mean and standard error were used to determine which descriptors better characterize the pain in the fibromyalgia.

Results and Discussion: The result of the content analysis was the construction of categories of analysis regarding the perceptions of: diagnosis, motivation, disease, feelings, thoughts and repercussions on the quality of life. The Descriptors of Pain instrument revealed the descriptors of higher attribution in the characterization of pain were inconvenient, spreading, pulsating, uncomfortable and persistent and the descriptors with the lower attribution were miserable, demoniac, cursed, terrifying and frightening. The two instruments showed the clients' tendency in perceiving and reporting the pain regarding to the sensorial-discriminating characteristics. In addition, data related to the importance of the family's and the health professional's roles in managing the pain were presented.

Conclusion: The need to stimulate the perception and expression of clients regarding the pain in its multidimensionality was perceived. It is concluded that the management of pain must be performed considering the complexity of the phenomenon in terms of the triad health team-client-family.

Abstract: 497

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S147

FACTORS TO HELP PRIMARY CARE PHYSICIANS DETECTING FIBROMYALGIA IN ROUTINE PRACTICE

R. Baron¹, B. Arnould², C. Alegre³, E. Choy⁴, G. Cruccu⁵, J. Desmeules⁶, C. Dias-Barbosa⁷, J. Margaux⁸, S. Richards⁹, E. Serra¹⁰, M. Spaeth¹¹, S. Perrot¹²

¹ *Division of Neurological Pain Research and Therapy, Christian-Albrechts University, Kiel, Germany*

² *Mapi Values, Lyon, France*

³ *Public health, Hospital Universitari Valle Hebron, Barcelona, Spain*

⁴ *Rheumatology, King's College London, London, United Kingdom*

⁵ *Department of Neurological Sciences, La Sapienza University, Roma, Italy*

⁶ *Clinical pharmacology and toxicology & Multidisciplinary pain center, Geneva University Hospital, Geneva, Switzerland*

⁷ *Mapi Values, Lyon, France*

⁸ *Rheumatology, Erasme Hospital, Brussels, Belgium*

⁹ *Rheumatology Poole Hospital NHS Trust, Poole, United Kingdom*

¹⁰ *Pain Unit, North Hospital, Amiens, France*

¹¹ *Rheumatology, Gräefelfing, Germany*

¹² *Internal Department and Pain Unit, Hôpital Hôtel Dieu, Paris, France*

Background and Aims: Fibromyalgia (FM) diagnosis remains challenging, especially among primary care physicians (PCPs), because of symptom heterogeneity, co-morbidities and overlapping of FM symptoms with other disorders (e.g. rheumatoid arthritis and other psychiatric and pain-causing conditions). A screening tool was developed to help European PCPs identify FM patients.

Methods: A European multidisciplinary expert group was set up to provide clinical expertise, define methodology, and identify key issues around FM detection. Comprehensive literature review, clinician focus groups (N = 6), and face-to-face interviews with English (UK), German and French-speaking patients (N = 29) were conducted to determine the FM screening tool content. The tool was developed in French, German and English, based on patients' wording, and tested for comprehension in FM-diagnosed (N = 11) and FM-suspected (N = 4) patients from respective countries.

Results: High consistency was found between clinicians and patients across countries. Pain constituted the major factor; in terms of occurrence, intensity, perception, location, worsening and relieving factors, and impact on everyday life. Other important factors identified were fatigue, FM-associated symptoms, physical/emotional situations affecting patients' condition, and patients' personal history and attitude.

Conclusion: Beside pain description and perception and the symptomatic picture, investigation of multiple factors such as patients' history, attitude and quality of life, and socio-demographics is essential to identify FM. By capturing simultaneously all these factors, the European FM screening tool should help PCPs to detect FM patients early and improve their management. Quantitative validation of the tool is currently underway.

The work was funded by Pfizer Limited.

Abstract: 499

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S148

FIBROMYALGIA AND DEPRESSION: WHAT RELATION? A CLINICAL CASE REPORT

S. Moreira, **M. Branco**, A. Regalado^{1,2}

¹ *Centro Hospitalar do Porto - Hospital Santo António, Porto, Portugal*

² *Chronic Pain Unit, Porto, Portugal*

Background and Aims: Fibromyalgia is a chronic pain condition whose main features are widespread musculoskeletal pain described as persistent, diffuse, deep and most often continuous with periodical exacerbations. Depression is described in 40% of fibromyalgia patients compared to 20% of patients hospitalized for other medical conditions. We want to reflect and discuss the relation between depression and fibromyalgia, and the importance of psychological assessment of fibromyalgia patients.

Methods: Discussion of a 36 years-old-woman clinical case.

Results: Patient complained of persistent widespread musculoskeletal pain, headaches, physical fatigue and insomnia for four years. Clinical observation showed 11 tender points to digital palpation. She was undergoing antidepressant therapy (fluoxetine) since the diagnostic. Pain and physical disability were her major complaints, and did not decrease significantly with analgesic medication. We decided to propose individual psychotherapy. Patient started doing exercise with an improvement in physical functioning, started working and decided to stop fluoxetine. At 10th session referred more pain complaints, headache, anxiety and insomnia. She never thought about a relation between emotional condition and the disease. Psychotherapy brought up the recent oncologic terminal disease of a family member that reminded her of the loss of her best friend in a car accident, 10 years ago. She expressed anger, sadness and started using an antidepressant (Duloxetine) again. Pain decreased significantly.

Conclusions: A multidisciplinary approach was fundamental to diagnose a clinical depression that seemed to have an important role in the maintenance of pain complaints. Psychological and psychiatric support should be considered in fibromyalgia patient's treatment.

Abstract: 513

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S151

FIBROMYALGIA AND PSYCHOSOCIAL VARIABLES

P. Oliveira, M.Eí. Costa

Centre of Psychology of Oporto University, Portugal

Fibromyalgia is a musculoskeletal chronic pain syndrome of unknown etiology and cure, which is estimated to affect 2-4% of the adult population, mainly women. Fibromyalgia is characterized by widespread musculoskeletal pain and anatomical defined tender points, but also by fatigue, morning stiffness, disturbed sleep, and cognitive disturbance. Our main goals were to assess the prevalence and associations among psychosocial variables namely, health status perception, emotional distress, negative affect, positive affect, social support, and coping with chronic pain. On the other hand, we intended to access illness representations, as well as life stories of fibromyalgia patients. A mixed methodological approach was used. The quantitative study included 128 fibromyalgia patients, 52 rheumatoid arthritis patients, and 91 healthy controls who completed a set of self-report measures. In the qualitative study 20 fibromyalgia patients were interviewed. Results have shown that fibromyalgia patients have significantly lower levels of health status perception and positive affect, as well as significantly higher levels of emotional distress, negative affect, avoidance, and worrying. Concerning to qualitative study, we have found support for the presence of predisposing, triggering, and maintenance factors in participants' life stories. Furthermore, relating to illness representations four categories have emerged, specifically: (a) finding a diagnosis: fibromyalgia, (b) a changed life (c) coping with fibromyalgia and, (d) perspectives about a new reality. Overall, we point out the usefulness of a biopsychosocial approach on assessment and intervention on fibromyalgia patients in order to improve their quality of life.

Abstract: 977

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S275

**FIBROMYALGIA PATIENTS' COMMUNICATION OF CUES AND CONCERNS
IN THEIR FIRST CONSULTATION WITH A PAIN CLINIC NURSE. AN
OBSERVATIONAL STUDY**

H. Eide¹, T. Sibbern², A. Finset³, T. Rustøen⁴

¹ *Oslo University College, Oslo, Norway*

² *Diakonhjemmet University College, Oslo, Norway*

³ *University of Oslo, Oslo, Norway*

⁴ *Oslo University Hospital, Oslo, Norway*

The aims of this study were to gain insight in what kind of worries and concerns patients with fibromyalgia presented in a first consultation at a pain clinic, how these were displayed, and possible predictors. 59 first visit consultations (50 women, mean age 48 years, Sd 11) with 5 clinical nurse specialists were videotaped and coded with the Verona Coding Definitions of Emotional Sequences and Burlinson's Scale for Comforting Strategies (BSCS). Patients also filled in questionnaires about pain, overall health (Sf 36), and satisfaction with the consultation.

The patients had a worst pain level of 9.7 on a numeric rating scale from 0 to 10. Each patient displayed a mean of 3.6 concerns (explicitly expressed negative emotions) and 10.6 cues (hints to negative emotions) during the consultation, mostly about pain, interpersonal relationships, and emotional reactions. The nurses responded most often with implicitly acknowledging the perspective of the patient (intermediate empathy level according to BSCS). Concerns were more often responded to with reflections of emotion (high empathy level) ($p = 0.008$) than cues. Regression analyses of predictors of cues and concerns indicate that patients' negative evaluation of overall health corresponds with many cues and concerns in the consultations. No other psychosocial or health predictors or nurse related factors were significantly related to expression of emotion.

This is one of the first studies of real time communication with fibromyalgia patients. The patients reported what was at stake in their lives, mostly communicated as hints to emotion.

Oral Presentation

Free Presentations 04: Treatment approaches (conservative and other)

Abstract: 94

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S36

FROM ACUTE MUSCULOSKELETAL PAIN TO CHRONIC WIDESPREAD PAIN AND FIBROMYALGIA: APPLICATION OF PAIN NEUROPHYSIOLOGY IN REHABILITATION PRACTICE

J. Nijs¹, B. Van Houdenhove²

¹ *Vrije Universiteit Brussel Department of Human Physiology, Brussels, Belgium*

² *Katholieke Universiteit Leuven, faculty of medicine, Leuven, Belgium*

Background and aims: During the past decade, scientific research has provided new insight into the development from an acute, localized musculoskeletal disorder towards chronic widespread pain/fibromyalgia (FM).

Methods: An in-depth review of basic and clinical research was performed to design a theoretical framework for rehabilitation in these patients.

Results: Chronic widespread pain/FM is characterised by sensitisation of central pain pathways. It is explained that rehabilitation might be able to influence the process of chronicity in 3 different ways. (I) In order to prevent chronicity in (sub)acute musculoskeletal disorders, it seems crucial to limit the time course of afferent stimulation of peripheral nociceptors. (II) In case of chronic widespread pain and established sensitisation of central pain pathways, relatively minor injuries/trauma at any location are likely to sustain the process of central sensitisation and should be treated appropriately with rehabilitation accounting for the decreased sensory threshold. Inappropriate pain beliefs should be addressed and exercise interventions should account for the process of central sensitisation. (III) However, therapists ignoring the processes involved in the development and maintenance of chronic widespread pain/FM, may cause more harm than benefit to the patient by triggering or sustaining central sensitisation.

Conclusions: Our current understanding of the transition from acute musculoskeletal pain to chronic widespread pain/FM can be used to steer the content of conservative interventions. Findings from basic sciences like neurophysiology can be incorporated into clinical practice.

Abstract: 500

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S148

HIPPOCAMPUS DYSFUNCTION MAY EXPLAIN SYMPTOMS OF FIBROMYALGIA SYNDROME

Y. Emad¹, Y. Ragab², F. Zein³, A. Saad⁴, A. Abou-Zeid⁵, J.J. Rasker⁶

¹ *Rheumatology and Rehabilitation Department Faculty of Medicine Cairo University & Dr. Erfan and Bagedo General Hospital Jeddah, KSA, Jeddah, Egypt*

² *Department of Radiology, Cairo University, Cairo, Egypt*

³ *Department of Radiology, Cairo University, Cairo, Egypt*

⁴ *Internal Medicine Department, Cairo University, Cairo, Egypt*

⁵ *Department of Public Health, Cairo University, Cairo, Egypt*

⁶ *University Twente, Enschede, Netherlands*

Background and Aim: The hippocampus plays crucial roles in maintenance of cognitive functions, sleep regulation and pain perception. Magnetic resonance spectroscopy (1H-MRS) was used to investigate dysfunction of hippocampus in patients with fibromyalgia syndrome (FM) and to compare these findings with healthy controls.

Methods: In 15 FM patients and 10 healthy age-matched control females controls, 1H-MRS was used to assess N-acetylaspartate, choline, creatine and their ratios from both hippocampi. Levels of metabolites and their ratios were compared between the groups. All patients and controls underwent psychological assessment to assess cognitive function, depression, and structured sleep interview, Fibromyalgia Impact Questionnaire (FIQ), number of tender points, and visual analog scale (VAS) for pain were assessed in all patients.

Results: NAA levels of right and left hippocampi differed significantly between patients and controls ($p < 0.05$). Cho levels in the right hippocampus were higher in the patient group than in controls ($p = 0.005$). NAA/Cho and NAA/Cr ratios differed significantly between patients and controls ($p < 0.05$), while the Cho/Cr ratio showed no differences. Significant correlations were found between language score and right Cho and right Cr levels ($p = 0.041$, $p = 0.006$, respectively).

Conclusion: The hippocampus was dysfunctional in patients with FM, as shown by lower NAA levels compared to controls, representing neuronal or axonal metabolic dysfunction.. we suggest that metabolic dysfunction of hippocampus may be implicated in the appearance of these symptoms associated with this puzzling syndrome.

Abstract: 940

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S266

HRV BIOFEEDBACK FOR FIBROMYALGIA

M. Johnson, E. Edwards

University of Auckland, Auckland, New Zealand

There is growing evidence that fibromyalgia (FM) is a condition that involves dysfunction in the stress response system, specifically involving the autonomic nervous system. Some evidence for the autonomic nervous system involvement derives from studies analysing heart rate variability (HRV) that show sympathetic hyper-reactivity in FM patients. There is also a pilot study that indicates HRV biofeedback might be helpful for patients with FM. In a series of 5 single FM cases, we investigated the efficacy of paced breathing, HRV biofeedback and a control condition for FM symptoms. Four of the five participants reported reduced average daily pain during the last two weeks of HRV biofeedback compared to baseline while three of five reported reduced stiffness and two reduced fatigue. Although individual scores varied, mean depression, anxiety, and stress scores as well as sleep disturbance and disability were all lowest by the end of HRV biofeedback compared to baseline, control and paced breathing. The findings provide additional support for HRV biofeedback as an intervention but design limitations argue the need for a larger controlled trial.

Abstract: 988

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S277

IMPACT OF THE INTERACTION BETWEEN SELFEFFICACY, SYMPTOMS, AND CATASTROPHIZING ON DISABILITY, QUALITY OF LIFE, AND HEALTH IN CHRONIC PAIN PATIENTS

B. Börsbo^{1,2}, B. Gerdle^{1,3}, M. Peolsson^{1,4}

¹ *Rehabilitation Medicine, IKE, Faculty of Health Sciences, Linköping, Sweden*

² *Department of Rehabilitation Medicine, County Hospital Ryhov, Jönköping, Sweden*

³ *Pain and Rehabilitation Centre, University Hospital, Linköping, Sweden*

⁴ *School for Technology and Health, Royal Institute of Technology, Stockholm, Sweden*

Background and Aims: To investigate the interactions between self-efficacy - including subcomponents - and symptoms (pain, depression, and anxiety), catastrophizing, disability, quality of life, and health in a population of chronic pain patients.

Method: 433 chronic pain patients including 47 patients with spinal cord injury-related pain, 150 with chronic whiplash-associated disorders, and 236 with fibromyalgia. The participants answered a postal questionnaire that provided background data, pain intensity and duration, and psychological- and health-related items.

Results: In the multivariate context, depression, anxiety, catastrophizing, and disability were intercorrelated. Self-efficacy correlated positively with variables of quality of life and general health. These two groups of variables were negatively correlated. The pain variables - duration of pain, pain intensity, and spreading of pain - formed a third group of variables. Self-efficacy function was negatively correlated to these three pain variables. When regressing disability, quality of life, and health, we found that self-efficacy had a positive impact whereas symptoms, catastrophizing, and pain had a negative influence on these aspects. Different patterns of influencing variables were discerned for the three different analyses, and specific patterns of the subscales of self-efficacy corresponded to specific patterns of negative factors for the outcome of disability, quality of life, and health.

Conclusion: There is a complex interaction of psychological factors and symptoms and their positive and negative influence on disability, quality of life, and health. The results indicate that it might be important to assess and influence both enhancing and deteriorating factors to ensure an effective pain management programme.

Oral Presentation
Free Presentations 07: Anatomy and animal models

Abstract: 117

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S43

IMPLICIT OPERANT LEARNING OF CHANGES IN THERMO-NOCICEPTIVE SENSITIVITY IN FIBROMYALGIA PATIENTS WITH AND WITHOUT IRRITABLE BOWEL SYNDROME

S. Becker, D. Kleinboehl, D. Baus, M.F.J. Brunner, J.F. Ahlheim, R. Hoelzl

University of Mannheim, Otto Selz Institute for Applied Psychology, Laboratory for Clinical Psychophysiology, Mannheim, Germany

Background and Aims: Thermo-nociceptive sensitivity could be changed by implicit operant learning with contingent decrease and increase in pain intensity (intrinsic reinforcement) in healthy participants. Thus, it was assessed if these learning mechanisms were altered in fibromyalgia patients with and without comorbid irritable bowel syndrome.

Methods: Fibromyalgia patients with (13) and without (17) comorbid irritable bowel syndrome as well as healthy participants (29) took part in an operant conditioning procedure of enhanced sensitization and habituation in two separate sessions. Conditioning trials based on behavioral measurement of sensitization and habituation independent of subjective judgments. This was combined with standard methods of operant response shaping for enhanced sensitization or habituation, where reinforcement was implemented intrinsically by increase or decrease in heat-pain intensity contingent on criterion responses.

Results: Healthy participants learned changes in thermo-nociceptive sensitivity according to the operant learning conditions. In contrast, fibromyalgia patients with irritable bowel syndrome showed no signs of operant learning and in fibromyalgia patients without irritable bowel syndrome, sensitization occurred in both learning conditions with sensitization being, unexpectedly, even more intense under the habituation condition.

Conclusions: Pain perception can be shaped by implicit operant reinforcement in healthy participants, while fibromyalgia patients differ in their ability to learn enhancement of sensitization and habituation dependent. Implicit operant learning can be assumed to be important in the development and persistence of nociceptive hypersensitivity, but mechanisms seem to be altered in chronic pain.

Abstract: 948

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S268

INTERACTION BETWEEN APATHY AND MENTAL FLEXIBILITY ON PAIN COPING STRATEGIES IN FIBROMYALGIA (FM)

S. Baudic¹, A. Mhalla¹, D. Ciampi de Andrade¹, S. Perrot², N. Attal¹, D. Bouhassira¹

¹ *Inserm U 792 Hopital Ambroise Paré, Boulogne Cedex, France*

² *Service de Médecine Interne et Consultation de la Douleur, AP-HP, Hôtel-Dieu, Université Descartes Paris, Paris, France*

Aim of study: To examine the influence of apathy (reduction of voluntary behaviours sustained by a lack of motivation not attributable to diminished level of consciousness, cognitive impairment or emotional distress) on cognitive functions in the FM patients.

Methods: Thirty-nine consecutive FM women (age: 50.1±9.9, disease duration: 9.8±8.9) were evaluated by the Auditory Verbal Learning Test (learning), Trail Making Test A (focused attention) and B (mental flexibility) and Stroop Color Word Test (SCWT, selective attention, mental flexibility). They also completed the chronic pain acceptance questionnaire (CPAQ); survey of pain attitudes (SOPA-B) and multidimensional pain coping strategic questionnaire (MLPC). Apathy was measured by the Starkstein's scale.

Results: 54% of the patients had signs of mild to moderate apathy (mean: 18.5±5.5). The apathy score was correlated to the Trail Making Test B only. There were no differences between the patients with and without apathy on cognitive tests. The apathy score was also correlated to the CPAQ, MLPC and SOPA-B. Finally, the Trail Making Test B was related with the CPAQ and SOPA-B, and the SCWT with the SOPA-B.

Conclusion: Apathy appears to have a little impact on cognitive functions in FM patients. But, its influence on pain coping strategies may be more important. Furthermore, flexibility seems to be implicated in pain coping strategies. Apathy and flexibility should be considered as they could interfere with successful clinical management. Because of apathy or inflexibility, dysfunctional behaviours persist despite their disabling effects.

Abstract: 257

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S81

INTRAVENOUS LIDOCAINE ASSOCIATED WITH AMITRIPTILINE ON PAIN INTENSITY AND PLASMA CONCENTRATIONS OF SEROTONINE, NORADRENALINE AND DOPAMINE IN FIBROMYALGIA PATIENTS

R.K. Sakata, R. Vlainich, A. Issy

Federal University of São Paulo, São Paulo, Brazil

Background and Objectives: The main effect of lidocaine is central antihyperalgesic effect. The aim of the present study was to evaluate the effect of IV lidocaine associated with amitriptyline on pain intensity and plasma serotonin, norepinephrine, and dopamine in fibromyalgic patients.

Methods: Thirty patients participated in this randomized double-blinded study. All patients used 25 mg amitriptyline; G1 patients received saline, and G2, 240 mg lidocaine, once a week, for 4 weeks.

Results: Pain intensity reduced after treatment in G1 (T0: 7.0 ± 1.2 ; T4: 4.0 ± 2.1), and G2 (T0: 7.6 ± 0.8 e T4: 4.1 ± 2.3). Serotonin plasma concentrations were similar in T0 (G1: 42.7 ± 32.3 ; G2: 65.9 ± 41.1 ng/mL) and T4 (G1: 63.7 ± 32.1 ; G2: 76.7 ± 55.6), as norepinephrine in T0 (G1: 189.5 ± 108.6 ; G2: 171.9 ± 131.0 pg/mL) and T4 (G1: 167.5 ± 85.5 ; G2: 191.7 ± 142.3 pg/mL); dopamine levels was higher in T4 (45.7 ± 36.9 g/mL) than in T0 (17.1 ± 9.1 pg/mL) in G1; and there was no difference in T4 (34.7 ± 33.6) and T0 (25.8 ± 15.5) in G2.

Conclusion: The association of 240 mg IV lidocaine (1/week) with 25 mg amitriptyline for 4 weeks didn't modified pain intensity and plasma concentrations of serotonin, noradrenaline, and dopamine in fibromyalgia patients.

Abstract: 511

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S151

KETAMINE FOR THE TREATMENT OF FIBROMYALGIA SYNDROME

Mó. Mayo Moldes, A. Carregal, T. Fernandez, J.C. Carballo

Hospital Meixoeiro, Vigo, Spain

Background: Fibromyalgia (FMS) is a widespread chronic pain disorder. The use of NMDA antagonists have been recommended.

Aims: To assess the efficacy and safety of low-dose (0.4 mg/kg) i.v. ketamine in FMS. The primary outcomes were the correlation between basal status and changes in pain (VAS), and other variables (sleep, anxiety, depression, headache, stiffness, muscle cramps, brain fog, dry mouth, rhinitis and pharyngitis) before and after infusion of ketamine, and 7 days, 1, 3 and 6 months.

Methods: Prospective, open-label, non-controlled study. 21 patients were included and received a short course (5 days) ketamine infusion administered over 30 min, under monitorization. One patient was excluded for a adverse effect. Data were compared with McNemar and Wilcoxon Signed Ranks tests.

Results: Post-infusion average pain ratings were significantly improved over baseline (Table 1); as were several fibromyalgia descriptors: depression, headache, stiffness, muscle cramps (table 2). The percentage of subjective improvement at 3 and 6 months was 50% vs 33%.

Table 1: Average pain ratings 7 days, 1, 3 and 6 months. ($P \leq 0.001$)

	0 days	7 days	1 month	3 months	6 months
VAS rating	73±14	46±25	48±24	39±22	47±16

Table 2: Fibromyalgia descriptors with significant improvement. (N = 20; $P_s < 0.05$)

	depression					headache				
	0	7d.	1m	3m	6m	0	7d.	1m	3m	6m
N	17	9	6	8	9	17	12	9	5	7

	stiffness					muscle cramps				
	0	7d.	1m	3m	6m	0	7d.	1m	3m	6m
N	19	11	7	10	11	16	7	3	4	6

Ketamine reduced significantly the pain of fibromyalgia syndrome and improved other patient-reported conditions.

Abstract: 498

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S147

MILNACIPRAN FOR THE TREATMENT OF FIBROMYALGIA SYNDROME: A EUROPEAN MULTICENTER, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

J.C. Branco¹, S. Perrot², O. Airaksinen³, P. Sarzi Puttini⁴, M. Galissié⁵, S. Lugardon⁵, A. Montagne⁵, O. Vitton⁵, Y. Mainguy⁵

¹ Hospital Egas Moniz Departamento de Reumatologia, Lisboa, Portugal

² Hôpital Hôtel Dieu, Paris Cedex 04, France

³ Suomen Oma Lääkäri Oy, Kuopio, Finland

⁴ Ospedale Luigi Sacco U.O Reumatologia, Milano, Italy

⁵ Institut de Recherche Pierre Fabre (IRPF), Labège, France

Background and Aims: Milnacipran, a dual reuptake inhibitor of norepinephrine and serotonin, has been approved by the US FDA for the management of fibromyalgia (FM). This study investigated the efficacy and safety of milnacipran in a FM European population. The protocol was approved by each center's IRB. Each patient gave written informed consent.

Methods: 83 sites (13 European countries) randomized 884 FM patients to placebo or milnacipran 200 mg/day for 12 weeks (after 4-week up-titration). The primary analysis used a sequential testing procedure involving a 2-measure composite response criterion (pain VAS + Global Patient Improvement of Change-PGIC (eDiary), then the change in the FM Impact Questionnaire (FIQ) total score (eDiary). Composite responders were defined as individuals concurrently having $\geq 30\%$ improvement from baseline in pain and a rating of "very much improved" or "much improved" on the PGIC.

Results: Milnacipran, significantly increased the primary efficacy composite criterion ($P = 0.0003$) and the FIQ total score ($P = .015$). Secondary analyses showed milnacipran significantly improved on multiple FM domains at the endpoint as compared to placebo as follows: pain scores on eDiary ($p \leq 0.001$), Brief Pain Inventory - Pain Interference ($p < 0.02$), SF-36 Mental ($p < 0.01$) and Physical ($p < 0.05$) components, Multidimensional Fatigue Inventory total score ($p < 0.01$), FIQ Physical function subscore ($p < 0.05$) and Multiple Ability Self-Report Questionnaire cognition complaints total score ($p < 0.05$), non-refreshing sleep (eDiary, $p < 0.01$). Milnacipran was well tolerated, the majority of adverse events reported (mainly nausea and hyperhidrosis) being mild to moderate in severity.

Conclusions: Milnacipran 200 mg/d is an effective and safe treatment for the multiple symptoms of FM. The study was supported by and performed in collaboration with Pierre Fabre. O. Vitton, M. Galissié, S. Lugardon, A. Montagne, Y. Mainguy are Pierre Fabre employees

Abstract: 540

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S159

MUSCLE PAIN IN CHILDREN AND ADOLESCENTS

B. Horlé¹, C. Wood²

¹ *Service de Pédiatrie Centre Hospitalier de Brive-la-Gaillarde, Brive-la-Gaillarde, France*

² *Unité d'Evaluation et de Traitement de la Douleur Centre Hospitalier Universitaire Robert Debré, 75 019 Paris, France*

Acute muscle pain is reported in 6.1% of schoolchildren. It is mainly of traumatic origin. The incidence of chronic muscle pain, however, is variable, depending on its localization. It is frequently of non-traumatic origin.

The clinical approach is essential for diagnosis. It is important to watch the child walk and move. Examination should look for muscle tenderness, trophicity and swelling, as well as oedema, deformed articulation and haematomas. If muscle trigger points are found, they evoke myofascial syndrome. Diffuse muscle pain could be a sign of fibromyalgia.

In case of chronic pain, psychosomatic symptoms like fatigue and anxiety or associated pain symptoms like headache or abdominal pain should be asked for.

Certain factors can predispose to chronic pain: low pain threshold, female gender, physical hyperactivity or lack of physical exercise, negative coping strategies, physical or sexual abuse, anterior pain experiences, poor social background, sleeping problems and imitation of parental attitude towards pain. They should also be investigated for.

In some cases paraclinical examinations are indicated for differential diagnosis.

Once the diagnosis of "muscle pain" established, it is important to reassure the child and parents that the prognosis is good even though the symptomatology is painful. The negative impact of stress on pain should also be explained.

Medical treatments and analgesics can be prescribed, but rest should be avoided.

Complementary therapies like physiotherapy, acupuncture, relaxation or hypnosis are essential and based on an individual approach. Psychological follow-up should be proposed in case of chronic pain as it is a helpful support to develop coping strategies.

Abstract: 537

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S158

MUSCLE TRIGGER POINTS IN SUBJECTS WITH FIBROMYALGIA SYNDROME: PRELIMINARY RESULTS

C. Fernández-de-las-Peñas¹, C. Alonso-Blanco¹, J. Fernández-Carnero¹, P. Zarco², M. Flórez-García²

¹ *Universidad Rey Juan Carlos, Alcorcón, Spain*

² *Fundación Hospital Alcorcón, Alcorcón, Spain*

Background and Aim: It is suggested that muscle trigger points (TrPs) can be involved in fibromyalgia syndrome (FMS). Our aim was to investigate in a blinded design the presence of TrPs in 12 pair of muscles in FMS when compared to controls.

Methods: Ten women (age: 48±8 years) diagnosed with FMS according to the ACR criteria and 10 healthy women (age: 47±9 years) participated. TrPs in upper trapezius, sternocleidomastoid, suboccipital, splenius capitis, levator scapulae, scalene, temporalis, masseter, extensor carpi radialis brevis, extensor digitorum communis, piriformis and tibialis anterior muscles were bilaterally identified according to Simons et al. criteria: hyperirritable spot in a taut band, local twitch response and referred pain. TrPs were active if the referred pain reproduced pain symptoms, whereas TrPs were latent when the referred pain did not reproduce symptoms.

Results: The mean number of TrPs in FMS patients was 9.4 (SD: 1.9) active TrPs and 1.5 (SD: 2.0) latent TrPs. Controls only exhibited latent TrPs (1.5±0.5). Significant difference between groups were found for active ($P < 0.001$), but not latent TrPs ($P = 0.8$). Active TrPs in the upper trapezius ($n = 9$, $n = 6$ right/left side), extensor carpi radialis brevis ($n = 8$, $n = 7$), masseter ($n = 6$, $n = 5$) and piriformis ($n = 5$, $n = 5$) muscles were the most prevalent within FMS subjects.

Conclusions: The referred pain elicited from active muscle TrPs may be implicated in the genesis of FMS.

Abstract: 860

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S245

NEUROMODULATION OF REFRACTORY NEUROPATHIC PAIN CONDITIONS. EARLY OUTCOMES FROM C2 AREA STIMULATION, SUBCUTANEOUS AND COMBINED SUBCUTANEOUS AND SPINAL CORD STIMULATION

J. Salmon

Achieve Pain Control Group Bethesda Hospital, Claremont WA, Australia

Background: Central nervous system mechanisms and pathology interactive with the psychosocial environment are currently considered to be the principal origins of the more severe and disabling persistent pain conditions.

Spinal cord stimulation treatment of neuropathic pain, particularly post spinal surgery, is now well established and accepted with a level 1 evidence base and recent endorsement by NICE. However, for many patients it remains difficult to achieve effective stimulation coverage of head and truncal regions of the body and diffuse neuropathic pain states such as fibromyalgia have not been previously considered candidates for neuromodulation by electrical stimulation approaches.

During the last 10 years occipital nerves/region stimulation has become relatively well-established for the treatment of occipital region neuropathic pain and also increasingly for chronic migraine and related cranial central neuropathic pain syndromes. PET studies have demonstrated that C2 stimulation alters brain stem region neural activity.

Recently there have been anecdotal reports of potent responses to subcutaneous implanted electrode stimulation in areas of neuropathic pain on the trunk, head and limbs which were previously unresponsive to spinal cord stimulation and other modalities and also reports of severe fibromyalgia symptoms responding significantly to upper occipital region stimulation (C2 area).

Method: Retrospective review of clinical outcomes for a variety of patients with refractory and/or diffuse neuropathic pain states implanted with C2 area and/or subcutaneous and spinal cord stimulation systems over the last two years.

Results and Conclusions To be collated and presented.

Financial support from St Jude Medical (ANS) to attend conference applied for.

Abstract: 950

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S268

PERSONALITY HARDINESS MODEL AS A COGNITIVE-BEHAVIORAL APPROACH WITH FIBROMYALGIA PATIENTS

B. Gokce Doering¹, I. Yegul²

¹ *Ege University, Department of Algology, School of Medicine, izmir, Turkey*

² *Ege University, Faculty of Medicine, Izmir, Turkey*

Introduction: A cognitive-behavioral treatment model for chronic pain was investigated in fibromyalgia patients. The aim of this study was to assess the effectiveness of the model on treatment and enhancement of self control over chronic pain by changing pain related attitude on skills. Personality Hardiness, depression, anxiety and communication skills of patients investigated in this study.

Methods: 10 patients suffering from fibromyalgia were included in this study. Subjects were chosen from Ege University Department of Algology. Zung depression scale, modified somatic perception test, personality hardiness questionnaire and communication skills test were used in the present study. Cognitive-Behavioral approach (personality hardiness training, progressive relaxation, communication skills, problem solving techniques) was applied to the patients. The program was performed 10 weeks and 2 hours per week.

Results: Semi-depression, anxiety and somatization were found before treatment. Personality hardiness training was used as a stress coping method. Control, commitment and challenge subscales were evaluated. Helplessness, passivity and over control skills, perceiving the stress as a threat, giving up and alienation skills were found in this group. Good balance was found between three skills after treatment.

Abstract: 504

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S149

PHYSICAL AND PSYCHOLOGICAL STRESS AS A TRIGGER FOR PATIENTS WITH FIBROMYALGIA: REVIEW OF 22 CASES

C. Gaudet, G. Vargas-Schaffer

Hôtel Dieu du CHUM, Montreal, Canada

Background and Aims: Fibromyalgia represented in Rheumatology 8 to 10% of new diagnoses. The pain is the cornerstone of clinical or diffuse or localized pain in all cases, persistent pain, intense, rebel in the various medical treatments or even surgery. The main objective of this review of cases is to establish the relationship between a physical or psychological stress and the emergence of fibromyalgia.

Materials and Method: We studied a total of 24 cases of patients referred Rheumatology service at the clinic of CHUM. Two cases were excluded because they did not have any history of fibromyalgia.

Result: The sample was formed by 17 women and 5 men. In 90% of cases, there is a stressor before the outbreak of the disease. Of these cases, 50% were a psychological stressor (violence, abuse, PTSD); 50% were physical stress (column trauma, surgery, cancer, hepatitis C). The family history was positive for a parent of first degree with chronic pain in 10 patients, therefore 45%. The positive family history is also found that the trauma is physical and/or psychological. Morbidity found were: irritable colon 36.36% (8/22), menstrual changes 76.47% (13/17), respiratory disorders 31.81% (7/22), and headaches 50% (11/22). All of these morbidities were equal, that trigger physical or psychological except for migraine found most often with the trigger psychological (70%).

Conclusion: Review of these 22 cases suggests that fibromyalgia is a stress-related illness and the stress may be physical and/or psychological.

Oral Presentation

Topical Seminar: Potential implications of pain brain imaging in the clinic

Abstract: 61

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S26

POTENTIAL IMPLICATIONS OF PAIN BRAIN IMAGING IN THE CLINIC: LOW BACK PAIN AND FIBROMYALGIA

P. Schweinhardt

Alan Edwards Centre for Research on Pain, McGill University, Montreal, Canada

Fibromyalgia belongs to the so-called 'functional pain syndromes', a term that is used to describe pain conditions for which no organic cause can be found. Similarly, chronic low back pain is in many instances disproportional to observable pathology, which might even be completely absent. In recent years, however, it has become clear that patients with functional pain syndromes exhibit functional, structural, and biochemical brain alterations. Interestingly, some of these brain changes overlap with findings in patients with stress-related disorders, such as post-traumatic stress disorder or depression. This might point at etiological commonalities of functional pain syndromes and stress-related disorders. In this talk, I will describe some of the brain alterations observed in functional pain syndromes as well as how they might relate to the symptoms commonly experienced by the patients. For example, we have observed dysfunctions of dopaminergic neurotransmission in fibromyalgia (Wood et al., 2007). While healthy subjects released dopamine during an experimental pain challenge, fibromyalgia patients showed a substantial lack of the dopamine response. Dysfunctional dopaminergic systems could not only contribute to the patients' pain but also to mood disturbances or cognitive impairments. Cognitive difficulties are indeed frequently reported by patients with fibromyalgia. Structural brain alterations, especially decreases in gray matter, have repeatedly been observed in patients with fibromyalgia (e.g. Kuchinad et al., 2007) and chronic low back pain (e.g. Apkarian et al.) in pain- and stress-related areas. Such structural alterations could potentially contribute to dyscognition. We are currently undertaking a study in patients with fibromyalgia to investigate the relationship between structural and functional brain alterations and cognitive impairment.

Reference: Wood et al., Fibromyalgia patients show an abnormal dopamine response to pain. Eur J Neurosci, 2007. 25(12): p. 3576-82.

Reference: Kuchinad et al., Accelerated brain gray matter loss in fibromyalgia patients: premature aging of the brain? J Neurosci. 2007 Apr 11; 27(15): 4004-7.

Reference: Apkarian et al., Chronic back pain is associated with decreased prefrontal and thalamic gray matter density. J Neurosci. 2004 Nov 17; 24(46): 10410-5.

Abstract: 225

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S73

RATE ANALYSIS IN GENETIC POLYMORPHISMS OF GENES GSTM1, GSTT1, COMT, 5-HTT IN PATIENTS DIAGNOSED WITH FIBROMYALGIA. COMPARISON WITH CONTROL GROUP

N. Albesa^{1,3}, A. Corno²

¹ *Madrid, Spain*

² *Análisis Genéticos ANCOR, Madrid, Spain*

³ *Clínica Ruber, Madrid, Spain*

Results: From the comparative evaluation of these genes' rates in both treatment and control groups (which has to be completed with a statistic analysis), we could appreciate:

- A. Higher rate of GSTT1 null polymorphism (gene absence) in the treatment group (42.05%) as compared to the control group (20.50%). In case that this difference is found to be significant, it would mean a lower ability to eliminate potential etiologic agents of the disease or modifiers for clinical course.
- B. Higher rate of COMT Val/Met heterocygotes in the treatment group (87.61%) as compared to the control population (64.36%). The presence of Val/Val homocygotes was lower (0.02%) in fibromyalgic patients than in healthy subjects (21.78%). This would speak of the role of Met-allele presence and Val-allele absence in the disease, confirming the results of other clinical trials.
- C. In healthy subjects, the presence of SS homocygotes was higher (22.34% vs 16.00%), while the presence of LL homocygotes was lower (23.40% vs 34.00%). This fact suggests an active participation of the S allele in the disease (higher levels of depression and psychological distress). It may also support the thesis that there is an implication of altered serotonin metabolism in the disease (decreased levels of tryptophan and serotonin have been associated with fibromyalgia).

If these differences turn to be statistically significant, they would prove that the alteration of detoxification routes, catecholamine catabolism and synthesis of serotonin is implied with the onset of the disease or with its symptoms.

Abstract: 509

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S150

RECOGNIZING FIBROMYALGIA IN MULTIPLE SCLEROSIS

K. Kosma¹, G. Papadopoulos¹, A. Sianni¹, K. Liatsos², M. Anastasiou³

¹ *Department of Neurology, Dromokaitio Psychiatric Hospital of Athens, Athens, Greece*

² *"Mitera" Maternity Hospital of Athens, Athens, Greece*

³ *"Thriasio", Department of Aneesthesiology, General Hospital of Athens, Athens, Greece*

Introduction: Fibromyalgia is a chronic pain disorder, characterized among others by tiredness, sleep and emotional disturbances. If these symptoms are present in a sufferer from Multiple Sclerosis (MS) they could be attributed to the disease itself and thus fibromyalgia in these patients can easily be misdiagnosed and mistreated.

Case report: We report a 47-year-old female patient with primary progressive multiple sclerosis (PPMS) who presented with widespread musculoskeletal pain since 6 months. At first, she was complaining for low back pain, fatigue and muscle pain after exertion. For the last 5 months reported pain in her neck, shoulders and arms with gnawing sensation and pain in her knees, legs and feet with a burning-aching sensation. Stiffness was almost present every day. Additionally, the pain awakened the patient frequently at night. Her neurological examination revealed otherwise only a mild gait disturbance. The diagnosis of fibromyalgia was then considered possible, since it requires a history of at least 3 months of widespread pain, and tenderness in at least 11 of 18 tender-point sites. The patient was administered duloxetine in up to 60 mg daily and pregabalin in up to 150 mg daily and showed great improvement 3 weeks after initiation of treatment.

Discussion and Conclusions: Despite the fact that clinical manifestations such as pain, stiffness and fatigue are common in patients with MS, the possibility of another cause must always be taken into consideration, especially if the symptoms cannot be easily attributed to the lesions of MS.

Oral Presentation

Free Presentations 11: Treatment approaches (invasive)

Abstract: 144

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S50

REPETITIVE TRANSCRANIAL MAGNETIC STIMULATION (rTMS) OF THE MOTOR CORTEX IMPROVES CRPS PAIN

H. Picarelli^{1,2}, M. Jacobsen Teixeira^{1,2}, M.L. Myczkowski^{1,3}, T. Barreira Luvisotto^{1,3}, L.T. Yeng^{1,2}, E. Talamoni Fonoff^{1,2}, **D. Ciampi de Andrade**^{1,2,3}, S. Pridmore⁴, M.A. Marcolin^{1,3}

¹ *Institute of Psychiatry Hospital das Clínicas of the University of São Paulo (USP), Brazil*

² *Division of Functional Neurosurgery of Institute of Psychiatry, Department of Neurology, USP., São Paulo, Brazil*

³ *Laboratory of Transcranial Magnetic Stimulation, Department of Psychiatry, USP., São Paulo, Brazil*

⁴ *Division of Psychiatry, University of Tasmania, Hobart, Tasmania, Australia*

Background and aims: Evidence is being gathered to support the use of repetitive sessions of rTMS to relieve non-neuropathic pain conditions such as fibromyalgia, and complex regional pain syndrome type I (CRPS-I). There are only a few studies evaluating the efficacy of repetitive sessions of rTMS. They showed that its analgesic effect outlasted the stimulation period for more than a week. In the present study we assessed, for the first time, the analgesic effects of ten consecutive sessions of rTMS in patients with refractory CRPS-I under a standardized evidence-based baseline treatment.

Methods: Twenty-three patients presenting with CRPS of the hand were treated with conventional treatment plus either sham-rTMS (srTMS) or real rTMS (rrTMS) over the motor cortex opposite to the affected limb. The following parameters were used: stimulations at 100% MT, 10 Hz, 10 s trains, 25 trains/day, for ten consecutive days.

Results: There was significant reduction in visual analogical scale (VAS) scores favoring the rrTMS group up to the seventh day after stimulation ($p < 0.05$). The mean pain reduction during sessions in the VAS scale was 4.65 cm and 2.18 cm in the rrTMS and srTMS groups, respectively ($p < 0.05$). Improvement in VAS scores was independent of other variables (PIQ-6, DASH and Hamilton questionnaires) except for improvement in emotional aspects in the SF-36 questionnaire.

Conclusions: Real rTMS sessions were able to reduce pain intensity in patients with refractory CRPS-I during the stimulation period and up to seven days after the end of the stimulation.

Abstract: 503

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S149

ROPINIROLE IN THE TREATMENT OF REFRACTORY FIBROMYALGIA: A CASE SERIES

J.M. Garcia-Leiva¹, R. Molina-Barea², C.Ma. Rodriguez-Lopez¹, P. Morillas-Arques³, J. Garcia-Carrillo¹, E.P. Calandre¹

¹ *Institute of Neuroscience, University of Granada, Granada,* ² *Hospital San Cecilio, Granada,* ³ *Hospital Ciudad de Jaén, Jaén, Spain*

Background and Aims: The purpose of the present study was to evaluate the effectiveness and tolerability of ropinirole, a dopamine receptor agonist, in fibromyalgia patients refractory to standard drugs such as antidepressants and/or pregabalin.

Methods: Twenty three fibromyalgia patients, 18 women and 5 men aged 27-67 years, received ropinirole in a starting dose of 0.25 mg/day subsequently adjusted according to patients' response, during 12 weeks. Outcome variables included the Fibromyalgia Impact Questionnaire (FIQ), the Brief Pain Inventory (BPI), the Hospital Anxiety and Depression Scale (HADS) and the Short Form Health Survey SF-36. Adverse drug reactions were recorded. Data analysis was done on the Intention-To-Treat sample which included all the patients who started the treatment.

Results: Final ropinirole daily dose ranged from 1 to 4 (2.55±0.86) mg. Five (22%) patients withdrew before the study end due to drug-related side effects. At endpoint significant decreases were found in the FIQ total score (-12.9, p = 0.016), in BPI average pain severity (-1.15, p = 0.019) and global interference scores (-1.02, p = 0.023), and in the HADS anxiety score (-2.35, p = 0.0005). Significant increases were found in the items of bodily pain (7.6, p = 0.034), general health (5.3, p = 0.0098), mental health (8.7, p = 0.029), and vitality (8.00, p = 0.026) of the SF-36. Seventeen (74%) patients reported adverse reactions; most frequently reported side effects included dizziness (43%), nausea (31%), headache (19%), sedation (15%).

Conclusions: In this sample of highly refractory patients, ropinirole improved fibromyalgia symptomatology and quality of life. However, tolerability was poor.

Abstract: 216

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S70

SOCIAL SUPPORT MODULATES BRAIN ACTIVATION IN FIBROMYALGIA PATIENTS

P. Montoya¹, **W. Larbig**², C. Sitges¹, R. Veit², N. Birbaumer²

¹ *Research Institute on Health Sciences (IUNICS) University of Balearic Islands, Palma, Spain*

² *Institute of Medical Psychology and Behavioral Neurobiology, University of Tuebingen, Tuebingen, Germany*

Previous research has shown that fibromyalgia is characterized by an abnormal processing of somatosensory information and that pain sensitivity in these patients may be modulated by affective factors. Recently, it has been further observed that affective components of the neural pain network are more activated than sensory components during the experience of another's pain in healthy controls. In the present study, we investigated whether the presence vs. absence of patient's significant other may also influence brain activity elicited by non-painful somatosensory stimulation in fibromyalgia. Ten female patients with fibromyalgia (aged 51.2 yrs) and nine female healthy controls (aged 55.3 yrs) were examined using fMRI during the application of vibratory stimuli at the elbow (considered as a tender point in fibromyalgia) and finger (control point). Significant greater activations were found in insula, anterior cingulate cortex (ACC), and secondary somatosensory cortex (SII) in fibromyalgia patients compared to healthy controls only when somatosensory stimuli were applied at the elbow in presence of patient's significant other, but no when stimuli were applied in absence of patient's significant other, or when stimuli were applied at the finger. These data suggest that social support from significant others may activate both sensory and affective components of the pain network in fibromyalgia. Furthermore, we concluded that social support could play a relevant role for the maintenance of pain in fibromyalgia. Research was supported by the Spanish Ministerio de Ciencia e Innovación and European Funds (Plan Nacional de I+D+I; ref.: SEJ2007-62312).

Abstract: 496

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S147

STRESS-RELATED LATENCY IN SENSORY AND AFFECTIVE DIMENSIONS OF REPORTED PAIN IN PATIENTS WITH FIBROMYALGIA SYNDROME

C. Pyle, A. Moe, M. Terao, E. Luppino, C. Athing, R. Allen

Department of Physical Therapy University of Puget Sound, Tacoma, WA, United States

Background & Aims: Patients with fibromyalgia syndrome (FS) experience variable persistent pain, yet causes of episodic pain flares are often inexplicable. Stress is suggested as a trigger, however correlations between pain intensity and same-day stress are low. Recent FS case studies report notable increases in pain ten days following stressful episodes. One case yielded psychoendocrine evidence that the ten-day delay may be delayed influence of stress-related thyroxine release on nociceptor excitability and cerebation rate. This study's aim was to assess the impact of stress across time on latent pain intensity changes and affective pain responses in a larger FS patient sample.

Methods: 38 patients with FS participating in a multidisciplinary pain program (34 females, 4 males) completed the following inventories daily over 4 weeks: Daily Stress Index (DSI), Visual-Analog Pain (VASP), McGill Pain Questionnaire Short Form (MPQSF). Serial-lag correlations between DSI and VASP scores and between DSI and MPQSF-A assessed the impact of daily stress across time on the intensity and affective response to episodic pain flares.

Results: Pain intensity was not correlated with same-day stress scores ($r = +0.106$). However, serial-lag correlations revealed a significant relationship between stress and pain flares occurring ten days later ($r = +0.481$). Affective responses to pain showed little relationship to same-day stress ($r = +0.106$), yet significant peaks ten days after high stress days ($r = +0.589$).

Conclusion: Daily stress increases are associated with delayed episodic pain flares and pronounced affective responses to pain occurring ten days later in patients with FS.

Abstract: 445

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S134

STRUCTURAL BRAIN CHANGES IN PATIENTS WITH RHEUMATOID ARTHRITIS

K. Wartolowska^{1,3}, M.G. Hough¹, P. Wordsworth², I. Tracey^{1,3}

¹ *Centre for Functional Magnetic Resonance Imaging of the Brain, Oxford, United Kingdom*

² *Nuffield Orthopaedic Centre, Oxford, United Kingdom*

³ *Nuffield Department of Anaesthetics, Oxford, United Kingdom*

Introduction: Recent studies demonstrated that chronic pain leads to possible structural brain changes in diseases such as lower back pain, migraine and fibromyalgia. We used two automated methods to investigate whether morphometric changes occur in patients with rheumatoid arthritis (RA).

Methods: We recruited 28 patients with severe RA, and 25 age- and sex-matched healthy controls. High-resolution MP-RAGE images were acquired on a 3T scanner Tim Trio (Siemens, Erlangen). Data were analyzed using FSL_VBM, a voxel-based morphometry style analysis and FreeSurfer, a surface-based morphometry. To investigate the effect of disease duration, a model with disease duration as a regressor of interest was used in the patients group.

Results: There were no local structural grey-matter differences between patients and controls in the FSL_VBM. The FreeSurfer analysis however revealed decrease in grey-matter thickness in both parahippocampal gyri. Moreover, RA patients had significantly smaller brains compared to controls, estimated using intra-cranial volume (ICV). In the patient group, disease duration, when controlled for age, significantly correlated with ICV ($r = 0.44$ $p = 0.019$) and there was a trend for ASF ($r = -0.36$ $p = 0.055$). Furthermore, in the patients group the disease duration regressor negatively correlated with grey matter density in the thalamus.

Conclusions: These results suggest that there are global brain differences associated with RA. However, it is not clear whether these changes represent an accelerated rate of atrophy as observed in fibromyalgia, the effect of systemic inflammation and vasculopathy similar to lupus erythematosus or rather intrinsic differences between RA patients and healthy controls.

Oral Presentation

Topical Seminar: Endogenous pain controlling systems

Abstract: 54

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S24

STUDIES IN PATIENTS

D. Yarnitsky

Dept of Neurology Rambam Medical Center Technion Faculty of Medicine, Haifa, Israel

Psychophysical tests of endogenous pain controlling systems had been applied in several pain disorders. Studies have shown a less efficient DNIC-like function in patients with idiopathic pain syndromes, such as tension headache, fibromyalgia, irritable bowel syndrome etc. Tests were applied either at pain site or remote from it, and represent a systemically deranged pain modulation. These findings raised the question of whether this dysfunction is primary to the pain syndrome, or, alternatively, caused by it. Some evidence is now available to support the first option: 1. Several studies have shown a correlation between psychophysical pain parameters such as pain threshold and magnitude estimation of experimental suprathreshold pain stimuli, obtained before surgery, and acute post operative pain. 2. One study showing correlation between DNIC-like efficiency before surgery and chronic post operative pain in thoracotomy patients. These studies support the thinking that deranged pain processing, specifically non efficient DNIC, make the subject susceptible to acquire pain. In support of the alternative is the report on improvement of DNIC efficiency after surgical treatment of painful joint disease that relieved pain. This suggests that DNIC reacts to the clinical pain state, rather than be involved in its generation. New data available along these lines will be presented and the issue of chicken and egg between pain inhibitory modulation state and prevalence of clinical pain will be discussed. In addition, findings on changes in endogenous pain inhibitory function and dysfunction in neuropathic pain patients will be presented and discussed in relation to therapeutic considerations.

Abstract: 1013

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S284

SYSTEMATIC REVIEW AND META-ANALYSIS OF PSYCHOLOGICAL TREATMENTS FOR PERSISTENT OR RECURRENT PAIN IN CHILDREN AND ADOLESCENTS

A.C.C. Williams¹, C. Eccleston², S. Morley³, T. Palermo⁴, A. Lewandowski⁴

¹ *University College London, Research Department of Clinical, Educational & Health Psychology, London, United Kingdom*

² *University of Bath, Bath, United Kingdom*

³ *University of Leeds, Leeds, United Kingdom*

⁴ *Division of Psychology, Children's Hospital Boston, Boston, United States*

Background and Aims: The psychological treatment of children and adolescents with persistent and recurrent pain, mainly headache and abdominal pain, is expanding so that a 2003 systematic review and meta-analysis required updating. This was completed in the Cochrane format using only randomized controlled trials (RCTs). Pain can be rated as severe and can cause distressed mood, and reduced participation in normal activities.

Methods: We searched widely for RCTs up to August 2008 comparing a psychological treatment with placebo, waiting list or standard medical care. All studies were rated for quality, and data were extracted on pain, disability, and mood outcomes.

Results: Thirty-four RCTs were recovered; 29 met the inclusion criteria, 20 of which treated headache (including migraine); the remainder (non-headache) treated abdominal pain, fibromyalgia, and pain from sickle cell disease. The total number of participants was 1432. For headache pain, treatment versus control gave an NNT of 2.57 (CI 2.2 to 3.13) immediately post-treatment and 1.99 (CI 1.63 to 2.72) at follow-up. For non-headache pain, the effect size was -0.94 (95% CI -1.43 to -0.44) immediately after treatment, and -1.08 (95% CI -1.84 to -0.33) at follow-up. Where measured, there were no significant improvements in distress or disability.

Conclusions: Psychological treatments are effective in pain control for children with headache, musculoskeletal and recurrent abdominal pain and benefits appear to be maintained. There is little evidence available to estimate effects on disability or mood.

Abstract: 514

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S152

THE EFFECT OF MILNACIPRAN ON TENDERNESS IN FIBROMYALGIA: A PSYCHOPHYSICAL AND FMRI ANALYSIS

F. Petzke¹, R.H. Gracely², K. Jensen³, E. Kosek³, M. Ingvar⁴, H. Marcus¹, E. Choy⁵, S.C.R. Williams⁶, M. Groc⁷, A. Montagne⁷, O. Vitton⁷, Y. Mainguy⁷

¹ Pain Clinic Department of Anesthesiology University Hospital of Cologne, Cologne, Germany

² Center for Neurosensory Disorders, Chapel Hill, United States

³ Karolinska Institute Department of Neurosciences, Stockholm, Sweden

⁴ Karolinska Institute Department of Neurosciences, Stockholm, Sweden

⁵ King's College Hospital Academic Department of Rheumatology Weston Education Centre, London, United Kingdom

⁶ Institute of Psychiatry Centre for Neuroimaging Neurosciences, London, United Kingdom

⁷ Institut de Recherche Pierre Fabre (IRPF), Labège, France

Background and Aims: Milnacipran, a serotonin and a norepinephrine reuptake inhibitor has been approved by the US FDA for the management of fibromyalgia (FM). This study evaluated the association of tenderness and spontaneous pain in FM using psychophysical ratings and functional magnetic resonance imaging (fMRI) measures of brain activity before and after treatment. The study protocol was approved by each center's Institutional Review Board. Each patient gave informed consent.

Methods: 92 right-handed FMS female patients participated in a 13-week, multicenter, double-blind, randomized trial assessing the effects of milnacipran 200 mg/d compared to placebo. At baseline and endpoint, each participant rated the pressure-evoked pain intensity of non-painful and painful pressure stimuli randomly applied to the left thumbnail to calculate subjectively equal pain sensations (VAS 50 mm), that was delivered during fMRI scanning before and after treatment.

Results: Milnacipran reduced pain-evoked tenderness in comparison to placebo, an effect that approached statistical significance ($p = 0.11$). fMRI analyses revealed significantly increased brain activity following milnacipran treatment in multiple brain regions involved with pain modulation. Placebo increased activity only in a parietal region and mid insula. Comparison between the effects of milnacipran and placebo showed increased activity in a large region of posterior cingulate/precuneus ($p < 0.05$)

Conclusions: Milnacipran exerted a normalizing effect in FM patients, reducing tenderness and increasing activity in brain regions involved in pain modulation, suggesting an association between the mechanisms mediating tenderness and pain and related symptoms of FM.

This study was supported by and performed in collaboration with Pierre Fabre. M. Groc, A. Montagne, O. Vitton, Y. Mainguy: Pierre Fabre employees

Oral Presentation

Topical Seminar: Central hypersensitivity in musculoskeletal pain

Abstract: 21

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S9

Topical Seminar Summary: CENTRAL HYPERSENSITIVITY IN MUSCULOSKELETAL PAIN

M. Curatolo¹, A.H. Dickenson², L. Arendt-Nielsen³

¹ University Department of Anaesthesiology and Pain Therapy, University of Bern, Inselspital, Bern, Switzerland

² University College London, Dept Pharmacology, London, United Kingdom

³ Aalborg University, Aalborg, Denmark

Introduction: There is consistent evidence from animal studies that tissue inflammation and nerve damage induce plasticity changes in the nociceptive system leading to hypersensitivity [1]. These findings have been confirmed in several human studies [2]. Clinically, sensitization is characterized by: (1) decrease in the response threshold (i.e. an otherwise innocuous stimulus evokes pain); (2) increased response to suprathreshold stimuli (i.e. an otherwise moderately painful stimulus is perceived as severely painful); and (3) enlargement in the referred pain areas. All these manifestations have clinical relevance.

The purposes of the workshop are: (1) to review the neurobiologic mechanisms underlying hypersensitivity states in musculoskeletal disorders; (2) to review the methods to assess central hypersensitivity in patients; (3) to present the published evidence on central hypersensitivity in patients; and (4) to highlight the clinical implications in terms of role of central hypersensitivity in pain and disability, perspectives of assessment in individual patients and possible treatment modalities. The workshop ultimately aims at elucidating the bridges between basic research and clinical practice for this relevant pain mechanism.

Mechanisms of Sensitization: A peripheral nociceptor can be sensitized in damaged tissues by the release of algogenic substances, inflammatory mediators or damage/degeneration of the terminals [1]. When a peripheral nociceptor is sensitized, the firing to a given stimulus is increased and prolonged, and the threshold for firing is lowered.

Nociceptive input can alter the function of transmitter release from their central terminals so that excitatory amino acids, neuropeptides and synaptic modulators are augmented, thus increasing neuronal excitability [1].

Increased levels of protein production mediate a later transcription-dependent phase [1]. The inhibitory controls within the spinal cord are reduced, leading to increased nociceptive activity travelling to the brain [3]. As a result of all these changes, non-nociceptive input can activate pain pathways, and low-levels of nociceptive stimuli can produce exaggerated pain.

The activation of silent synapses leads to the convergence of input from more than one source to the same neurons, thereby determining pain and hyperalgesia at areas outside the injured region (expansion of receptive fields) [4].

Generalized expression of cyclooxygenase-2 (COX-2) in the spinal cord can follow local tissue inflammation and may be responsible for neuronal hyperexcitability in the whole spinal cord [5].

Descending controls allow a "top-down" influence on spinal processing and form a link between higher functions such as cognition and emotions and pain transmission. Diffuse noxious inhibitory control (DNIC) is expressed as pain inhibition produced by a noxious stimulus applied to a remote body region. Activation of the excitatory 5HT₃ receptors in the spinal cord by serotonin released from descending pathways has been suggested to underlie one descending excitatory drive [6].

Human Data: In patients with regional chronic pain states, a reduction in pain thresholds after stimulation of areas very distant to the site of primary pain has been observed. For instance, pain thresholds measured at the lower limb are reduced in chronic neck pain [7]. In these patients, spinal reflexes of the lower limb that reflect nociceptive processes at the spinal cord are enhanced [8]. These findings are strongly suggestive for a generalized facilitation of nociceptive processes in the central nervous system of patients with regional pain.

Temporal summation (increased responses to repeated stimuli) occurs when repetition of a stimulus increases pain perception. A single non-painful stimulus is thus perceived as painful when repeated [9]. Temporal summation is facilitated in different chronic musculoskeletal pain conditions, such as fibromyalgia [8] and neck pain after whiplash injury [7, 8].

The areas of referred pain after application of a standardized stimulus are dramatically expanded in chronic pain patients, compared with healthy subjects. This has been observed in different chronic pain conditions, such as neck pain after whiplash injury, fibromyalgia and osteoarthritis [2]. Recently, a model to investigate receptive fields in humans using nociceptive spinal reflexes has been developed [10]. This method can be used to study the role of expansion of receptive fields in the pathophysiology of human pain states.

Alterations of DNIC can be detected in humans and have been found in different chronic pain conditions, such as fibromyalgia [11] and osteoarthritis of the hip [12].

Clinical Aspects: Central sensitization may explain exaggerated symptoms in the presence of modest tissue damage. Importantly, generalized hypersensitivity can be a predictor of poor outcome after a whiplash injury [13]. Furthermore, alteration in DNIC may be predictive for the development of chronic pain after thoracotomy [14]. Thus, these assessments can contribute to screening patients for an aggressive treatment approach, either in the frame of clinical research or for therapeutic purposes. The assessment of central sensitization in patients can be based on the measurement of pain reactions to standardized stimuli (quantitative sensory testing). In a large investigation that characterized the somatosensory phenotype of patients with neuropathic pain, reference values from 180 healthy subjects were obtained [15]. More recently, we defined the reference values of electrophysiological assessments of ventral hypersensitivity in 300 pain-free subjects (Neziri et al, Eur J Pain, in press). These data can be used to detect central hypersensitivity in individual patients.

Pain drawings that illustrate areas with sensory abnormalities and the extent of the pain areas can be helpful to assess indirectly disturbances in the central pain processing. Exaggerated spread of pain and hyperalgesia is strongly suggestive for clinically relevant central sensitization.

Up-regulation of ion channels in the peripheral nerve and central spinal terminals is involved in central sensitization: these sites are targets of the anticonvulsants carbamazepine (sodium channels), gabapentin, and pregabalin (calcium channels). These drugs are effective not only in neuropathic pain, but also for other conditions such as fibromyalgia [16]. Anticonvulsants may therefore interfere with sensitization processes that are common to different pain conditions.

Antidepressants inhibit the re-uptake of serotonin and noradrenalin, thereby enhancing descending inhibition. They are typically effective in neuropathic pain. However, antidepressants are superior to placebo also in fibromyalgia [17], a condition that is associated with altered endogenous modulation and central hypersensitivity. Thus these drugs are potentially effective in patients with alterations in endogenous pain control mechanisms.

Conclusions: Hypersensitivity of the nociceptive system is an important determinant of musculoskeletal pain and disability. Translational research is providing clinicians with tools for quantifying these disturbances in individual patients. Once this step has been made, treatment strategies need to be tailored on specific disturbances of nociceptive processes.

- Reference:
1. Woolf CJ, Salter MW. Neuronal plasticity: increasing the gain in pain. *Science*. 2000;288:1765-9.
 2. Curatolo M, Arendt-Nielsen L, Petersen-Felix S. Central hypersensitivity in chronic pain: mechanisms and clinical implications. *Phys Med Rehabil Clin N Am*. 2006 May;17(2):287-302.
 3. Zeilhofer HU, Zeilhofer UB. Spinal dis-inhibition in inflammatory pain. *Neurosci Lett*. 2008 Jun 6;437(3):170-4.
 4. Hoheisel U, Koch K, Mense S. Functional reorganization in the rat dorsal horn during an experimental myositis. *Pain*. 1994 Oct;59(1):111-8.
 5. Samad TA, Moore KA, Sapirstein A, Billet S, Allchorne A, Poole S, et al. Interleukin-1beta-mediated induction of Cox-2 in the CNS contributes to inflammatory pain hypersensitivity. *Nature*. 2001;410:471-5.
 6. Suzuki R, Morcuende S, Webber M, Hunt SP, Dickenson AH. Superficial NK1-expressing neurons control spinal excitability through activation of descending pathways. *Nat Neurosci*. 2002;5:1319-26.
 7. Curatolo M, Petersen-Felix S, Arendt-Nielsen L, Gianni C, Zbinden AM, Radanov BP. Central hypersensitivity in chronic pain after whiplash injury. *Clin J Pain*. 2001;17:306-15.
 8. Banic B, Petersen-Felix S, Andersen OK, Radanov BP, Villiger PM, Arendt-Nielsen L, et al. Evidence for spinal cord hypersensitivity in chronic pain after whiplash injury and in fibromyalgia. *Pain*. 2004;107:7-15.
 9. Price D, Staud R, Robinson M, Mauderli A, Cannon R, Vierck C. Enhanced temporal summation of second pain and its central modulation in fibromyalgia patients. *Pain*. 2002;99:49-59.
 10. Neziri AY, Curatolo M, Bergadano A, Petersen-Felix S, Dickenson AH, Arendt-Nielsen L, et al. New method for quantification and statistical analysis of nociceptive reflex receptive fields in humans. *J Neurosci Methods*. 2009;178:24-30.
 11. Kosek E, Hansson P. Modulatory influence on somatosensory perception from vibration and heterotopic noxious conditioning stimulation (HNCS) in fibromyalgia patients and healthy subjects. *Pain*. 1997 Mar;70(1):41-51.
 12. Kosek E, Ordeberg G. Lack of pressure pain modulation by heterotopic noxious conditioning stimulation in patients with painful osteoarthritis before, but not following, surgical pain relief. *Pain*. 2000 Oct;88(1):69-78.

13. Sterling M, Jull G, Vicenzino B, Kenardy J. Sensory hypersensitivity occurs soon after whiplash injury and is associated with poor recovery. *Pain*. 2003;104:509-17.
14. Yarnitsky D, Crispel Y, Eisenberg E, Granovsky Y, Ben-Nun A, Sprecher E, et al. Prediction of chronic post-operative pain: pre-operative DNIC testing identifies patients at risk. *Pain*. 2008 Aug 15;138(1):22-8.
15. Rolke R, Baron R, Maier C, Tolle TR, Treede RD, Beyer A, et al. Quantitative sensory testing in the German Research Network on Neuropathic Pain (DFNS): Standardized protocol and reference values. *Pain*. 2006 May 10;123:231-43.
16. Arnold LM, Goldenberg DL, Stanford SB, Lalonde JK, Sandhu HS, Keck PE, Jr., et al. Gabapentin in the treatment of fibromyalgia: a randomized, double-blind, placebo-controlled, multicenter trial. *Arthritis Rheum*. 2007 Apr;56(4):1336-44.
17. Arnold LM, Rosen A, Pritchett YL, D'Souza DN, Goldstein DJ, Iyengar S, et al. A randomized, double-blind, placebo-controlled trial of duloxetine in the treatment of women with fibromyalgia with or without major depressive disorder. *Pain*. 2005 Dec 15;119(1-3):5-15.

Oral Presentation
Topical Seminar: Fibromyalgia syndrome

Abstract: 11

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S5

Topical Seminar Summary: FIBROMYALGIA SYNDROME

P. Sarzi Puttini, W. Häuser, K. Lawson, H. Sprott

Dept Rheum Inst Phys Med Univ Hosp Zurich, Zurich, Switzerland

Dear Colleagues, I would like to welcome you our topical seminar about Fibromyalgia Syndrome. It is extremely important to speak about this chronic pain condition of unknown origin which causes amplitude of problems in both the management of the disease, as well as in society in general. Therefore, today we have invited very distinguished international speakers: Prof. Sarzi Puttini will speak about the pharmacological treatment of fibromyalgia, Dr. Häuser will analyse the evidence of published therapies for this condition, and last but not least, Dr. Lawson will speak about fibromyalgia as a "condition" und not an accumulation of diverse symptoms. We are looking forward to inspiring you with our thoughts in respect to your daily clinical practise.

Fibromyalgia (FM) is a prevalent disorder that is characterized by widespread pain along with numerous other symptoms, including fatigue, poor sleep, mood disorders, and stiffness. Previous guidelines for the management of fibromyalgia recommended an approach that integrates pharmacologic and nonpharmacologic therapies selected according to the symptoms experienced by individual patients. Currently, it is not possible to draw definite conclusions concerning the best pharmacological approach to managing FM because results of randomized clinical trials present methodological limitations and therapeutic programs are too heterogeneous for adequate comparison. However, a variety of pharmacological treatments including antidepressants, nonsteroidal anti-inflammatory drugs (NSAIDs), opioids, sedatives, muscle relaxants and antiepileptics have been used to treat FM with varying results. Pregabalin, duloxetine and milnacipran are the only FDA approved drugs for fibromyalgia management, and it is reasonable to start treatment with one of these drugs. All three drugs have shown similar efficacy in ameliorating pain, but their abilities to manage other fibromyalgia symptoms differ greatly, which, along with their different pharmacodynamic and safety profiles, often make one a better initial choice than the others for an individual patient.

The use of steroids and nonsteroidal anti-inflammatory drugs (NSAIDs) in FM has had disappointing outcomes. Opioids are meant to improve function in FM patients who are impaired by pain, even though there is an open debate about their usefulness and safety as a "specific" medication for fibromyalgia patients. Tramadol, in particular, was beneficial for FM patient. It is an atypical pain reliever that differs from other narcotics in its action on the central nervous system, specifically, on reuptake of serotonin and norepinephrine. Antidepressants that increase 5-HT and NE mediated neurotransmission are commonly used to treat FM and other chronic pain conditions, particularly neuropathic pain. Inhibition of both the 5-HT and NE reuptake transporters using tricyclic antidepressants (TCA) or SNRIs (serotonergic and noradrenergic reuptake inhibitors), seems more effective in treating pain, and FM, in general, than inhibition of either transporter alone using selective serotonergic (SSRIs) or noradrenergic (NARIs) reuptake inhibitors. However, the efficacy of TCAs is counterbalanced by side effects, while the better-tolerated SSRIs demonstrate less effectiveness in treating fibromyalgia. Antiepileptic drugs (i.e., gabapentin and pregabalin) act at a number of sites that may be relevant to pain. The precise mechanism of their analgesic effect remains unclear, but it is thought that they limit neuronal excitation and enhance inhibition. The relevant sites of action include voltagegated ion channels (i.e., sodium and calcium channels), ligand-gated ion channels, excitatory receptor for glutamate and Nmethyl-D-aspartate, the inhibitory receptors for gamma-aminobutyric acid (GABA) and glycine. Serotonergic receptors have been implicated in processing information and in the development of pain in FM, and randomised, controlled trials have found that tropisetron, a 5-hydroxytryptophan intermediate metabolite of L-tryptophan, is more effective than placebo. Despite the suggestion of relative growth hormone (GH) deficiency in FM patients and reports of improvements after the administration of GH injections, the enthusiasm for this approach has been dampened by the appearance of adverse effects, the need for frequent injections, and its high cost. Low doses of a β -blocker have been tried in selected cases with prominent autonomic symptoms, such as palpitations and orthostatic tachycardia; however, the effects are not known. Lidocaine hydrochloride injections, botulinum toxin injections, are sometimes offered to patients with FM. The success of the current treatments for FM is still limited, and there is a need for the

development of new drugs that are targeted at the CNS, and that undergo efficacy and toxicity testing in long-term, comparative trials involving large numbers of patients. The nature of FM suggests that an individualized, multimodal approach that includes both pharmacologic and nonpharmacologic therapies seems to be the most appropriate treatment strategy to date.

Guidelines on the management of fibromyalgia syndrome should be based on the best available evidence.

The clinical relevance (effect sizes, representativeness of study samples, in- and exclusion criteria of studies, acceptance [drop out rates]), methodological quality of pharmacological (amitriptyline, duloxetine, milnacipran, pregabalin) and non-pharmacological (acupuncture, aerobic exercise, balneotherapy, cognitive-behavioral therapy [CBT], hypnotherapy, multicomponent therapy) randomised controlled trials (RCT's) were compared.

We screened MEDLINE, PsychInfo, SCOPUS, www.clinicaltrials.org and the Cochrane Library (through January 2009) and the reference sections of original studies, systematic reviews and metaanalyses. Effects on pain, fatigue, sleep, depressed mood and health-related quality of life were summarized using standardized mean differences.

The exclusion criteria and the study samples of non-pharmacological studies were less restrictive than the ones of pharmacological studies. The drop-out rates were lower in passive therapies (acupuncture, balneotherapy) than in active or pharmacological treatments. The precise effect sizes are presented in the symposium. Despite large differences of the effect sizes at the end of treatment, the 95% confidence intervals of all treatment modalities overlapped. It is important to note that follow-ups after the cessation of therapy were not conducted by pharmacological trials. There is evidence that the positive effects of aerobic exercise, balneotherapy, CBT, hypnotherapy, multicomponent therapy decline with time, but substantial effect sizes can be demonstrated up to one year after therapy. The frequency of side effects of pharmacological therapy is higher than the ones of non-pharmacological treatment options. Rare but severe side effects of pharmacological therapy such as liver failure and suicide have to be considered. There are effective therapies available for the short-term treatment of FMS. The choice of treatment options should be embedded in a patient-centered approach with shared decision-making taking into consideration the preferences of the patient, the local availabilities and costs as well as the potential side effects. The question how a life-long disorder should be treated in the long-run cannot be answered until now by RCT's.

Fibromyalgia (FM) is a common, complex and difficult to treat chronic widespread pain disorder with many auxiliary symptoms. It is a condition of heightened generalized sensitization to sensory input presenting as a complex of symptoms including pain, sleep dysfunction and fatigue, with the complication of co-morbidities such as depression, anxiety, temporomandibular joint disorder and irritable bowel syndrome. The pathophysiology has been proposed to be associated with dysfunction of the central nervous system pain modulatory systems, dysfunction of the neuroendocrine system and dysautonomia. Many of the current and emerging drugs used to treat FM remain largely empiric and have been focused to the management of discrete symptoms rather than the condition. Approved pharmacological therapies are focused towards the modulation of noradrenaline and serotonin levels or an action on the α_2 -d subunit of calcium channels. Although drugs such as pregabalin, duloxetine and milnacipran demonstrate a degree of multidimensional efficacy in the treatment of this condition, many therapeutic agents often fail to provide acceptable efficacy in the majority of the patient population. This is demonstrated by the number-needed-to-treat data (NNT values 4-11) obtained during clinical trials. Evidence suggests that current pharmacological monotherapy is not sufficient to address the complexity of FM adequately. Multifactorial conditions, such as FM, therefore appear to require the concomitant modulation of multiple biochemical processes to achieve acceptable levels of resolution. An alternate consideration is that FM is a cluster of pathophysiological subgroups that respond to tailored monotherapy management.

Reference: Häuser W, Bernardy K, Üçeyler N, Sommer C. Treatment of fibromyalgia syndrome with antidepressants - a meta-analysis. JAMA 301 (2009) 198-209
Häuser W, Bernardy K, Offenbächer M, Arnold B, Schiltenswolf M. Efficacy of multicomponent treatment of fibromyalgia syndrome - a meta-analysis of randomised controlled trials. Arthritis Rheum 61 (2009) 216-224.

Oral Presentation

Topical Seminar: Inflammatory mechanisms in musculoskeletal pain

Abstract: 35

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S16

Topical Seminar Summary: INFLAMMATORY MECHANISMS IN MUSCULOSKELETAL PAIN

C. Sommer¹, B. Rydevik², B. Gerdle³, M. Schiltenswolf⁴

¹ *Department of Neurology University of Wuerzburg, Wuerzburg, Germany*

² *Department of Orthopaedics, Institute of Clinical Sciences, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden*

³ *Department of Clinical and Experimental Medicine Faculty of Health Sciences, Linköping, Sweden*

⁴ *Orthopädische Universitätsklinik Heidelberg, Heidelberg, Germany*

In this topical seminar, we will focus on inflammatory aspects of musculoskeletal pain. Bjorn Rydevik (Gothenburg, Sweden) will summarize the current knowledge on inflammatory mechanisms in discogenic pain and sciatica. In contrast to previous concepts of a pure mechanical injury of nerve roots by a herniated disk, it has become clear that nucleus pulposus releases inflammatory mediators which may induce structural and functional damage in nerve roots in the absence of mechanical deformation. Bjorn Rydevik, Kjell Olmarker and coworkers have intensely studied the role of the proinflammatory cytokines such as tumor necrosis factor-alpha (TNF-alpha) in this context. Evidence from animal models and from human studies will be provided. The impact of the findings for clinical treatment of discogenic pain and sciatica will be discussed. Besides low back pain, neck and shoulder pain continue to be a major problem for people with repetitive and stressful work tasks. Specifically, myalgia of the trapezius muscle is a frequent complaint. The pathophysiology of myalgia in this region is not very well known. The group of Björn Gerdle (Linköping, Sweden) has pioneered investigations in this area by using microdialysis to investigate the presence of algescic and inflammatory mediators in trapezius muscles in patients with chronic neck and shoulder pain. In particular, the role of glutamate and serotonin will be discussed, also in the context of whiplash-associated pain. While systemic cytokine profiles have been investigated in a number of chronic pain disorders, the group of Marcus Schiltenswolf (Heidelberg, Germany) was the first to perform a prospective long term study and to correlate certain cytokine levels to outcome measures. Intriguingly, multidisciplinary pain therapy modified the cytokine profile in patients with fibromyalgia syndrome. Specifically, elevated levels of TNF-alpha and interleukin-8 normalized with treatment. The impact of these findings will be discussed in relation to the use of biomarkers as outcome measures in the treatment of chronic pain and to clinical trials with cytokine antagonists in pain.

Oral Presentation

Topical Seminar: Pelvic and urogenital pain mechanisms - from bench to bedside

Abstract: 31

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S15

Topical Seminar Summary: PELVIC AND UROGENITAL PAIN MECHANISMS - FROM BENCH TO BEDSIDE

U. Wesselmann¹, [M.A. Giamberardino](#)², M. Granot³

¹ *University of Alabama at Birmingham, Dept. of Anesthesiology, Birmingham, United States*

² *G. D'Annunzio University of Chieti, Dept. of Medicine and Science of Aging, Chieti, Italy*

³ *University of Haifa, Faculty of Welfare and Health Sciences, Mount Carmel, Haifa, Israel*

Chronic pelvic and urogenital pain is a common and debilitating problem. This topical seminar will highlight recent studies that will lead to new insights into the pathophysiological mechanisms and to improved treatment avenues. Dr. Granot: What can we learn from psychophysical testing about the pathophysiological mechanisms of vulvodynia? The exact mechanisms associated with vulvodynia are still obscure. Current evidence obtained from psychophysical and brain imaging studies points to systemic pain hypersensitivity. The enhanced pain sensitivity to noxious stimuli applied to visceral and somatic tissues points to sensory pain alterations arising from peripheral and central levels. It has been suggested that less-efficient endogenous modulation processing play a role in vulvodynia. It may be hypothesized that increased afferent excitability together with dysfunctional pain modulation leads to the development of such pain disorders. The proposition that neurogenic inflammation, as well as central sensitization facilitates plasticity in pain modulation pathways will be considered via the application of advanced quantitative sensory testing. The possible role of psychophysical tests to explore mechanisms associated with the pathogenesis, characteristics of clinical presentation and out-come measures of vulvodynia patients will be addressed. Dr. Wesselmann: Interstitial Cystitis (IC): beyond the bladder! IC is a chronic pain syndrome of unknown cause, characterized by suprapubic pain, urinary urgency and increased urinary frequency. There are currently no consistently effective treatments for IC available. Published data suggest that altered sensory processing plays a role in the development and maintenance of this condition (Wesselmann, U., *Urology*, 57 (6A), 2001; Warren, J. W. et al., *J. Urol.*, 180, 2008). Dr. Wesselmann will present studies demonstrating that quantitative sensory testing techniques can be applied to female patients with IC to identify selective changes in sensory processing. Viscero-visceral and viscerosomatic interactions observed in these studies may account for the co-morbidities described in a subgroup of women with IC. Dr. Giamberardino: Pain from the reproductive organs in women. This lecture will describe the clinical profile, pathophysiological and therapeutic aspects of two very common pain conditions from the reproductive organs in women, namely primary dysmenorrhea and endometriosis and discuss their interaction with pain states from the digestive tract (irritable bowel syndrome) and urinary tract (urinary calculosis). The frequent co-occurrence of pelvic pain and other (non-visceral) pain states, such as headache and fibromyalgia will be addressed. The presence of multiple painful conditions - pelvic and extrapelvic - in the same patient produces not only complex pictures of spontaneous symptoms but also somatic tissue hyperalgesia of different degrees and diffusion (skin/subcutis/ muscle; painful and nonpainful areas), which persists in the interval between pain episodes often rendering these patients over-reactive towards pain stimuli on a constant basis. The author will describe different associations of pain conditions from the reproductive area and other districts in women, and report the results on the somatic sensory evaluation. These results suggest different levels of central sensitization in the various painful syndrome associations and may have potential important implications for the therapeutic approach to women suffering from pelvic plus extrapelvic pain.

Ursula Wesselmann is supported by NIH grants DK066641 (NIDDK), HD39699 (NICHD) and the Office of Research for Women's Health.

Oral Presentation

Topical Seminar: Transcranial Magnetic Stimulation: a new therapeutic approach for chronic pain?

Abstract: 27

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S12

Topical Seminar Summary: TRANSCRANIAL MAGNETIC STIMULATION: A NEW THERAPEUTIC APPROACH FOR CHRONIC PAIN?

D. Bouhassira¹, L. Garcia Larrea², D. Ciampi de Andrade³

¹ INSERM U-792 Hopital Ambroise Pare Centre d'Evaluation et de Traitement de la Douleur, Boulogne-Billancourt, France

² INSERM U879, University Claude Bernard, Lyon, France

³ São Paulo University, São Paulo, Brazil

Repetitive transcranial magnetic stimulation (rTMS) is a safe non-invasive technique for stimulating the cerebral cortex. In addition to its uses in cognitive neuroscience, the clinical applications of rTMS have rapidly expanded over the last few years. This technique was initially proposed and has been most thoroughly studied for the treatment of depression. However, rTMS may also be useful for the treatment of other psychiatric and neurological conditions, including schizophrenia, Parkinson's disease and tinnitus. Furthermore, recent studies have shown that rTMS applied to the motor cortex can induce analgesic effects in patients with chronic pain syndromes. In this topical seminar we will first summarize the data from recent clinical studies suggesting that rTMS of the primary motor cortex is a potentially effective alternative treatment option not only in patients with focal neuropathic pain, but also in patients with chronic widespread pain related to fibromyalgia. Then, the putative mechanisms underlying the analgesic effects of rTMS will be reviewed. In particular, the effects of rTMS on central pain modulatory systems and on cortical excitability will be detailed. Finally, the practical aspects of rTMS applications in the clinical setting, including type of equipment, site, frequency, intensity of stimulation that may optimize analgesic effects will be addressed.

Abstract: 761

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S220

VALIDATING IMPACT RECOMMENDATIONS FOR MINIMAL, MODERATE OR SUBSTANTIAL BENEFIT

S. Derry¹, **A. Moore**¹, S. Straube², H. McQuay¹

¹ *University of Oxford, Oxford, United Kingdom*

² *University of Göttingen, Göttingen, Germany*

Background: In 2008 the IMMPACT group defined provisional benchmarks for interpreting change in chronic pain clinical trial outcome measures. For pain intensity (PI), a moderately important change was defined as $\geq 30\%$ decrease in PI, and a substantial improvement was $\geq 50\%$ decrease. For patient global impression of change (PGIC) a moderately important change was much improved, and substantial was very much improved.

Methods: Individual patient meta-analysis of four randomised trials of pregabalin in fibromyalgia with 2757 patients over 8-12 weeks. IMMPACT criteria of minimal, moderate, and substantial benefit were calculated for each patient using baseline and end of trial weekly average PI measures, and PGIC at end of trial. Results were calculated separately for placebo, and 300, 450, and 600 mg pregabalin daily.

Results: For minimal benefit, PGIC and PI gave the same proportion of patients for pregabalin 600 mg, but about 50% more for placebo and pregabalin 300 and 450 mg doses. For moderate benefit, PGIC and PI gave very similar results. For substantial benefit, PGIC consistently produced fewer patients than PI, by 30-50%.

Conclusions: IMMPACT provisional benchmarks for minimal, moderate, and substantial benefits can be measured by using reduction in PI and by PGIC at the end of the trial. For moderate improvement there is good evidence that both scales produce the same result in fibromyalgia, but PGIC definitions overstate minimal benefit and understate substantial benefit relative to PI definitions. Validation in other pain conditions is needed.

Abstract: 502

Citation: European Journal of Pain, Volume 13, Supplement 1, September 2009, Page S149

WIDESPREAD HEAT AND COLD HYPERALGESIA IN PEOPLE WITH FIBROMYALGIA SYNDROME: A PILOT STUDY

C. Fernández-de-las-Peñas¹, **J. Fernández-Carnero**¹, M. Flórez-García², P. Zarco², M. Morales-Cabezas¹, L. Arendt-Nielsen³

¹ *Universidad Rey Juan Carlos, Alcorcón, Spain*

² *Fundación Hospital Alcorcón, Alcorcón, Spain*

³ *Center for Sensory-Motor Interaction (SMI), Aalborg, Denmark*

Background and Aim: Previous studies investigating thermal thresholds in FMS have analyzed data from the arm, but not other locations. Our aim of this pilot study was to assess in a blinded design the presence of widespread heat and cold hyperalgesia in people with FMS as compared to healthy subjects.

Methods: Eight women (age: 51±9 years) diagnosed with FMS according to the ACR criteria and 8 healthy women (age: 52±8 years) were included. Heat (HPT) and cold (CPT) pain thresholds were bilaterally tested with a Thermotest System (Somedic©) over the cervical spine, over the wrist and over the tibialis anterior muscle. The mean of 3 determinations at each point was calculated and used for analysis. The order of the points' assessment was randomized. A 2-way ANOVA was used for analyse differences between groups (patients or controls) and sides (dominant or non-dominant).

Results: The ANOVA showed significant differences between groups, for HPT over the carpal tunnel ($F = 5.5$; $P = 0.03$) and tibialis anterior ($F = 2.7$; $P = 0.04$), but not when measured over the cervical spine ($F = 2.1$; $P = 0.09$). Significant differences between groups were found for CPT over the cervical spine ($F = 7.9$; $P < 0.001$), wrist ($F = 20.1$; $P < 0.001$) and tibialis anterior muscle ($F = 47.1$; $P < 0.001$).

Conclusions: Our findings suggest widespread thermal hyperalgesia in patients with FMS. Widespread heat and cold hyperalgesia further reflect impairment in central nociceptive processing in FMS.